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Heterolytic Fragmentation. A Class of Organic Reactions

BY C. A. GROB AND P. W. SCHIESS [*]

Heterolytic fragmentation is a widespread but neglected class of organic reactions. It involves the regulated cleavage of molecules containing certain combinations of atoms such as carbon, oxygen, nitrogen, sulfur, phosphorus, silicon, boron and halogens. Fragmentation reactions are useful in degradation and structure elucidation, some are also of preparative value. A knowledge of the structural and electronic requirements makes it possible to predict and influence the course of reactions. From a theoretical viewpoint the recognition of heterolytic fragmentation has lead to the classification and correlation of a large number of apparently diverse reactions. Selected cases are reviewed in this article.

I. Definition

On the basis of mechanistic principles most reactions in organic chemistry can be reduced to a relatively small number of reaction classes. Those most extensively studied and therefore known in greatest detail are substitution, addition, elimination and rearrangement. In this manner a vast number of chemical transformations has been correlated, a development which has deeply influenced teaching and research.

About ten years ago a further reaction class was defined and termed fragmentation, since it involves the cleavage of a molecule symbolized by a–b–c–d–X into three fragments a–b, c=d and X[1]. The letters a,b,c, and d denote a sequence of atoms such as C, O, N, S, P, or B. However, fragmentation also occurs with compounds containing metal atoms[2]. In heterolytic fragmentation, which is by far the most common type in solution, X leaves with the electron pair by which it was originally attached to the rest of the molecule, *i.e.* as a nucleofuge[3]. X thereby becomes more negative by one charge unit and is converted into a nucleofugal fragment. This is usually an anion such as a halide, carboxylate and sulfonate ion. Neutral nucleofugal fragments derive from diazonium-, oxonium-, ammonium- and sulfonium-groups (Scheme 1).

Scheme 1. Heterolytic fragmentation.



Electrofugal groups and fragments		Middle and unsaturated groups and fragments		*Nucleofugal* groups and fragments	
a–b–	a⇀b or a → b	–c–d–	c=d	–X	X
HO–CR_2–	O=CR_2	–CR_2–CR_2–	R_2C=CR_2	–Cl	$Cl^{\ominus}$
RO–CR_2–	RO$^{\oplus}$=CR_2	–CR=CR–	RC≡CR	–Br	$Br^{\ominus}$
HOOC–	CO_2	–CR_2–NR–	R_2C=NR	–I	$I^{\ominus}$
R_2N–CR_2–	$R_2N^{\oplus}$=CR_2	–CR=N–	RC≡N	–SO_3R	$RSO_3^{\ominus}$
R_3C–	$R_3C^{\oplus}$	–CR_2–O–	R_2C=O	–OCOR	$RCOO^{\ominus}$
RCO–	RC$^{\oplus}$=O	–CO–O–	CO_2	–$OH_2^{\oplus}$	H_2O
$R_2C^{\ominus}$–CR_2–	R_2C=CR_2	–N=N–	N_2	–$NR_3^{\oplus}$	NR_3
H_2N–NH–	HN=NH	–CO–	C=O	–$SR_2^{\oplus}$	SR_2
HN=N–	N_2			–N$^{\oplus}$≡N	N_2

The electron deficiency on atom d resulting from the departure of X leads to heterolytic cleavage of the bond between b and c, with formation of an unsaturated fragment c=d and a fragment a–b. The latter leaves without the bonding electron pair, *i.e.* as an electro-

[*] Prof. Dr. C. A. Grob and Doz. Dr. P. W. Schiess
Institut für Organische Chemie der Universität
St. Johanns-Ring 19
4056 Basel (Switzerland)

[1] *C. A. Grob* and *W. Baumann*, Helv. chim. Acta *38*, 594 (1955); *C. A. Grob*, Experientia *13*, 126 (1957); "Theoretical Organic Chemistry" Report on the Kekulé Symposium, Butterworth, London 1958, p. 114; *C. A. Grob* and *F. Ostermayer*, Helv. chim. Acta *45*, 1119 (1962).

[2] The cleavage of carbonium ions into a smaller cationic fragment and an olefin in accordance with R_3C–C–C–X → $R_3C^{\oplus}$ + C=C was first recognized as a possible secondary reaction of carbonium ions by *F. C. Whitmore* and *E. E. Stahly*, J. Amer. Chem. Soc. *55*, 4153 (1933); *67*, 2158 (1945). *V. I. Maksimov*, Tetrahedron *21*, 687 (1965), has recently attempted to interpret fragmentations as cases of σ,σ-conjugation as defined by *A. N. Nesmeyanov*, Vestnik Moskovskogo Univ. Ser. II *132*, 5 (1950). This term is evidently intended to describe the electromeric participation of a σ bond β to an unsaturated center which is formed in the transition state. It would therefore correspond to hyperconjugation, which does not necessarily lead to fragmentation, *i.e.* cleavage of a σ bond.

fuge[3], becoming one unit of charge more positive in the process. Electrofugal fragments are therefore frequently cations.

Typical electrofugal fragments are carbonyl compounds (often formed as their conjugate acids), carbon dioxide, imonium-, carbonium-, and acylium-ions, olefins, diimine, and nitrogen (Scheme 1). Silicon, phosphorus, boron derivatives, and organometal ions also act as electrofugal fragments. The ease with which an electrofugal fragment a–b is formed will depend on the stabilization of the incipient positive charge on b due to the inductive or conjugative effect of a. This structural unit is frequently a hydroxyl, amino, alkyl, or aryl group. The displacement of electrons from a towards b, *i.e.*

a→b or ä–b

promotes the release of the unsaturated fragment c=d.

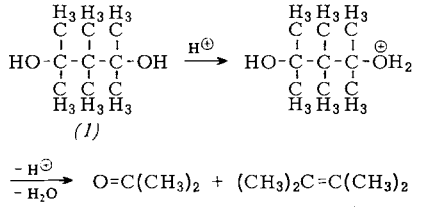
Unsaturated fragments frequently encountered are olefins, acetylenes, imines, and nitriles. Less common are carbonyl compounds, carbon dioxide, carbon monoxide and nitrogen (Scheme 1). At present more than sixty fragmentable systems are known which differ only with respect to the groups a–b and c–d. By taking into account variations of the nucleofugal group X, a far greater number of cases can be cited from the literature. Since new examples are constantly being found, a system of classification is urgently needed. The system adopted in this review is based on the nature of the three fragments in the following order: 1. middle-, 2. electrofugal- and 3. nucleofugal-fragment.

Fragmentation reactions[4] can also be classified according to mechanistic criteria, since, like elimination reactions[5], they can proceed by three basic mechanisms These differ in the order in which the fragments are released. Thus one-step and two-step processes can be distinguished depending on whether a–b and X depart simultaneously from c–d or whether a–b or X depart successively[5a]. In this review of a selected number of fragmentation reactions, questions related to mechanism will be considered only insofar as they are essential to the understanding of the particular reaction. Moreover, homolytic fragmentation and the fragmentation patterns resulting from electron impact and detected by mass spectrometry will not be discussed, since different principles are involved in these cases.

II. Olefin-Forming Fragmentations (a–b–C–C–X)

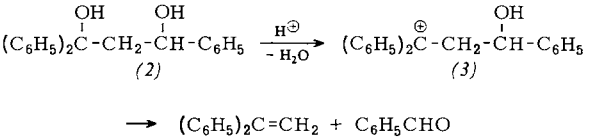
a) H–O–C–C–C–X

In many olefin-forming systems, the electron-donating part is a hydroxyl group or an alkoxide oxygen atom. In these cases the electrofugal fragment is a carbonyl compound. Probably one of the earliest examples is the acid-catalysed fragmentation of tetramethyl-2,4-pentanediol *(1)* into acetone and dimethyl-2-butene[6]:

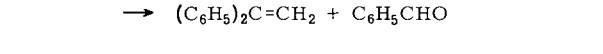


(1)

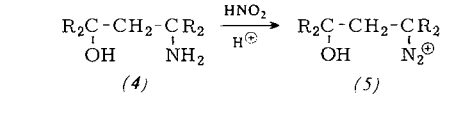
In unsymmetrical 1,3-diols, the nucleofugal fragment is usually formed from the hydroxyl group on the more highly substituted carbon atom, as is shown by the exclusive formation of benzaldehyde and 1,1-diphenylethylene when 1,1,3-triphenyl-1,3-propanediol *(2)* is heated with acid. This suggests that the fragmentation proceeds *via* the more stable tertiary carbonium ion *(3)*[7]:



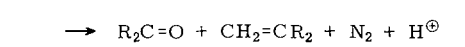
(2) *(3)*



However, fragmentation can also occur *via* the diazonium salt *(5)* as in the deamination of γ-aminoalcohols *(4)* with nitrous acid[8]. The yields vary, and depend on the substituents R and on stereochemical factors.



(4) *(5)*



[3] Whereas the terms nucleophile and electrophile refer to the role of reagents in bond formation the complementary terms nucleofuge and electrofuge refer to bond cleavage, specifically to the partitioning of the electrons which formed the original bond. The term leaving group is inadequate, since in fragmentation two different kinds of leaving group are involved: *J. Mathieu, A. Allais,* and *J. Valls,* Angew. Chem. *72,* 71 (1960).

[4] According to the above definition, heterolytic fragmentation is a generalization of heterolytic elimination. An elimination involves the removal of a nucleofugal group X and an electrofugal atom, usually a proton, from the β-position, whereas in fragmentation the electrofugal fragment is a group of atoms. If the chain a–b–c–d=X contains a double bond between d and X, the group X does not leave the molecule on heterolysis of the b–c bond. The molecule then breaks down into only two fragments. Reactions of this type, such as the retroaldol reaction $^{\ominus}O-C-C-C=O \rightarrow O=C + C=C-O^{\ominus}$, are 1,2-eliminations where a resonance stabilized nucleofugal group is liberated. They are therefore not considered in the present review.

[5] *C. K. Ingold*: Structure and Mechanism in Organic Chemistry. Cornell University Press, Cornell 1953, p. 419.

[5a] Mechanistic and stereochemical aspects of heterolytic fragmentation will be discussed in a later article.

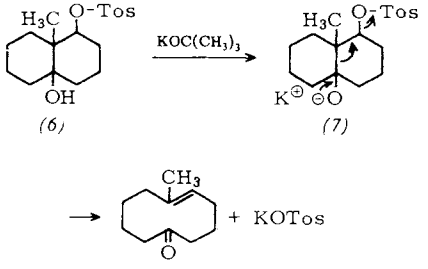
[6] *A. Slawjanow*, J. Russ. Phys. Chem. Soc. *39*, 140 (1907); Chem. Abstr. *1*, 2077 (1907).

[7] *J. English* and *F. V. Brutcher*, J. Amer. chem. Soc. *74*, 4279 (1952).

[8] *J. English* and *A.D.Bliss*, J. Amer. chem. Soc. *78*, 4057 (1956); *R. R. Burford, F. R. Hewgill,* and *P. R. Jefferies*, J. chem. Soc. (London) *1957*, 2937.

In this as in many other cases, fragmentation is accompanied by substitution and elimination.

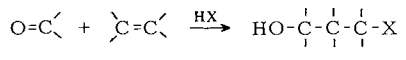
Many fragmentations, such as that of the bicyclic γ-hydroxytosylate *(6)*, are brought about by a strong base, *e.g.* potassium t-butoxide [9]; the reacting substrate is therefore the anion *(7)*.



(6) *(7)*

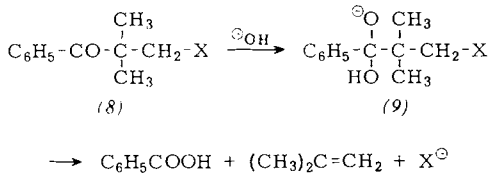
In such cases the fragmentation is also of preparative use, since it permits the stereospecific synthesis of medium-sized unsaturated rings that are otherwise difficult to obtain.

The reverse of this fragmentation, *i.e.* the condensation of an olefin with an aldehyde or ketone in the presence of an acid, is possible in many cases [10]. (When formaldehyde is used as the carbonyl component, this is known as the Prins reaction).



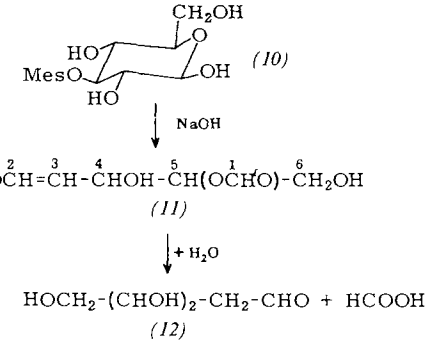
b) O=C—C—C—X

Aldehydes and ketones bearing a nucleofugal group in the β position can be cleaved into acids and olefins by treatment with alkali. This reaction is observed in particular when the usual 1,2-elimination of HX with formation of the α,β-unsaturated carbonyl compound is difficult or prevented by structural factors. Thus it has been shown that, on treatment with sodium hydroxide, 3-bromo-2,2-dimethyl-1-phenyl-1-propane[*(8a)* X = Br] (ω-bromopivalophenone) or the trimethylammonium iodide [*(8b)*, X = $N(CH_3)_3{}^{\oplus}I^{\ominus}$] breaks down *via* the adduct *(9)* into benzoic acid and isobutene [11]. This



(8) *(9)*

Another example is 3-mesyl-D-glucose, whose hemiacetal form *(10)* is cleaved by sodium hydroxide into the enol *(11)*, the precursor of 2-deoxy-D-ribose *(12)*, and formic acid [12].



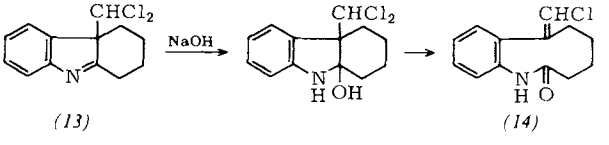
(10)

(11)

(12)

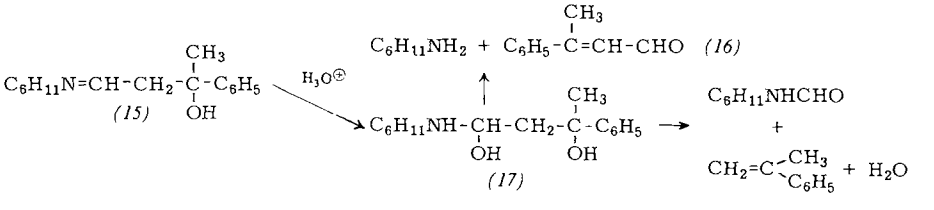
c) —N=C—C—C—X

Imines (Schiff bases) containing a nucleofugal group in the β-position also become fragmentable after addition of a nucleophile. Thus the 3*H*-indole derivative *(13)* reacts with sodium hydroxide to form the unsaturated nine-membered lactam *(14)* [13].



(13) *(14)*

Fragmentation occurs as an undesirable side reaction in the preparation of unsaturated aldehydes by aldol condensation of an acetaldimine with ketones. For example, on treatment with acid, the β-hydroxyaldimine



(15) *(16)* *(17)*

is an example of a compound that becomes fragmentable only after an active electrofugal group has been formed by the addition of a nucleophile.

(15) not only undergoes hydrolysis and dehydration to *(16)*, but also suffers fragmentation with formation of cyclohexylformamide and α-methylstyrene [14]. The common reactive substrate is undoubtedly the product resulting from the addition of water *(17)*.

[9] *P. S. Wharton* and *G. A. Hiegel*, J. org. Chemistry *30*, 3254 (1965); *E. J. Corey, R. B. Mitra*, and *H. Uda*, J. Amer. chem. Soc. *86*, 485 (1964).

[10] Cf., *e.g.*, *H. Stetter, J. Gärtner*, and *P. Tacke*, Angew. Chem. *77*, 171 (1965); Angew. Chem. internat. Edit. *4*, 153 (1965).

[11] *F. Nerdel, H. Goetz*, and *M. Wolff*, Liebigs Ann. Chem. *632*, 65 (1960); *F. Nerdel, D. Frank*, and *H. J. Lengert*, Chem. Ber. *98*, 728 (1965).

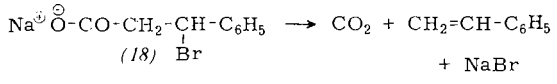
[12] *D. C. Smith*, J. chem. Soc. (London) *1957*, 2690; *E. Hardegger et al.*, Helv. chim. Acta *40*, 1815 (1957).

[13] *M. F. Bartlett, D. F. Dickel*, and *W. I. Taylor*, J. Amer. chem. Soc. *80*, 126 (1958).

[14] *G. Wittig* and *H. D. Frommeld*, Chem. Ber. *97*, 3548 (1964).

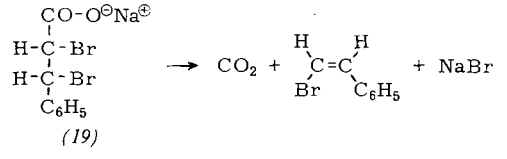
d) H—O—CO—C—C—X

Many β-halocarboxylic acids undergo decarboxylation to an olefin when their salts are heated in solution. One of the earliest examples is the formation of styrene from 3-bromo-3-phenyl propionic acid *(18)* in aqueous soda [15].



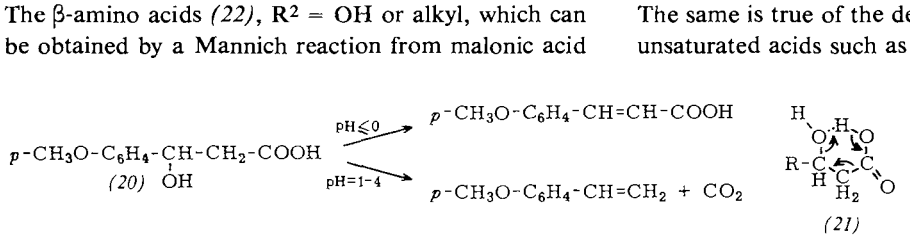
(18)

The sodium salt of the *erythro* form of dibromohydrocinnamic acid *(19)* is stereospecifically decarboxylated in a non-polar solvent such as acetone to *cis*-bromostyrene [16].



(19)

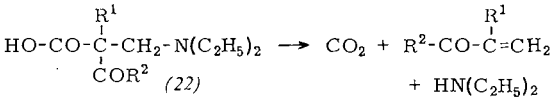
In β-hydroxycarboxylic acids decarboxylation competes successfully with the elimination of water to form the α,β-unsaturated acid. Whereas 3-hydroxy-3-(*p*-methoxyphenyl)propionic acid *(20)* is dehydrated to the cinnamic acid derivative in strongly acidic solution, the main reaction in weakly acidic solution is decarboxylation to *p*-methoxystyrene. In this case the reactive substrate is presumably *(21)*, which contains an internal hydrogen bond [17].



(20)

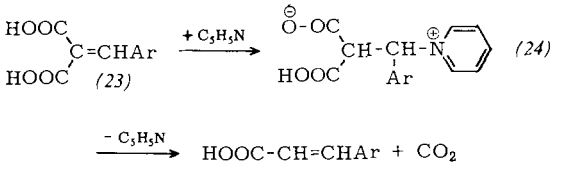
(21)

The β-amino acids *(22)*, R^2 = OH or alkyl, which can be obtained by a Mannich reaction from malonic acid and β-keto acids [18], undergo spontaneous decarboxylation to form α,β-unsaturated carbonyl compounds.



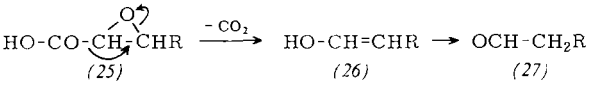
(22)

Arylethylenedicarboxylic acids *(23)* also readily undergo decarboxylation when heated with pyridine. The reactive substrate in this case is the zwitterion *(24)* which contains the nucleofugal pyridinium group β to the carboxyl group [19].



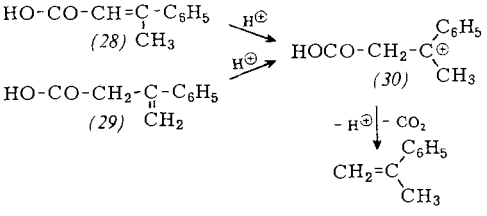
(23) *(24)*

An interesting variant of these reactions is the Darzen reaction. α,β-Epoxy acids (glycidic acids) such as *(25)* are readily decarboxylated to the aldehyde with one less carbon atom [20]. In this case the nucleofugal oxygen atom of the epoxide group remains attached to the unsaturated fragment, so that the primary product is an enol *(26)*, the precursor of the aldehyde *(27)*.



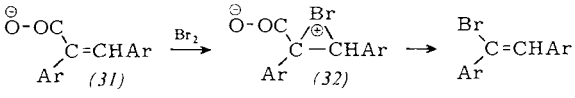
(25) *(26)* *(27)*

In principle, any carboxylic acid having a carbonium ion center in the β-position can undergo decarboxylation, as is shown by the acid-catalysed fragmentation of the α,β- and β,γ-unsaturated acids *(28)* and *(29)* [21]. In both cases the olefinic double bond is protonated to form the β-carbonium ion *(30)*.



(28) *(29)* *(30)*

The same is true of the decarboxylation of salts of α,β-unsaturated acids such as *(31)* with bromine [22] to the bromo olefin, which presumably proceeds *via* a bromonium ion *(32)*.



(31) *(32)*

e) R—O—C—C—C—X

The role of the electron-donating atom a of the electrofugal group a–b can occasionally be assumed by an ether oxygen atom. Thus when the tosylate *(33)* is heated with dimethyl sulfoxide, very little of the ex-

[15] *R. Fittig* and *F. Binder*, Liebigs Ann. Chem. *195*, 131 (1879).

[16] *S. J. Cristol* and *W. P. Norris*, J. Amer. chem. Soc. *75*, 632, 2645 (1953); *E. Grovenstein* and *D. E. Lee*, *ibid.* *75*, 2639 (1953).

[17] *D. S. Noyce*, *P. A. King*, and *G. L. Woo*, J. org. Chemistry *26*, 632 (1961).

[18] *H. Hellmann*, *F. Lingens*, and *K. Teichmann*, Angew. Chem. *70*, 247 (1958); *C. Szantay* and *J. Rohaly*, Chem. Ber. *96*, 1788 (1963).

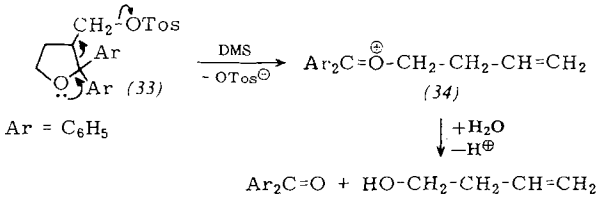
[19] *E. J. Corey* and *G. Fraenkel*, J. Amer. chem. Soc. *75*, 1168 (1953).

[20] *M. S. Newman* and *B. J. Magerlein*, Org. Reactions *5*, 413 (1949).

[21] *W. S. Johnson* and *W. E. Heinz*, J. Amer. chem. Soc. *71*, 2913 (1949).

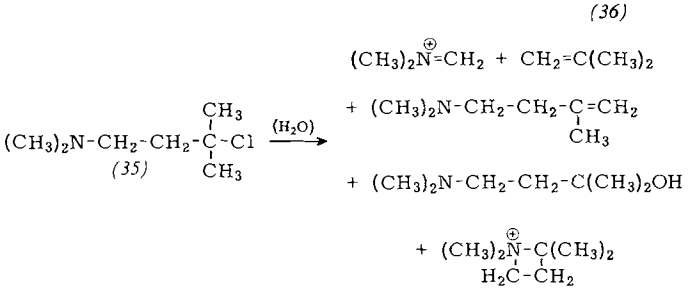
[22] *J. D. Berman* and *C. C. Price*, J. Amer. chem. Soc. *79*, 5474 (1957).

pected aldehyde is formed; instead fragmentation to the oxonium salt *(34)* yields benzophenone and 3-buten-1-ol [23].



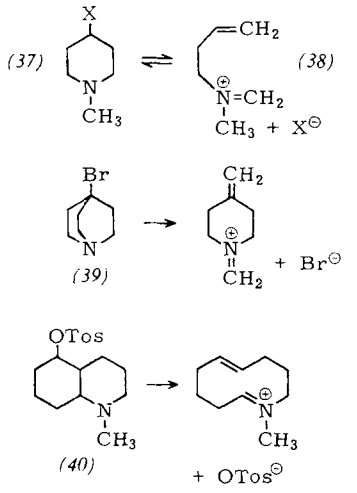
f) R_2N—C—C—C—X

The most thoroughly studied fragmentation reactions include those of γ-amino halides and sulfonates [24]. Several cleavages of this type have been observed in alkaloids [25]. They also occur, accompanied by side reactions, with acyclic γ-amino halides. For example, the solvolysis of *N*-(3-chloro-3-methylbutyl)dimethylamine *(35)* in 80 % aqueous ethanol leads to the fragmentation product isobutylene *(36)* in about 40 % yield, together with the amino olefin, the alcohol, and the azetidinium salt [26].



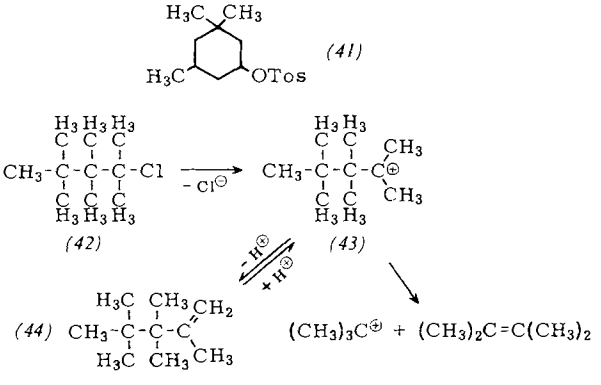
Under solvolytic conditions, cyclic γ-amino halides such as 4-chloro-1-methylpiperidine [*(37)*, X = Cl] [27] and 4-bromoquinuclidine *(39)* [28], as well as *N*-methyl-5α-tosyloxy-*trans*-decahydroquinoline *(40)* [29], undergo quantitative fragmentation to imonium salts or their hydrolysis products, *i.e.* amino olefins, aldehydes, and ketones.

The reverse of this reaction, *i.e.* the Mannich olefin condensation, proceeds particularly readily when it leads to ring closure, as in the reaction *(38)* → *(37)*, X = OH.



g) R_3C—C—C—X

The fragmentation of propanol derivatives containing a tertiary γ–C atom should yield relatively stable carbonium ions $R_3C^{\oplus}$ (R = alkyl or aryl) in addition to olefins. However, experience has shown that the electrofugal activity of ordinary carbonium ions is not sufficient for cleavage. Thus no fragmentation could be observed in the solvolysis either of *cis*- and *trans*-3,3,5-trimethylcyclohexyltosylate *(41)* [30] or of 2-chloropentamethylpentane *(42)* [31]. In this last case further reaction of the intermediate carbonium ion *(43)* leads only to the olefin *(44)*. However, if the carbonium ion *(43)* is repeatedly reformed by protonation of the olefin *(44)*, the thermodynamically more favorable fragmentation to the t-butyl cation and dimethyl-2-butene takes place [31].



Fragmentation can also occur in strained compounds [30], as is shown by the formation of β-terpineol *(48)* and limonene *(49)* on treatment of α-pinene *(45)* [*] with acid [32] and on deamination of *endo*-bornylamine *(46)* with nitrous acid [33]. In both cases fragmentation leads to the formation of the carbonium ion *(47)*, the precursor of *(48)* and *(49)*.

[23] *R. K. Hill* and *S. Barcza*, J. org. Chemistry *27*, 317 (1962); cf., *eg.*, *R. F. Zürcher* and *J. Kalvoda*, Helv. chim. Acta *44*, 198 (1961).

[24] Cf. *C. A. Grob et al.*, Helv. chim. Acta *45*, 1119 (1962) and later publications on fragmentation reactions.

[25] *H. S. Mosher*, *R. Forker*, *H. R. Williams*, and *T. S. Oakwood*, J. Amer. chem. Soc. *74*, 4627 (1952); *M. F. Bartlett*, *E. Schlittler*, *R. Sklar*, *W. I. Taylor*, *R. L. S. Amai*, and *E. Wenkert*, J. Amer. chem. Soc. *82*, 3793 (1960).

[26] *C. A. Grob*, *F. Ostermeyer*, and *W. Raudenbusch*, Helv. chim. Acta *45*, 1672 (1962).

[27] *R. D'Arcy*, *C. A. Grob*, *T. Kaffenberger*, and *V. Krasnobajew*, Helv. chim. Acta *49*, 185 (1966).

[28] *P. Brenneisen*, *C. A. Grob*, *R. A. Jackson*, and *M. Ohta*, Helv. chim. Acta *48*, 146 (1965).

[29] *C. A. Grob*, *H. R. Kiefer*, *H. Lutz*, and *H. Wilkens*, Tetrahedron Letters *1964*, 2901.

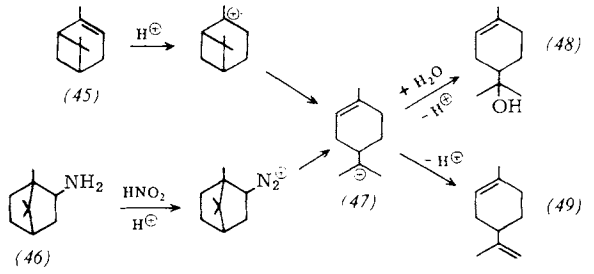
[30] *C. A. Grob*, *W. Schwarz*, and *H. P. Fischer*, Helv. chim. Acta *47*, 1385 (1964).

[31] *V. J. Shiner* and *G. F. Meier*, J. org. Chemistry *31*, 137 (1966).

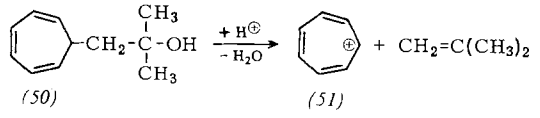
[*] This type of fragmentation is not initiated by the withdrawal of a nucleofuge, but by the addition of an electrophile to a double bond.

[32] *G. Wagner*, Ber. dtsch. chem. Ges. *27*, 1944 (1894); *G. Valkanas* and *N. Iconomou*, Helv. chim. Acta *46*, 1089 (1963).

[33] *W. Hückel* and *F. Nerdel*, Liebigs Ann. Chem. *528*, 57 (1937); *W. Hückel* and *J. Scheel*, *ibid.* *664*, 19 (1963).

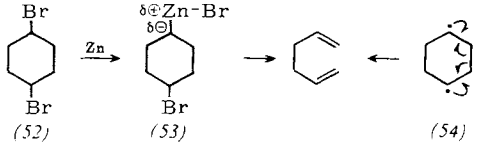


A special case is that of 2-methyl-3-tropyl-2-propanol *(50)*, which undergoes fragmentation with perchloric acid to form the very stable tropylium ion *(51)* and isobutene [34].

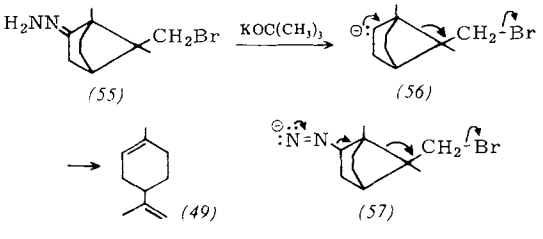


h) $-\overset{\ominus}{\ddot{C}}-C-C-C-X$

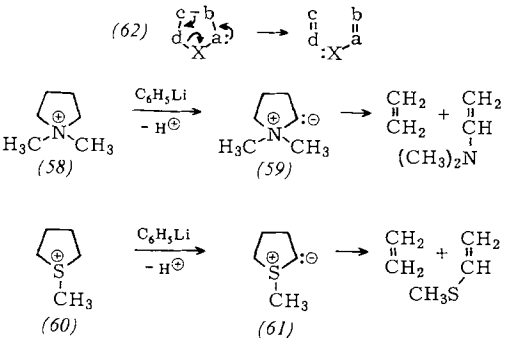
This class includes fragmentations induced by the formation of a carbanion center on the δ-carbon atom. The cleavage of 1,4-dihalides by zinc or an alkali metal possibly follows this path [35]. In the reaction of *cis*- and *trans*-1,4-dibromocyclohexane *(52)* with zinc, which yields 1,5-hexadiene exclusively, the fragmentable substrate might be the organozinc compound *(53)*. However, a reaction pathway *via* the 1,4-diradical *(54)* is not excluded since, like other 1,4-diradicals, it could undergo homolysis to form the hexadiene.



Another example is provided by the fragmentation of *trans*-8-bromocamphor hydrazone *(55)* to limonene in the Wolff-Kishner reduction [36]. If, as is generally assumed [37], the carbanion *(56)* occurs as an intermediate in this reaction, this represents a heterolytic five-center fragmentation. However a seven-center mechanism as indicated in *(57)* cannot be ruled out.

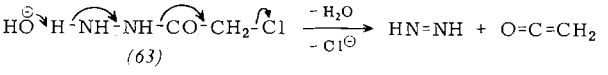


The decomposition of the five-membered cyclic ylides *(59)* [38] and *(61)* [39], which result from the action of phenyl-lithium on the ammonium *(58)* and sulfonium *(60)* ions respectively, may be regarded as fragmentations. In the first case dimethylvinylamine is formed in addition to ethylene, while methyl vinyl sulfide is formed in the second case. Since the nucleofugal group X remains attached to the atom a as in *(62)*, only two fragments are formed [40].

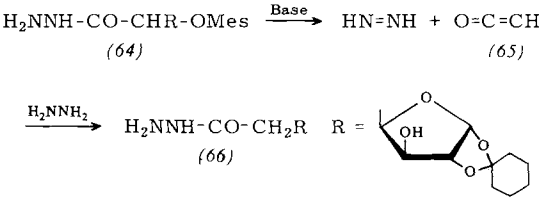


i) $H-N-N-C-C-X$ or $\overset{\ominus}{\ddot{N}}-N-C-C-X$

It has recently been found that diimine HN=NH can assume the role of the electrofuge in an olefin-forming fragmentation. Thus the treatment of chloroacetyl hydrazide *(63)* with aqueous sodium hydroxide leads to the formation of acetic acid besides nitrogen and hydrazine, the secondary products of ketene and diimine [41].



The recently described conversion of 1,2-*O*,*O*-cyclohexylidene-5-*O*-mesyl-D-glucofuranuronyl hydrazide *(64)* into the 5-deoxy compound *(66)* by treatment with hydrazine can be explained by a similar base-induced fragmentation to diimine and the sugar ketene *(65)*, which is the precursor of the deoxy acid hydrazide *(66)* [42].



k) $HN=N-C-C-X$ or $\overset{\ominus}{N}=\ddot{N}-C-C-X$

It has long been known that the Wolff-Kishner reduction of aldehydes and ketones containing a nucleofugal group α to the carbonyl group yields olefins instead of saturated compounds [43]. Suitable nucleofugal groups are a halogen atom, a hydroxyl, amino, even an epoxy

[34] *K. Conrow*, J. Amer. chem. Soc. *81*, 5461 (1959).

[35] *C.A.Grob* and *W.Baumann*, Helv. chim. Acta *38*, 594 (1955).

[36] *D. M. Gustavson* and *W. F. Erman*, J. org. Chemistry *30*, 1665 (1965).

[37] *W. Seibert*, Chem. Ber. *81*, 266 (1948).

[38] *G. Wittig* and *W.Tochtermann*, Chem. Ber. *94*, 1692 (1961); *F. Weygand* and *H. Daniel*, *ibid. 94*, 1688 (1961); Liebigs Ann. Chem. *671*, 111 (1964); *H. Daniel*, *ibid. 673*, 92 (1964).

[39] *F. Weygand* and *H. Daniel*, Chem. Ber. *94*, 3145 (1961).

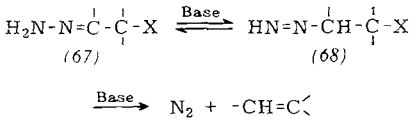
[40] For other examples, cf. *P. S. Wharton*, *G. A. Hiegel*, and *R. S. Ramaswami*, J. org. Chemistry *29*, 2441 (1964).

[41] *R. Buyle*, Helv. chim. Acta *47*, 2449 (1964).

[42] *H. Paulsen* and *D. Stoye*, Chem. Ber. *99*, 908 (1966).

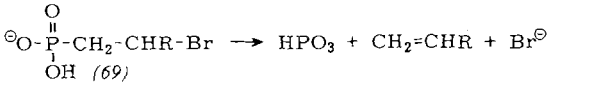
[43] *N. J. Leonard* and *S. Gelfand*, J. Amer. chem. Soc. *77*, 3272 (1955).

group[44] or a cyclopropane ring[45]. The base-induced formation of nitrogen and olefin can be formulated as a fragmentation of the tautomer *(68)* of the hydrazone *(67)*. The electrofugal activity of nitrogen is so high that this reaction proceeds even with notoriously poor nucleofugal groups such as OH and NR_2.



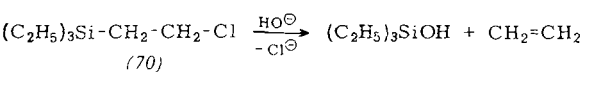
l) H—O—P—C—C—X

β-Halophosphonic acids such as *(69)* behave in the same manner as the corresponding carboxylic acids. Relatively stable in aqueous solution, they react rapidly in alkaline media with liberation of olefin and metaphosphate[46, 47].



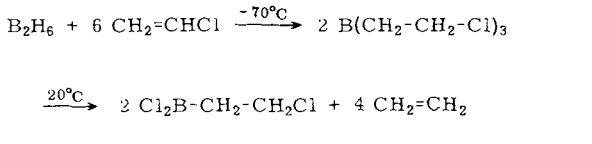
m) R_3Si—C—C—X

β-Haloalkylsilanes such as *(70)* undergo base-induced cleavage to silanols and olefins[48].



n) B—C—C—X

β-Chloroalkylboron derivatives, which are formed by hydroboration of vinyl chlorides are also known to decompose with formation of olefins[49].



[44] *P. S. Wharton* and *D. H. Bohlen*, J. org. Chemistry *26*, 3615 (1961).

[45] *S. M. Kupchan* and *E. Abushanab*, Tetrahedron Letters *1965*, 3075.

[46] *J. B. Conant* and *B. B. Coyne*, J. Amer. chem. Soc. *44*, 2530 (1922).

[47] *J.-A. Maynard* and *J. M. Swan*, Austral. J. Chem. *16*, 596 (1963).

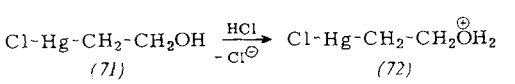
[48] *L. H. Sommer*, *D. L. Bailey*, and *F. C. Whitmore*, J. Amer. chem. Soc. *70*, 2869 (1948); *L. H. Sommer*, *L. J. Tyler*, and *F. C. Whitmore*, *ibid. 70*, 2872 (1948).

[49] *M. F. Hawthorne* and *J. A. Dupont*, J. Amer. chem. Soc. *80*, 5830 (1958). Cf. also *J. A. Marshall* and *G. L. Bundy*, *ibid. 88*, 4291 (1966).

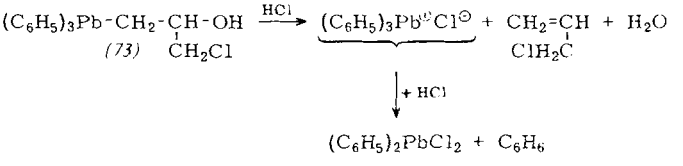
o) R—M—C—C—X

A series of organometallic compounds (M = metal) having a nucleofugal group on the β-carbon atom suffer cleavage of the metal-carbon bond. A metal cation, which may be regarded as an electrofugal fragment, and an olefin are thus formed. These reactions may therefore be regarded as fragmentations.

For example, β-hydroxyethylmercuric chloride *(71)*, which is stable in neutral media, undergoes cleavage *via* the oxonium salt *(72)* in acidic solution, with formation of $HgCl_2$ and ethylene[50].



The relatively stable (3-chloro-2-hydroxypropyl)-triphenyllead *(73)* undergoes a similar cleavage with hydrogen chloride in ether[51]:

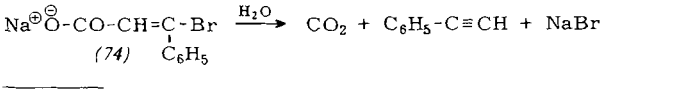


III. Alkyne-Forming Fragmentations (a—b—C≡C—X)[52]

These fragmentations are not so numerous as the olefin-forming fragmentations discussed in Section II, probably because in these cases the nucleofugal group is attached to an unsaturated carbon atom, and therefore ionizes with difficulty. Consequently, a reaction takes place only when the nucleofugal activity of X is particularly high or when a—b is an extremely active electrofugal group.

a) HO—CO—C≡C—X

This class includes α,β-unsaturated β-haloacids the anions of which can undergo decarboxylation. For example, both *cis*- and *trans*-β-bromocinnamic acid *(74)* give phenylacetylene as the main product when their salts are heated in water. Decarboxylation occurs much less readily in the case of β-halo crotonic and acrylic acids[53].



[50] *F. C. Whitmore*, Chem. Engng. News *26*, 668 (1948).

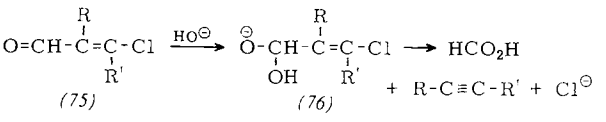
[51] *L. C. Willemsens* and *G. J. M. van der Kerk*: Investigations in the Field of Organolead Chemistry. International Lead Zinc Research Organisation, Inc., New York 1965, p. 56.

[52] Cf. also the review by *G. Köbrich*, Angew. Chem. *77*, 75 (1965); Angew. Chem. internat. Edit. *4*, 49 (1965).

[53] *C. A. Grob*, *J. Csapilla*, and *G. Cseh*, Helv. chim. Acta *47*, 1590 (1964).

b) O=C—C=C—X

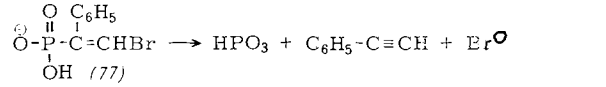
β-Halogenated α,β-unsaturated carbonyl compounds are systems that become fragmentable only upon addition of a nucleophile. Thus in the presence of aqueous sodium hydroxide, substituted β-chloroacroleins *(75)* decompose into formic acid and alkynes [54]. The reactive substrate is assumed to be the anion of the aldehyde hydrate *(76)*.



(75) *(76)*

c) HO—P—C=C—X

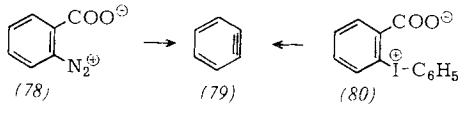
An example of this class of reactions is the formation of phenylacetylene from the salt of β-bromo-α-phenylvinylphosphonic acid *(77)*. The electrofugal fragment in this case is metaphosphoric acid [55].



(77)

d) $^{\ominus}$OCO-*o*-C_6H_4 $X^{\oplus}$

Alkyne-forming fragmentations include, at least formally, certain reactions used in the preparation of benzyne *(79)*. Thus this unstable compound is formed by mild decarboxylation of diazotized anthranilic acid *(78)* [56] or of diphenyliodonium-*o*-carboxylate *(80)* [57].



(78) *(79)* *(80)*

Both of these compounds contain combinations of very active electrofugal and nucleofugal groups. Whether benzyne is to be regarded as an acetylene derivative, however, is a matter of opinion.

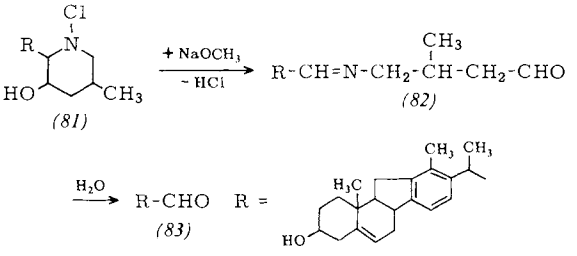
IV. Imine-Forming Fragmentations (a–b–C–N–X and a–b–N–C–X)

In the reactions discussed so far, the nucleofugal group X was attached to a carbon atom. In the following subclasses, however, the group X is attached to a heteroatom such as nitrogen or oxygen.

In these cases nucleophilic substitution no longer competes with fragmentation. Another difference is that cationic centers form much less readily on nitrogen or oxygen than on carbon. On the other hand, rearrangement involving a 1,2-shift of a group in the β position often competes with fragmentation in these systems.

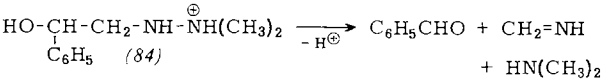
a) HO—C—C—N—X

The β-hydroxy-*N*-chloro amine *(81)* obtainable from veratramine, undergoes fragmentation with bases to form the imine *(82)*, which is hydrolysed to the aldehyde *(83)* [58].



(81) *(82)* *(83)*

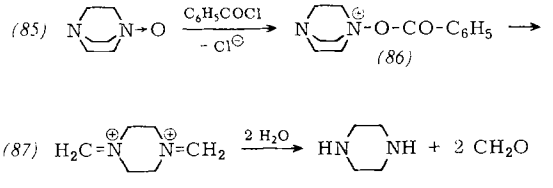
A similar acid-catalysed cleavage of *N,N'*-dimethyl-*N'*-(2-hydroxy-2-phenylethyl)hydrazinium ion *(84)* to benzaldehyde and formimine or its hydrolysis products has recently been formulated as a fragmentation [59].



(84)

b) N—C—C—N—X

Benzoylation of the *N*-oxide of 1,4-diazabicyclo[2.2.2]-octane *(85)* followed by hydrolysis yields piperazine and formaldehyde. This reaction may be regarded as a fragmentation of the ammonium salt *(86)* to the bisimonium salt *(87)* [60].



(85) *(86)* *(87)*

c) HO—CO—C—N—X

This class includes the oxidative decarboxylation of α-amino acids with halogenating agents such as hypochlorite or *N*-bromosuccinimide (NBS) [61]. *N*-halo-

[54] *K. Bodendorf* and *R. Mayer*, Chem. Ber. *98*, 3554 (1965).

[55] Cf. [46] and *E. Bergmann* and *A. Bondi*, Ber. dtsch. chem. Ges. *66*, 278 (1933).

[56] *M. Stiles* and *R. G. Miller*, J. Amer. chem. Soc. *82*, 3802 (1960); *M. Stiles*, *R. G. Miller*, and *U. Burckardt*, *ibid. 85*, 1792 (1963); *L. Friedman* and *F. M. Logullo*, *ibid. 85*, 1549 (1963).

[57] *E. LeGoff*, J. Amer. chem. Soc. *84*, 3786 (1962).

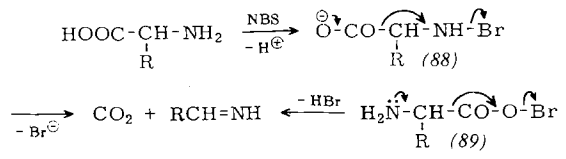
[58] *R. W. Franck* and *W. S. Johnson*, Tetrahedron Letters *1963*, 545; *T. Masamune*, *M. Takazugi*, and *Y. Mori*, *ibid. 1965*, 489.

[59] *W. H. Urry*, *P. Szecsi*, *C. Ikoku*, and *D. W. Moore*, J. Amer. chem. Soc. *86*, 2224 (1964)

[60] *R Huisgen* and *W. Kolbeck*, Tetrahedron Letters *1965*, 783.

[61] Cf. *A. Schönberg* and *R. Moubacher*, Chem. Reviews *50*, 261 (1952).

amino acids *(88)* may be assumed as intermediates, though fragmentation of the acyl hypobromite *(89)* cannot be ruled out.



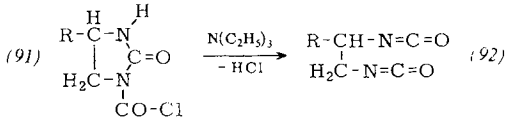
N-Arenesulfonylamino acids *(90)* also undergo fragmentation when heated in pyridine [62].



(90)

d) N—C—N—C—X

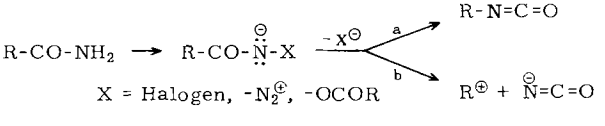
In the imine-forming fragmentations described above, the electrofugal group is attached to the carbon atom and the nucleofugal group to the nitrogen atom. However, cases are also known in which the positions of these two groups on the middle group are reversed. For example, the decomposition of the allophanyl chloride *(91)* into the diisocyanate *(92)* in the presence of triethylamine involves the formation of an N=C double bond. This reaction evidently is induced by the attack of the base on the H atom attached to nitrogen [63].



(91) *(92)*

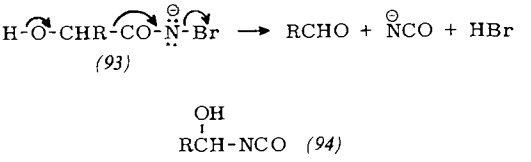
V. Fragmentations Leading to Cyanic Acids (a—b—CO—N—X)

In the Hofmann, Curtius, or Lossen degradation of amides, the release of the nucleofugal group from the nitrogen atom is normally accompanied by migration of the group R to form an isocyanate (route a):



X = Halogen, $-N_2^{\oplus}$, -OCOR

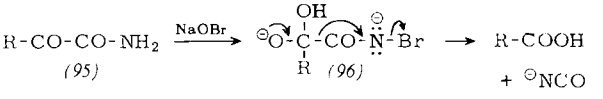
However, if R is an active electrofugal group, fragmentation can compete with the rearrangement. Such groups are present in amides of α-hydroxy, α-keto, α-amino, and α-halo acids. Thus in the Hofmann degradation of α-hydroxy carbonamides *(93)*, the expected rearrangement product α-hydroxy isocyanate *(94)* could not be detected [64], suggesting that direct fragmentation to the aldehyde and the cyanate ion has taken place in accordance with *(93)*.



(93)

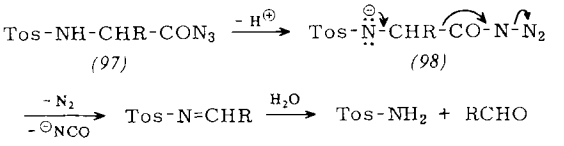
(94)

The formation of carboxylic acids and cyanate ions in the Hofmann degradation of α-keto carbonamides *(95)* in aqueous alkali solution [65] can also be formulated as a fragmentation as in *(96)*.



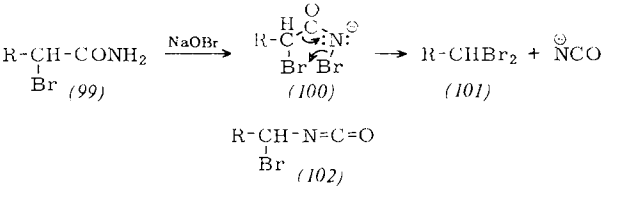
(95) *(96)*

Azides of *N*-tosyl-α-amino acids *(97)* are relatively stable in neutral solution. When alkali is added, however, they decompose to form an aldehyde, *p*-toluenesulfonamide, cyanate ion, and nitrogen [66], indicating a fragmentation in accordance with *(98)*.



(97) *(98)*

The formation of geminal dibromides *(101)* and cyanate ion in the Hofmann degradation of α-bromo carbonamides *(99)* has been explained by an intramolecular mechanism *(100)* [67]. In any case, the hypothetical rearrangement product *(102)* is stable under the conditions of the reaction, and therefore does not occur as an intermediate.



(99) *(100)* *(101)*

(102)

VI. Nitrile-Forming Fragmentations (a—b—C=N—X and a—b—N=C—X)

If the hydroxyl group of a ketoxime [*(103)*, X = OH] is converted into a more active nucleofugal group by protonation, esterification, or etherification, a Beckmann rearrangement (route a) generally takes place [68].

[62] *R. H. Wiley* and *R. P. Davis*, J. Amer. chem. Soc. *76*, 3496 (1954).

[63] *A. A. R. Sayigh, J. N. Tilley*, and *H. Ulrich*, J. org. Chemistry *29*, 3344 (1964).

[64] *C. L. Stevens, T. K. Mukherjee*, and *V. J. Traynelis*, J. Amer. chem. Soc. *78*, 2264 (1956).

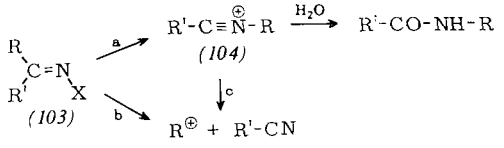
[65] *C. L. Arcus* and *B. S. Prydal*, J. chem. Soc. (London) *1954*, 4018.

[66] *A. F. Beecham*, J. Amer. chem. Soc. *79*, 3257, 3262 (1957).

[67] *D. A. Barr* and *R. N. Haszoldine*, J. chem. Soc. (London) *1957*, 30.

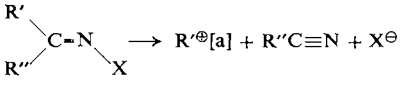
[68] Cf. *L. G. Donaruma* and *W. Z. Heldt*, Org. Reactions *11*, 1 (1960).

The group R that is *trans* to X migrates to form a nitrilium ion *(104)*, which reacts further with water to form the amide[69]. However, if R is an active electrofugal group it may be wholly or partially removed, with simultaneous formation of a nitrile (route b). Processes of this type are frequently referred to as second order Beckmann reactions. A more appropriate term would be Beckmann fragmentation[70].



This reaction occurs particularly with α-amino, α-hydroxy, α-alkoxy, α-oxo, α-imino, and α-carboxy ketoxime derivatives. A number of electrofugally substituted ketoximes are listed in Scheme 2, together with products resulting from Beckmann fragmentation and subsequent hydrolysis. Classes a to h are substantiated by several examples in the literature.

Scheme 2. Examples of Beckmann fragmentations.



	R'—	$R'^{\oplus}$	Hydrolysis products of $R'^{\oplus}$[b]	Ref.
a	$R_2N-\overset{|}{C}-$	$R_2N\overset{\oplus}{=}C\diagdown$	$R_2NH + O=C\diagdown$	[70]
b	$HO-\overset{|}{C}-$	$O=C\diagdown$		[71]
c	$RO-\overset{|}{C}-$	$RO\overset{\oplus}{=}C\diagdown$	$ROH + O=C\diagdown$	[72]
d	R—CO—	$RC\overset{\oplus}{=}O$	RCOOH	[73]
e	R—C(OH)— [c] Y	R—CO—Y		[74]
f	$RN=\overset{|}{C}-$	$RN\overset{\oplus}{\equiv}C-$	R—NH—CO—	[75]
g	HOOC—	CO_2		[76]
h	R_3C-	$R_3C^{\oplus}$	R_3COH	[69, 77]
i	$R_2\overset{\ominus}{C}-\overset{|}{C}-$	$R_2C=C\diagdown$		[78]
k	RS—C—	$RS\overset{\oplus}{=}C\diagdown$	$RSH + O=C\diagdown$	[79]

[a] The charge on R is more positive by one unit than in the starting compound but R need not be a cation.

[b] $H^{\oplus}$ is not listed.

[c] Y is a nucleophilic particle such as $RO^{\ominus}$, $R_2N^{\ominus}$, or $C\equiv N^{\ominus}$

[69] *C. A. Grob, H. P. Fischer, W. Raudenbusch*, and *J. Zergenyi*, Helv. chim. Acta *47*, 1003 (1964).

[70] *C. A. Grob et al.*, Helv. chim. Acta *45*, 2539 (1962); *46*, 936 1190 (1963).

[71] *A. Werner* and *Th. Detscheff*, Ber. dtsch. chem. Ges. *38*, 69 (1905); *A. H. Blatt* and *R. P. Barnes*, J. Amer. chem. Soc. *57*, 1330 (1935).

[72] *R. K. Hill*, J. org. Chemistry *27*, 29 (1962).

[73] *A.F.Ferris, G.S.Johnson*, and *F.E.Gould*, J. org. Chemistry *25*, 1813 (1960); *A. F. Ferris, ibid. 25*, 12 (1960).

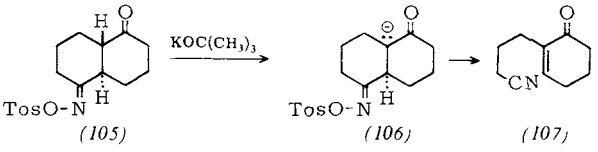
[74] *A. Hassner* and *W. A. Wentworth*, Chem. Commun. *1965*, 44.

[75] *Y. Sato* and *N. Ikekawa*, J. org. Chemistry *26*, 5058 (1961).

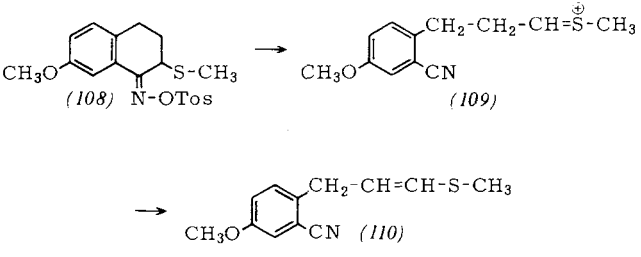
[76] *A. Werner* and *A. Piguet*, Ber. dtsch. chem. Ges. *37*, 4295 (1904); *A. F. Ferris et al.*, J. org. Chemistry *25*, 492, 496, 1302 (1960).

[77] *R.T. Conley* and *M. C. Annis*, J. org. Chemistry *27*, 1961 (1962); *R. K. Hill* and *O.T. Chortyk*, J. Amer. chem. Soc. *84*, 1064 (1962).

Case i, in which the electrofugal fragment contains an olefinic double bond, is new. A fragmentation of this type is observed with the compound *(105)*, which undergoes base-catalysed decomposition with formation of the unsaturated keto nitrile *(107)*[78]. The reactive substrate is undoubtedly the anion *(106)*.



The fact that a sulfur atom can induce fragmentation, as in case k, is shown by the recently described cleavage of the thioether *(108)* to the nitrile *(110)*, which presumably proceeds *via* the alkyl alkylidene sulfonium ion *(109)*[79].

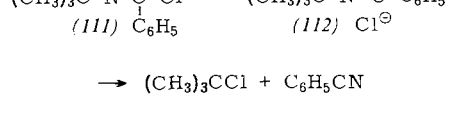


Finally, oximes with groups R of low electrofugal activity, such as α-alkylated and α-arylated ketoximes (class h in Scheme 2), frequently give fragmentation products. However, these are not formed by direct decomposition in accordance with route b, but by Beckmann rearrangement to the ion *(104)* (route a), which fragments to a greater or lesser extent (route c) depending on the reaction conditions. Amide formation is favored in a nucleophilic solvent such as water, whereas the fragmentation is favored in inert solvents and by reagents such as PCl_5 and $SOCl_2$, as well as by high temperatures[69].

In a series of nitrile-forming fragmentations, the electrofugal group is attached to the nitrogen atom and the nucleofugal group to the carbon atom of the middle group N=C.

a) $R_3C-N=C-X$

One such reaction is the fragmentation of *N*-t-butylimidoyl chloride *(111)* or of the nitrilium ion *(112)* formed from it, yielding t-butyl chloride or t-butanol, depending on the reaction conditions[80,69].



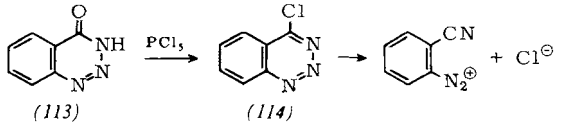
[78] *W. Eisele, C. A. Grob*, and *E. Renk*, Tetrahedron Letters *1963*, 75.

[79] *R. L. Autrey* and *P. W. Scullard*, J. Amer. chem. Soc. *87*, 3284 (1965); cf. also *M. Ohno, N. Naruse, S. Torimitsu*, and *I. Teresawa*, J. Amer. chem. Soc. *88*, 3168 (1966).

[80] *G. Schroeter*, Ber. dtsch. chem. Ges. *44*, 1201 (1911).

b) —R—N=N—N=C—X

In the fragmentation of 4-chlorobenzotriazine *(114)* which is formed by the reaction of the dihydrobenzotriazinone *(113)* with PCl_5 but cannot be isolated, a diazonium ion is split off as an electrofuge, with formation of a nitrile group [81].



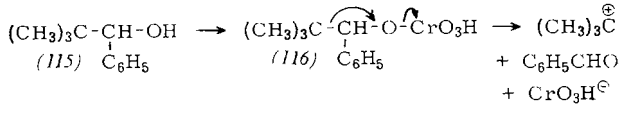
(113) *(114)*

VII. Carbonyl-Forming Fragmentations (a—b—C—O—X and a—b—O—C—X)

This class of fragmentations can be subdivided according to whether an aldehyde, a ketone, a carboxylic acid, or CO_2 is formed. In most cases the nucleofugal group X is attached to the oxygen atom of the middle group. Since the course of the reaction has been elucidated in very few cases and since this class of reactions is of less importance, only a few of the possible types are listed.

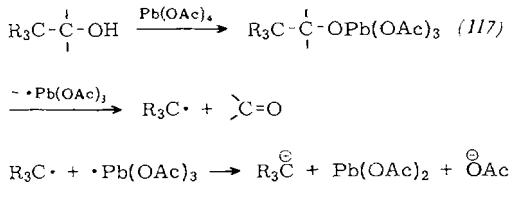
a) R_3C—C—O—X

The oxidation of secondary alcohols with chromic acid can lead to varying quantities of fragmentation products besides the expected ketone if the β carbon atom is highly substituted [82]. Thus the oxidation of 2,2-dimethyl-1-phenyl-1-propanol *(115)* gives a 67 % yield of benzaldehyde, together with the t-butyl cation and its secondary products. An ester of chromic acid *(116)* is assumed to occur as an intermediate [83].



(115) *(116)*

Similar fragmentations of secondary and tertiary alcohols to carbonyl compounds are brought about by lead tetraacetate. However the decomposition of the



(117)

[81] *D. Buckley* and *M. S. Gibson*, J. chem. Soc. (London) *1956*, 3242.

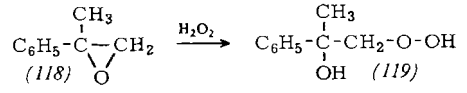
[82] *W. A. Mosher* and *H. A. Neidig*, J. Amer. chem. Soc. *72*, 4452 (1950).

[83] *P. T. Lansbury*, *V. A. Pattison*, and *J. W. Diehl*, Chem. and Ind. *1962*, 653.

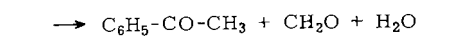
initially formed alkoxylead ester *(117)* appears to be a homolytic process, the resulting radical being oxidized to the carbonium ion in a second step [84].

b) HO—C—C—O—X

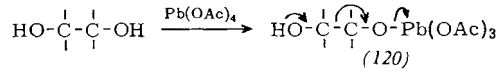
On treatment with alkaline hydrogen peroxide, α-methylstyrene oxide *(118)* decomposes into acetophenone and formaldehyde [85]. This reaction may be regarded as a fragmentation of the initially formed β-hydroxy hydroperoxide *(119)*.



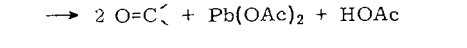
(118) *(119)*



The preferred mechanism for the cleavage of *cis*-1,2-diols [86] and of certain *trans*-1,2-diols *(120)* [87] with lead tetraacetate corresponds to a fragmentation:

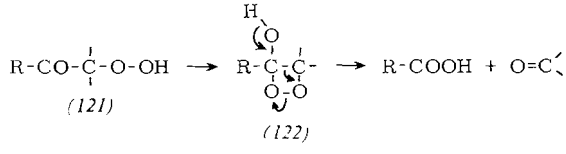


(120)



c) O=C—C—O—X

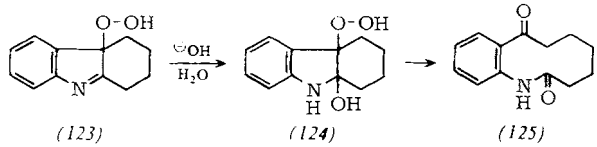
α-Hydroperoxyketones *(121)* formed by the oxidation of enolizable ketones with air undergo base-induced decomposition with formation of acids and carbonyl compounds [88]. In anhydrous alcohol the electrofugal fragment is the free acid and not the ester, suggesting that a cyclic intermediate *(122)* is formed.



(121) *(122)*

d) —N=C—C—O—X or —N—C(OH)—C—O—X

The 3*H*-indole hydroperoxide *(123)*, an α-hydroperoxyketimine, undergoes fragmentation of its water adduct *(124)* to give the lactam *(125)* [89].



(123) *(124)* *(125)*

[84] *K. Heusler* and *J. Kalvoda*, Angew. Chem. *76*, 518 (1964); Angew. Chem. internat. Edit. *3*, 525 (1964).

[85] *J. Hoffman*, J. Amer. chem. Soc. *79*, 504 (1957).

[86] *R. Criegee et al.*, Liebigs Ann. Chem. *599*, 81 (1956); *S. J. Angyal* and *R. J. Young*, J. Amer. chem. Soc. *81*, 5251 (1959).

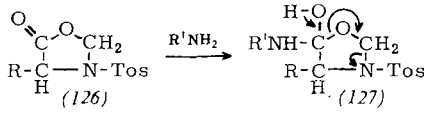
[87] *R. Criegee* and *R. Büchner*, Ber. dtsch. chem. Ges. *73*, 563 (1940).

[88] *W. v. E. Doering* and *R. M. Haines*, J. Amer. chem. Soc. *76*, 482 (1954); *E. Elkik*, Bull. Soc. chim. France *1959*, 933.

[89] *B. Witkop*, J. Amer. chem. Soc. *72*, 1428 (1950).

e) —N—C(OH)—O—C—X

The same system as in *(124)*, but with the sequence of atoms in the middle group reversed, is present in the intermediate *(127)* formed during the ring cleavage of *N*-tosyl-5-oxazolidones *(126)* with amines. This fragmentation reaction has found use in peptide synthesis [90].



(126) *(127)*

→ R NH-CO-CHR-NHTos + CH_2O

f) HO—CO—C—O—X

α-Hydroxy acids are degraded by oxidizing agents such as chromic acid [91], *N*-bromosuccinimide [92], sodium hypochlorite [93], or lead tetraacetate [94] into CO_2 and the carbonyl compound containing one carbon atom less. For example, the oxidation of lactic acid with chromic acid leads to acetaldehyde and carbon dioxide without intermediate formation of pyruvic acid [91,95]:

$$CH_3–CHOH–COOH \rightarrow CH_3CHO + CO_2$$

In this reaction it is not certain whether the oxidizing agent (Ox) attacks the carboxyl group as in *(128)*, the α-hydroxyl group as in *(129)*, or both groups *via* a cyclic intermediate.



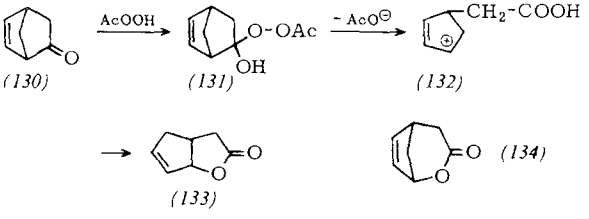
(128) *(129)*

α-Hydroxy peracids are well known to be unstable. Thus glycolic acid is decarboxylated to formaldehyde by hydrogen peroxide in acidic solution [96]. This reaction can be explained by fragmentation of the intermediate α-hydroxyperacetic acid in accordance with *(128)*, R = H, Ox = OH.

g) R_3C—C(OH)—O—X

The Bayer-Villiger oxidation of ketones to esters by peracids [97] can be superseded by fragmentation if there is an active electrofugal group α to the carbonyl group.

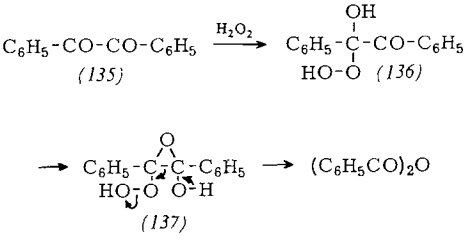
Thus the reaction of dehydronorcampher *(130)* with peracetic acid does not lead to the expected lactone *(134)*; instead, the adduct *(131)* undergoes fragmentation with formation of the carbonium ion *(132)*, the precursor of the lactone *(133)* which is isomeric with *(134)* [98].



(130) *(131)* *(132)* *(133)* *(134)*

h) O=C—C(OH)—O—X

α,β-Diketones such as *(135)* are oxidized by hydrogen peroxide or alkyl hydroperoxides to acid anhydrides [99]. This base-induced reaction probably proceeds *via* the adduct *(136)*, whose cyclic tautomer *(137)* satisfies the requirements for fragmentation to the anhydride [100].



(135) *(136)* *(137)*

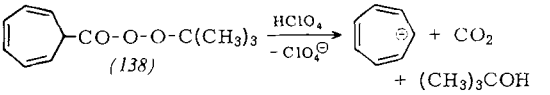
i) R_3C—CO—O—X

The oxidative decarboxylation of carboxylic acids with lead tetraacetate to form acetates and olefins has recently been recognized as a homolytic reaction [101].

$$2\ R–CH_2–CH_2–COOH \xrightarrow{Pb(OAc)_4} R–CH_2–CH_2–OAc + R–CH=CH_2$$

Consequently, it does not come within the scope of this discussion.

On the other hand, the acid catalysis observed in the decarboxylation of the peroxy ester *(138)* of norcara-



(138)

[90] *F. Micheel* and *H. Haneke*, Chem. Ber. *95*, 1009 (1962); *E. Dane*, *R. Heiss*, and *H. Schäfer*, Angew. Chem. *71*, 339 (1959).

[91] *F. H. Westheimer*, Chem. Reviews *45*, 419 (1949).

[92] *M. F. Abdel-Wahab* and *M. Z. Barakat*, Mh. Chem. *88*, 692 (1957); *M. Z. Barakat* and *M. F. Abdel-Wahab*, J. Amer. chem. Soc. *75*, 5731 (1953).

[93] *R. L. Whistler* and *R. Schweiger*, J. Amer. chem. Soc. *81*, 5190 (1959); J. org. Chemistry *26*, 1050 (1961).

[94] *H. Oeda*, Bull. Soc. chem. Japan *9*, 8 (1934).

[95] *E. T. Chapman* and *M. H. Smith*, J. chem. Soc. (London) *20*, 173 (1867).

[96] *H. S. Fry* and *K. L. Milstead*, J. Amer. chem. Soc. *57*, 2269 (1935).

[97] *C. H. Hassall*, Org. Reactions *9*, 73 (1957).

[98] *J. Meinwald* and *E. Frauenglass*, J. Amer. chem. Soc. *82*, 5235 (1960).

[99] *E. Weitz* and *A. Scheffer*, Ber. dtsch. chem. Ges. *54*, 2327 (1921); *R. P. Barnes* and *R. E. Lewis*, J. Amer. chem. Soc. *58*, 947 (1936).

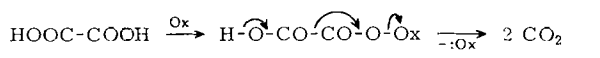
[100] *C. A. Bunton*, Nature (London) *163*, 444 (1949); *H. Kwart* and *N. J. Wegemer*, J. Amer. chem. Soc. *83*, 2746 (1961).

[101] *J. K. Kochi*, J. Amer. chem. Soc. *87*, 3609 (1965).

dienecarboxylic acid [which is formulated as a cycloheptatrienyl derivative to a tropylium salt points to heterolytic fragmentation [102].

k) HO—CO—CO—O—X

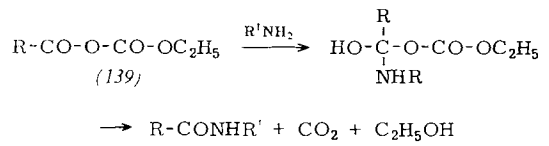
The bis-decarboxylation of oxalic acid by oxidizing agents such as permanganate can probably be formulated as fragmentation in the following manner:



In a group of CO_2-forming fragmentations, the electrofugal group is originally attached to the oxygen atom of the middle group, and the nucleofugal group to the carbon atom, as in the following examples.

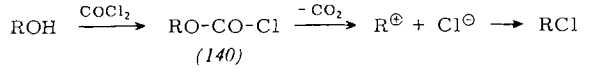
l) HO—C—O—CO—X

This type includes acylations of amines and alcohols by mixed anhydrides of carbonic acid *(139)* [103].



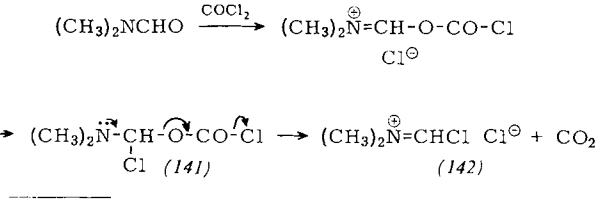
m) R_3C—O—CO—Cl

This group of CO_2-forming fragmentations also includes the decomposition of alkyl chlorocarbonates *(140)* to alkyl chlorides [104].



n) N—C—O—CO—X

The formation of *N,N*-dimethylformimidoyl chloride derivative *(142)* from dimethylformamide and phosgene is a CO_2-forming fragmentation and proceeds *via* the adduct *(141)* [105].



[102] *C. Rüchardt* and *H. Schwarzer*, Angew. Chem. *74*, 251 (1962); Angew. Chem. internat. Edit. *1*, 217 (1962); Chem. Ber. *99*, 1878 (1966).

[103] *D. A. Johnson*, J. Amer. chem. Soc. *75*, 3636 (1953); *R. A. Boissonnas*, Helv. chim. Acta *34*, 874 (1951).

[104] *K. B. Wiberg* and *T. M. Shryne*, J. Amer. chem. Soc. *77*, 2774 (1954).

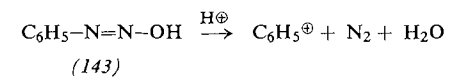
[105] *H. H. Bosshard, R. Mory, M. Schmid*, and *H. Zollinger*, Helv. chim. Acta *42*, 1653 (1959); *H. H. Bosshard* and *H. Zollinger, ibid. 42*, 1659 (1959).

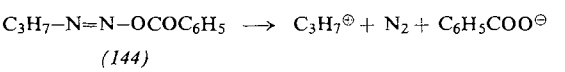
VIII. Nitrogen-Forming Fragmentations (a—b—N=N—X)

Owing to the high energy of formation of molecular nitrogen, azo compounds undergo fragmentation even when the leaving groups are as weakly electrofugal and nucleofugal as in the case of aryl and alkyl groups.

a) R—N=N—X

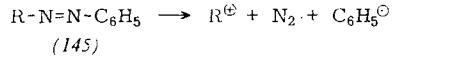
Aryldiazohydroxides *(143)* decompose in acidic solution into aryl cations and nitrogen. The same is true of esters of alkyldiazo hydroxides such as *(144)* [106].



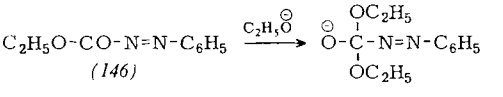


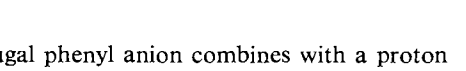
b) HO—C—N=N—Ar or HN—C—N=N—Ar

A number of base-induced fragmentations have recently been described in which phenyl anions are liberated together with nitrogen from phenylazo compounds *(145)* [107]. The reactive substrate is an anion formed by loss of a proton or by addition of a base such as sodium ethoxide, as is shown by the reaction of the ester *(146)*.



R = HOOC; CH_3CO-O-$C(CH_3)_2$; C_2H_5OOC; H_2N-CO; C_6H_5-CO





The nucleofugal phenyl anion combines with a proton to form benzene. An *o*-halophenyl anion may also form benzyne by loss of a halide ion.

IX. Other Heteroxide-Forming Fragmentations

Of the many possible atomic combinations, two examples, one with hydrogen and one with phosphorus, will be selected.

[106] *R. Huisgen* and *Ch. Rüchardt*, Liebigs Ann. Chem. *601*, 1 (1957); *H. Maskill, R. M. Southam*, and *M. C. Whiting*, Chem. Commun. *1965*, 496.

[107] *R. W. Hoffmann*, Chem. Ber. *97*, 2763 (1964); *98*, 222 (1965); *A. Angeli* and *Z. Jollés*, Ber. dtsch. chem. Ges. *62*, 2099 (1929).

a) $R_3C—O—SO—X$

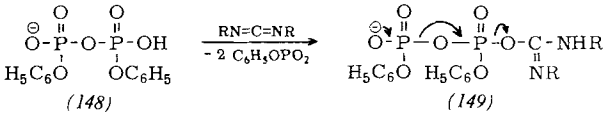
The formation of alkyl chlorides from alcohols and thionyl chloride proceeds *via* alkyl chlorosulfites *(147)*, the decomposition of which into alkyl chloride and sulfur dioxide constitutes a fragmentation [108].

$$R{-}OH \xrightarrow{SOCl_2} R{-}O{-}SO{-}Cl \xrightarrow{-SO_2} R^{\oplus} + Cl^{\ominus} \rightarrow R{-}Cl$$

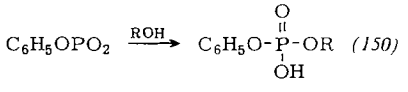
(147)

b) HO—P—O—P—X

Diaryl pyrophosphates *(148)* react with carbodiimides to form addition compounds *(149)*, which undergo fragmentation with formation of two molecules of an ester of metaphosphoric acid. The ester reacts with alcohols to give the unsymmetrical diester of phosphoric acid *(150)* [109]:



(148) *(149)*



(150)

X. α-Fragmentations

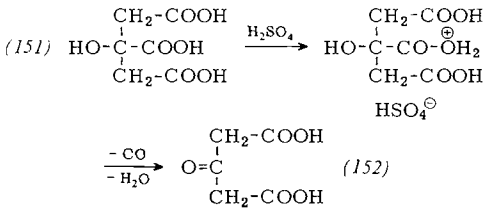
By analogy with α-eliminations, in which a proton and a nucleofugal group are removed from the same atom [110], it is possible to distinguish α-fragmentations. In this case the electrofugal and the nucleofugal groups are both removed from the same atom:

$$a{-}b{-}c{-}X \longrightarrow a{-}b + :c + :X$$

Since the valence of the atom c decreases by two in this type of fragmentation, the reaction will be observed when the lower valence state of c exhibits a certain stability. This applies *e.g.* to the carbon atom, when either carbon monoxide or an isocyanide is liberated as the unsaturated fragment. Most of the fragmentations of this type are therefore decarbonylations of carboxylic acids and their derivatives.

a) HO—C—CO—X

α-Hydroxy acids lose carbon monoxide in the presence of strong mineral acids with formation of aldehydes and ketones. For example, with concentrated sulfuric acid, citric acid *(151)* gives good yields of 3-oxopentanedicarboxylic acid *(152)* [111].



(151) *(152)*

b) O=C—CO—X

Similarly, α-keto acids are degraded by mineral acids to the next lower carboxylic acid. The decarbonylation of phenylglyoxylic acid *(153)* for example, can proceed stepwise [112].

$$C_6H_5{-}CO{-}COOH \xrightarrow{H^{\oplus}} C_6H_5{-}CO{-}CO{-}\overset{\oplus}{O}H_2 \xrightarrow{-H_2O}$$

(153)

$$C_6H_5{-}CO{-}\overset{\oplus}{C}O \xrightarrow{-CO} C_6H_5{-}\overset{\oplus}{C}O \xrightarrow{H_2O} C_6H_5COOH$$

The thermal decarbonylation of esters of oxalic acid may proceed in a similar manner [113].

c) HO—CO—CO—X

The acid-catalysed decomposition of the protonated form *(154)* of oxalic acid into CO and CO_2 is also an α-fragmentation.

$$HOCO{-}COOH \xrightarrow{H^{\oplus}} HOCO{-}CO{-}\overset{\oplus}{O}H_2 \xrightarrow[-H^{\oplus}]{}$$

(154)

$$CO_2 + CO + H_2O$$

Owing to the high electrofugal activity of the carboxyl group, the monochloride and the monoanhydride of oxalic acid [*(155)*, X = Cl or O–CO–COOH] are unstable [114].

HOCO–CO–X

(155)

d) N—C—CO—X

The acyl chlorides *(157)* of free α-(dialkylamino)acids *(156)* readily undergo decarbonylation during preparation, with formation of iminium salts [115].

[108] *E. S. Lewis* and *C. E. Boozer*, J. Amer. chem. Soc. *76*, 794 (1954); *D. J. Cram, ibid. 75*, 332 (1953).

[109] *F. Cramer, K. H. Scheit*, and *H. J. Baldauf*, Chem. Ber. *95*, 1657 (1962); *J. A. Shofield* and *A. Todd*, J. chem. Soc. (London) *1961*, 2316.

[110] *J. Hine*: Physical Organic Chemistry. McGraw-Hill, New York 1956, p. 131.

[111] *R. Adams, H. M. Chiles*, and *C. F. Rassweiler*, Org. Syntheses Coll. Vol. I, 9 (1932).

[112] *W. W. Elliott* and *D. L. Hammick*, J. chem. Soc. (London) *1951*, 3402; *K. Banholzer* and *H. Schmid*, Helv. chim. Acta *39*, 548 (1956).

[113] *M. Calvin* and *R. M. Lemmon*, J. Amer. chem. Soc. *69*, 1232 (1947).

[114] *I. Ugi* and *F. Beck*, Chem. Ber. *94*, 1839 (1961); *C. K. Rosenbaum* and *J. H. Walton*, J. Amer. chem. Soc. *52*, 3366 (1930).

[115] *N. A. Poddubnaya* and *V. I. Maksimov*, Ž. obšč. Chim. *29*, 3483 (1959); *V. I. Maksimov*, Tetrahedron *21*, 687 (1965).

$$R_2N-CHR'-COOH \xrightarrow{PCl_5} R_2N-CHR'-CO-Cl \xrightarrow{-CO}$$
(156) *(157)*

$$R_2\overset{\oplus}{N}=CHR'\ Cl^{\ominus}$$

A base-induced variant of this reaction is observed with chlorides of α-(*N*-arenesulfonyl)amino acids. Thus *N*-tosylphenylalanyl chloride *(158)* decomposes *via* the anion *(159)* to the *N*-tosylimine *(160)* [116].

$$\underset{(158)}{Tos-NH-\underset{\displaystyle CH_2-C_6H_5}{\underset{|}{CH}}-CO-Cl} \xrightarrow[-H_2O]{HO^{\ominus}} \underset{(159)}{Tos-\overset{\ominus}{N}-\underset{\displaystyle CH_2-C_6H_5}{\underset{|}{CH}}-CO-Cl}$$

$$\xrightarrow[-Cl^{\ominus}]{-CO} \underset{(160)}{Tos-N=CH-CH_2-C_6H_5}$$

e) $R_3C-CO-X$

Chlorides of tertiary carboxylic acids are decarbonylated in the presence of Friedel-Crafts catalysts such as $AlCl_3$. The intermediate acylium ion *(162)* formed from pivaloyl chloride *(161)* can be intercepted by anisole with formation of 1-(p-methoxyphenyl)-2,2-dimethyl-1-propanone. The less reactive solvent benzene is only alkylated by the t-butyl cations *(163)* formed by decarbonylation of *(162)* [117].

$$\underset{(161)}{(CH_3)_3C-CO-Cl} \xrightarrow[-Cl^{\ominus}]{AlCl_3} \underset{(162)}{(CH_3)_3C-C\overset{\oplus}{\equiv}O} \xrightarrow{-CO} \underset{(163)}{(CH_3)_3C^{\oplus}}$$

[116] *R. H. Wiley* and *R. P. Davis*, J. Amer. chem. Soc. *76*, 3496 (1954); *A. F. Beecham*, J. Amer. chem. Soc. *79*, 3257 (1957); Austral. J. Chem. *16*, 889 (1963).

[117] *E. Rothstein* and *R. W. Saville*, J. chem. Soc. (London) *1949*, 1946, 1950, 1954.

The reverse of this reaction, *i.e.* the formation of carboxylic acids by carbonylation of carbonium ions, is also known [118].

f) $O=C-CNR-X$

Mention finally should be made of an example of an α-fragmentation in which an isocyanide is formed as the unsaturated fragment. Thus acylformimidoyl chlorides such as *(164)* decompose when heated to form an acyl chloride and an isocyanide. At lower temperatures the reaction proceeds in the reverse direction, *i.e.* as a 1,1-addition [119].

$$\underset{(164)}{C_6H_5-CO-\underset{\displaystyle N-C_6H_5}{\underset{\|}{C}}-Cl} \rightleftharpoons C_6H_5-\overset{\oplus}{C}O + \overset{\ominus}{C}l + C_6H_5-N\equiv C$$

XI. Outlook

These examples do not exhaust the list of fragmentable systems. Other combinations of electrofugal and middle groups lead to further cases. New fragmentations are constantly being reported in the literature. As was mentioned in the introduction, detailed studies of the mechanism and stereochemistry of fragmentation reactions have been carried out in only a few cases. In view of their great variety, fragmentation reactions present a wide field for future investigations.

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German version: Angew. Chem. *79*, 1 (1967)
Translated by Express Translation Service, London

[118] *T. A. Ford, H. W. Jacobson*, and *F. C. McGrew*, J. Amer. chem. Soc. *70*, 3793 (1948); *H. Koch* and *W. Haaf*, Angew. Chem. *70*, 311 (1958).

[119] *I. Ugi* and *U. Fetzer*, Chem. Ber. *94*, 1116 (1961).

Diels-Alder Reactions II[**]: The Reaction Mechanism

BY J. SAUER[*]

The possible mechanisms of the preparatively so productive Diels-Alder reactions are discussed critically on the basis of experimental data. Although most of the facts can be explained readily by a synchronous mechanism, a number of problems remains.

A. Cycloadditions: Possible Mechanisms

B. Stereochemical Course of Diels-Alder Additions
1. The "*cis*" Principle
2. *Alder*'s "*endo*" Rule: Validity and Exceptions
3. Influence of Conformation on Diene Reactivity: *cisoid* and *transoid* Dienes
4. Partial Asymmetric Syntheses with Diels-Alder Reactions

C. Orientation Phenomena in Reactions of Unsymmetrical Components
1. 1-Substituted Dienes
2. 2-Substituted Butadienes
3. Disubstituted Dienes
4. Influence of Catalysts on Orientation Phenomena

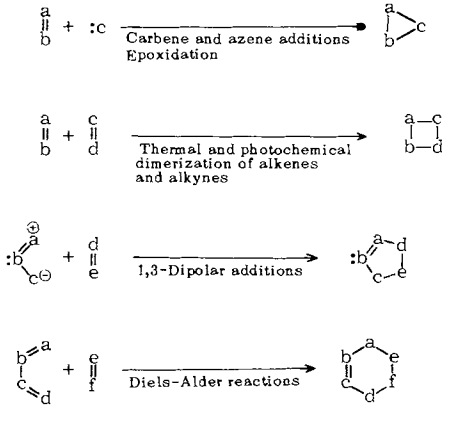
D. Kinetic Studies of Diels-Alder Reactions
1. The "Alder Rule": Influence of Activating Substituents in the Dienophile
2. Reactivity of Dienes towards Maleic Anhydride and Tetracyanoethylene
3. Diels-Alder Reactions with Inverse Electron Demand
4. Solvent Effects and Activation Parameters
5. Acceleration of Diels-Alder Reactions by Catalysts and Pressure

E. On the Mechanism of Diels-Alder Reactions
1. Rearrangements of Diels-Alder Adducts
2. Kinetic Isotope Effects
3. One-Step or Two-Step Reaction?

F. Conclusion

A. Cycloadditions: Possible Mechanisms

Cycloadditions (this term is defined in [1]) can be used to gain access to compounds of various ring sizes, as illustrated in the following examples for the formation of three-membered to six-membered rings.



In every case, two new σ bonds are formed between the reactants at the expense of π bonds. The reaction may follow one of several courses, which will be briefly outlined for the diene synthesis.

The new σ bonds between the reactants may be formed simultaneously in a multicenter mechanism, as indicated by route A. We are dealing, therefore, with a one-step reaction, whose energy profile contains only one activation barrier (Fig. 1a).

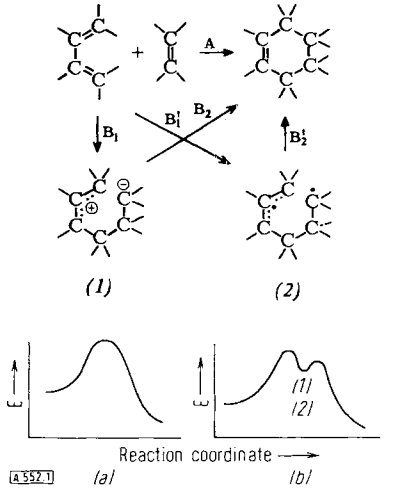


Fig. 1. Energy profile for (a) a one-step and (b) a two-step reaction.

Another possibility is that the two σ bonds are formed in two successive reaction steps. The energy profile of the two-step reaction (Fig. 1b), which contains two transition states, then includes a zwitterion *(1)* or biradical *(2)* intermediate. For *(2)*, we must in principle consider a singlet state (paired electrons) as well as a triplet species.

The following discussion of stereochemical and kinetic results, orientation phenomena in the combination of

[*] Doz. Dr. J. Sauer
Institut für Organische Chemie der Universität
Karlstraße 23
8 München 2 (Germany)

[**] Part I see [2].

[1] *R. Huisgen, R. Grashey,* and *J. Sauer* in *S. Patai*: The Chemistry of Alkenes. Interscience, London 1964, p. 739.

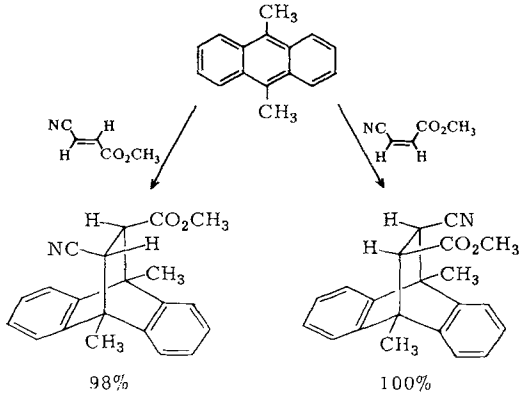
unsymmetrical reactants, catalyst effects, rearrangements, and isotope effects should provide some idea of what criteria may be used to distinguish between one-step and two-step reactions. As in Part I of this series [2], no attempt is made to survey all the existing data.

B. Stereochemical Course of Diels-Alder Additions

The stereochemical study of a reaction often presents an insight into its mechanism. *Alder* and his school made valuable contributions in this respect, which have been critically discussed, together with results obtained by other authors, by *Martin* and *Hill* [3]. The study of the stereochemical course of diene additions is sometimes difficult, owing to the ability of the adducts to redissociate [2] (examples occur with furans, fulvenes, and 9,10-disubstituted anthracenes as diene components). In many cases the 1:1 adducts resulting from a kinetically controlled and a thermodynamically controlled reaction are formed simultaneously, giving the impression that the Diels-Alder reaction yields a mixture of structural or stereoisomers. However, information about the stereochemical course of the reaction can be obtained only from the 1:1 adduct resulting from a kinetically controlled reaction.

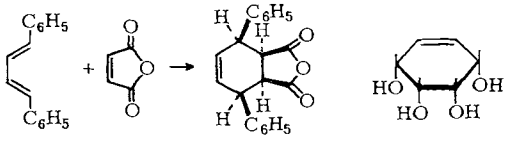
1. The "*cis*" Principle

It was recognized very early that the steric arrangement of substituents in the dienophile and in the diene is preserved in the 1:1 adduct, *i.e.* that diene additions are pure "*cis*" additions, and this observation was formulated by *Alder* and *Stein* as the "*cis*" principle [4]. *cis*- or *trans*-Dienophiles react with dienes to give 1:1 adducts in which the *cis* or *trans* arrangement of the substituents in the dienophile is retained; this is illustrated for the reactions of the isomeric methyl β-cyanoacrylates [5] (in boiling dioxane).



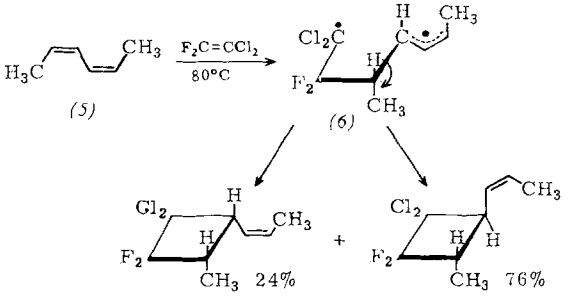
According to *Hendrickson*, the addition of *cis*- and *trans*-β-sulfoacrylic acid ($HO_3S-CH=CH-CO_2H$) to cyclopentadiene leads to the same adduct, in which the substituents of the dienophile are *trans* to each other [6]. This result, which is the only known exception to the "*cis*" principle, is remarkable from the mechanistic standpoint, but according to the author it requires further corroboration.

The *cis* principle applies also to substituents in the diene components, as is shown by many examples [3, 7]. In the 1:1 adduct *(3)*, which can be obtained almost quantitatively from *trans,trans*-1,4-diphenylbutadiene and maleic anhydride (in boiling benzene), the phenyl groups are *cis* to each other [8]. The synthesis of all-*cis*-3,4,5,6-cyclohexenetetrol *(4)* (Kondurit D) [9], the first step of which is the Diels-Alder reaction of vinylene carbonate with *trans,trans*-1,4-diacetoxybutadiene, is also stereoselective. Heterodienophiles also obey the "*cis*" principle in the addition to dienes [9a].



The almost universal strict *cis* addition can be readily explained by synchronous formation of the bonds between the two components in a one-step reaction (Section A, route A), but does not, in principle, rule out the possibility of a two-step reaction *via (1)* or *(2)*. If the step B_2 or B'_2 is much faster than rotation about C–C single bonds, the two-step mechanism should also lead to stereoselectivity.

Bartlett et al. [10] recently found a two-step mechanism with a biradical intermediate in cycloadditions leading to cyclobutane derivatives. In the reaction of the *cis-trans*-isomeric 1,4-dimethylbutadienes with 1,1-dichloro-2,2-difluoroethylene, the step leading to the formation of the four-membered ring is not stereoselective, as is illustrated for *cis,cis*-2,4-hexadiene *(5)*. The rate of rotation about a C–C single bond (indicated by a curved arrow) in the intermediate *(6)* is comparable with the rate of the second step in the two-step reaction, *i.e.* the ring closure, so that the stereoselectivity is partially lost.



[2] *J. Sauer*, Angew. Chem. *78*, 233 (1966); Angew. Chem. internat. Edit. *5*, 211 (1966).

[3] *J. G. Martin* and *R. K. Hill*, Chem. Reviews *61*, 537 (1961).

[4] *K. Alder* and *G. Stein*, Angew. Chem. *50*, 510 (1937).

[5] *J. Sauer*, *H. Wiest*, and *A. Mielert*, Chem. Ber. *97*, 3183 (1964).

[6] *J. B. Hendrickson*, J. Amer. chem. Soc. *84*, 653 (1962).

[7] *A. S. Onishchenko*: Diene Synthesis. Translated from the Russian by Israel Program for Scientific Translations, Jerusalem 1964; available through Oldbourne Press, London.

[8] *K. Alder* and *M. Schumacher*, Liebigs Ann. Chem. *571*, 87 (1951).

[9] *R. Criegee* and *P. Becher*, Chem. Ber. *90*, 2516 (1957).

[9a] *R. Daniels* and *K. A. Roseman*, Tetrahedron Letters *1966*, 1335.

[10] *L. K. Montgomery*, *K. Schueller*, and *P. D. Bartlett*, J.Amer. chem. Soc. *86*, 622 (1964); *P. D. Bartlett* and *L. K. Montgomery*, *ibid. 86*, 628 (1964).

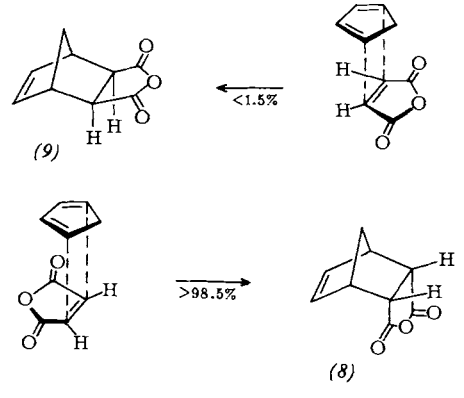
It is significant in this connection that the Diels-Alder reactions of *cis*- and *trans*-1,2-dichloroethylene with pentadiene, which could involve biradical intermediates *(7a)* and *(7b)*, respectively, of comparable stability, give strict *cis*-addition [11], *i.e.* there is no interconversion *(7a)* $\rightleftharpoons$ *(7b)*. The addition of hexachlorocyclopentadiene to α-methyl-β-deuterostyrene is also stereospecific.



(7a) *(7b)*

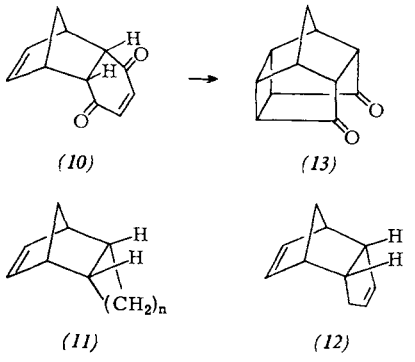
2. The Alder *"endo"* Rule: Validity and Exceptions

The combination of cyclic dienes with cyclic dienophiles could in principle follow two courses; in general, however, only one of these is actually realized. After a "sandwich-like" preorientation of the reactants, the dienophile is added in such a way as to give a "maximum concentration" of double bonds [4] in the transition state; according to *Alder* and *Stein* [4] this includes not only the π systems directly involved in the reaction, but also those of the "activating ligands" (see Section D). The addition of maleic anhydride to cyclopentadiene leads almost exclusively to the *endo* adduct *(8)*. The thermodynamically more stable *exo* compound *(9)* is formed in yields of less than 1.5 % [12].



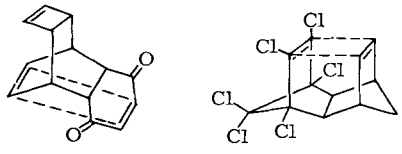
(9) *(8)*

Preferential or exclusive formation of the *endo* adduct is also found in the reactions of cyclopentadiene with *p*-benzoquinone, cyclopentene [13], and cyclopropene [14] to give *(10)*, *(11)*, n = 3, and *(11)*, n = 1, and in the dimerization of cyclopentadiene to form *(12)* [4]. The configurations of *(10)* and *(12)* were determined by photochemically induced cycloaddition to form a four-membered ring, as is illustrated for the conversion of *(10)* into *(13)* [15]. Cage compounds of the type *(13)* can be formed only by *endo* adducts. The *endo*



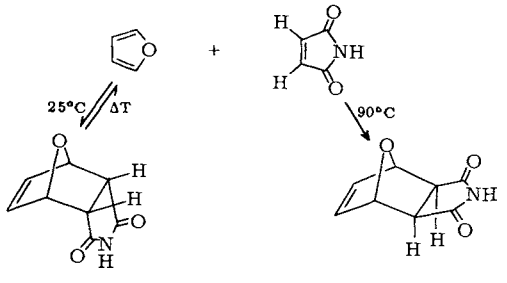
(10) *(13)* *(11)* *(12)*

configuration of the adducts *(14)* and *(15)* can be proved in the same way [15]; the π bonds that react are indicated by broken lines. The reaction of cyclohexadiene with cyclic dienophiles, like that of cyclopentadiene, also leads almost exclusively to the *endo* adducts.

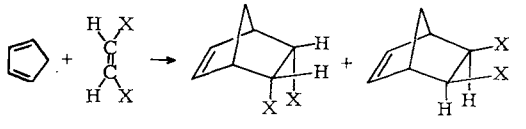


(14) *(15)*

The *endo* rule is only apparently violated by the reaction of the cyclic diene furan with the cyclic dienophiles maleic anhydride and maleimide [16] and by the diene additions of the fulvenes [17]. In these cases the adduct redissociates at temperatures only slightly above room temperature (more rapidly at 90 °C), permitting the conversion of the *endo* adduct resulting from the kinetically controlled reaction into the thermodynamically more stable *exo* isomer.



The reaction of cyclic dienes with *cis*-1,2-disubstituted olefins *(16)* obeys *Alder*'s *endo* rule only in part. For example, when X = C_6H_5–SO_2 or C_6H_5–CO the *endo*



(16) *(17)* *(18)*

adducts *(17)* are obtained with no spectroscopically detectable amounts of the *exo* isomers *(18)*, whereas in the reaction with the dimethyl ester or dinitrile of maleic

[11] *J. B. Lambert* and *J. D. Roberts*, Tetrahedron Letters *1965*, 1457.

[12] *H. Stockmann*, J. org. Chemistry *26*, 2025 (1961).

[13] *S. J. Cristol*, *W. K. Seifert*, and *S. B. Soloway*, J. Amer. chem. Soc. *82*, 2351 (1960).

[14] *K. B. Wiberg* and *W. J. Bartley*, J. Amer. chem. Soc. *82*, 6375 (1960).

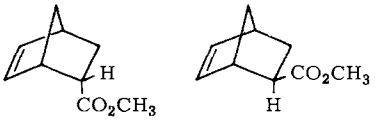
[15] *R. C. Cookson*, *E. Crundwell*, and *J. Hudec*, Chem. and Ind. *1958*, 1003; *R. C. Cookson* and *E. Crundwell*, *ibid. 1958*, 1004; *G. O. Schenck* and *R. Steinmetz*, Chem. Ber. *96*, 520 (1963); *R. C. Cookson*, *E. Crundwell*, and *R. R. Hill*, J. chem. Soc. (London) *1964*, 3062.

[16] *R. B. Woodward* and *H. Baer*, J. Amer. chem. Soc. *70*, 1161 (1948); *H. Kwart* and *I. Burchuk*, *ibid. 74*, 3094 (1952).

[17] *D. Craig*, *J. J. Shipman*, *J. Kiehl*, *F. Widmer*, *R. Fowler*, and *A. Hawthorne*, J. Amer. chem. Soc. *76*, 4573 (1954); *R. B. Woodward* and *H. Baer*, *ibid. 66*, 645 (1944).

acid *(16)*, X = CO_2CH_3 or CN, the adducts *(17)* and *(18)* are formed in the approximate ratio 75:25 [5]. Similar results were obtained with cyclohexadiene [18].

Cyclic dienes generally react with monosubstituted olefins to yield mixtures of isomers. Cyclopentadiene and methyl acrylate give *(19)* and *(20)* in the approxi-



(19) *(20)*

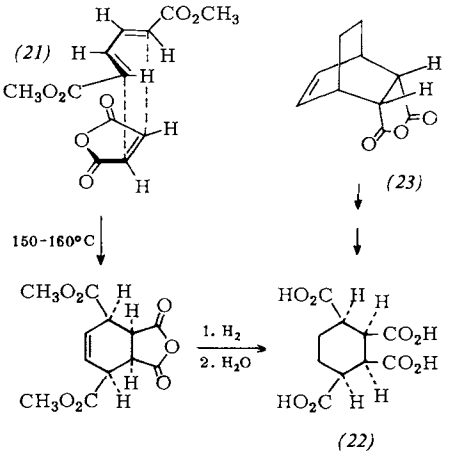
mate ratio 76:24 [19]; with acrylonitrile, the product ratio *endo*:*exo* = 60:40 approaches the statistical value [20], which is attained in the reaction of cyclohexadiene with acrylonitrile [20]. In these cases *Alder*'s rule is not valid. The stereochemical course of these Diels-Alder reactions is strongly influenced by the introduction of a methyl, phenyl, or chloro substituent into the α or β position of the acrylate [7, 21, 22].

Interesting solvent and catalyst effects on the stereochemistry of the addition of acrylates to cyclopentadiene have recently been recognized. *Berson* [22] showed that the proportion of the *endo* isomer *(19)* in the mixture increases with the polarity of the solvent. Since the activated complex leading to *(19)* has a higher dipole moment than that leading to *(20)*, the former is more strongly favored by an increase in solvating power of the solvent. *Berson* also derived a new empirical scale of solvent polarity [22] based on the *endo*:*exo* ratio, which can be determined accurately by gas chromatography; this scale parallels other solvent functions [23].

As will be explained in Section D 5, the rate of diene additions is considerably increased by addition of Lewis acids. It was only recently recognized that the ratio of the structurally isomeric or stereoisomeric 1:1 adducts also changes on addition of a catalyst [24, 25]. At 0 °C in dichloromethane, *(19)* and *(20)* are formed in the approximate ratio 80:20, whereas when catalysed by Lewis acids (10-mole-% of $AlCl_3 \cdot O(C_2H_5)_2$, $BF_3 \cdot O(C_2H_5)_2$, $SnCl_4$, or $TiCl_4$), the reaction gives a 95:5 mixture; at −70 °C in the presence of $AlCl_3 \cdot O(C_2H_5)_2$ or $BF_3 \cdot O(C_2H_5)_2$, practically pure *(19)* is formed [25].

Similar results are obtained in the addition reactions of methyl methacrylate, methyl crotonate, and maleic esters to cyclopentadiene [25a].

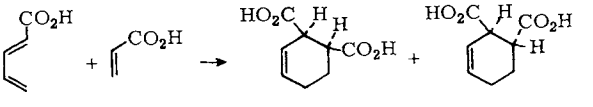
The *endo* rule is frequently satisfied also in the reaction of acyclic dienes with cyclic dienophiles, as has already been seen from the synthesis of Kondurit D *(4)* and the reaction of *trans,trans*-1,4-diphenylbutadiene with maleic anhydride (Section B.1). The addition of dimethyl *trans*-muconate *(21)* to maleic anhydride also proceeds in high yield and strictly in accordance with the *endo* rule, as shown by the all-*cis* arrangement of the carboxyl groups in the cyclohexanetetracarboxylic acid *(22)*



(22)

derived from the adduct. The configuration of *(22)* is confirmed by the oxidative degradation of the cyclohexadiene-maleic anhydride adduct *(23)*, the configuration of which is known [26].

Open-chain dienes and open-chain dienophiles obey the *endo* rule only at low temperatures, as shown in Table 1 for the reaction of *trans*-butadiene-1-carboxylic acid and acrylic acid [3, 7].



(24) *(25)*

Table 1. Effect of temperature on the stereochemistry of the reaction of *trans*-butadiene-1-carboxylic acid with acrylic acid.

Temperature (°C)	75	90	100	110	130
Ratio *(24)*:*(25)*	*(24)* only	7:1	4.5:1	2:1	1:1

No quantitative theoretical approach to *Alder*'s *endo* rule has yet been found. The exclusive *endo* addition of *p*-benzoquinone to cyclopentadiene has been attributed to dipole-induced dipole forces between the polar groups in the dienophile and the readily polarizable diene [27]; this phenomenon is now described, probably more accurately, as a "charge-transfer" interaction (see Section E 3). The fact that dienophiles *without* polar substituents, such as cyclopropene [14], cyclopentene [13], and even allyl bromide and

[18] *D. Albera, G. Luciani,* and *F. Montanari,* Boll. sci. Fac. Chim. ind. Bologna *18*, 52 (1960); Chem. Abstr. *55*, 27140e (1961).

[19] *C. D. Ver Nooy* and *C. S. Rondestvedt,* J. Amer. chem. Soc *77*, 3583 (1955); *A. C. Cope, E. Ciganek,* and *N. A. LeBel, ibid. 81*, 2799 (1959).

[20] *K. Alder, K. Heimbach,* and *R. Reubke,* Chem. Ber. *91*, 1516 (1958).

[21] *K. Alder* and *W. Günzl,* Chem. Ber. *93*. 809 (1960); *K. Alder, R. Hartmann,* and *W. Roth,* Liebigs Ann. Chem. *613*, 6 (1958).

[22] *J. A. Berson, Z. Hamlet,* and *W. A. Mueller,* J. Amer. chem. Soc. *84*, 297 (1962) give an excellent discussion of the stereochemical orientation phenomena and further references.

[23] *C. Reichardt,* Angew. Chem. *77*, 30 (1965); Angew. Chem. internat. Edit. *4*, 29 (1965), and literature cited there.

[24] *E. F. Lutz* and *G. M. Bailey,* J. Amer. chem. Soc. *86*, 3899 (1964).

[25] *J. Sauer* and *J. Kredel,* Angew. Chem. *77*, 1037 (1965); Angew. Chem. internat. Edit. *4*, 989 (1965); Tetrahedron Letters *1966*, 731.

[25a] *T. Inukai* and *T. Kojima,* J. org. Chemistry *31*, 2032 (1966).

[26] *K. Alder* and *H. Vagt,* Liebigs Ann. Chem. *571*, 153 (1951); *K. Alder, ibid. 571*, 157 (1951).

[27] *A. Wassermann,* J. chem. Soc. (London) *1935*, 1511; *1936*, 432; Diels-Alder-Reactions. Elsevier, New York 1965.

propene[28], react with cyclopentadiene to give exclusively or predominantly the *endo* adduct somewhat weakens the above working hypothesis[22].

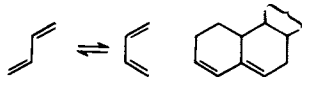
As pointed out earlier, the *endo*:*exo* ratio in the cyclopentadiene/methyl acrylate system depends on the solvent. The transition state with the higher overall dipole moment is passed preferentially in this kinetically controlled reaction. The fact that this energetically less favorable transition state occurs at all is evidence of a second orienting force, possibly the charge-transfer interaction. The combination of strongly polar reactants on the other hand, should proceed *via* a transition state with a very low overall dipole moment, as was shown by *Horner* and *Dürckheimer*[29] in the dimerization of various *o*-benzoquinones to the *endo* adduct.

It should be stressed at this point that the forces that dictate the steric course of the reaction are relatively weak. Even the preference of one isomer in the ratio 99:1, *i.e.* a practically stereospecific reaction, corresponds to a difference in activation energies of less than 3 kcal/mole for the two competing reaction mechanisms. In view of the many factors that can influence the formation of possible stereoisomers, an accurate prediction for new systems is not yet possible. The examples described above should be regarded rather as a guide.

Woodward and *Hoffmann*[29a] have recently attempted a quantitative MO treatment of the *endo* rule. They showed that *endo* addition is energetically more favorable in the reaction of dienes with dienophiles containing conjugated π systems. This treatment has not yet been applied to the *endo* addition of cyclopropene, cyclopentene, allyl bromide, or propene mentioned above.

3. Influence of Conformation on Diene Reactivity: *cisoid* and *transoid* Dienes

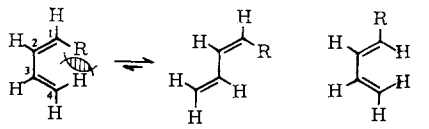
Open-chain 1,3-dienes exist in the conformational equilibrium *(26)* ⇌ *(27)*; only the *cisoid* conformer *(27)* can undergo diene addition[1,2,7]. Cycloaddition to form a six-membered ring is prevented if the conformation *(26)* is fixed, *e.g.* by incorporation into the polycyclic ring system of the steroids *(28)*. On the other hand, addition of the dienophile is



(26) *(27)* *(28)*

facilitated if the *cisoid* conformer is fixed (*e.g.* by incorporation of the diene system into a ring or by fusion of a ring on positions 2 and 3 of the diene, see Section D 2). Substituents in acyclic dienes can cause a considerable change in the rates of diene additions, not only as a result of their electronic effects, but also by displacement of the above equilibrium as a result of purely steric influences.

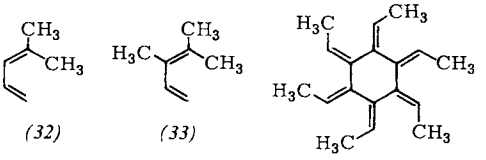
In preparative studies *cis*-1-substituted butadienes *(29)* are found to be much less reactive diene components than their *trans* isomers *(31)*. As R becomes more bulky the equilibrium *(29)* ⇌ *(30)* is displaced in favor of the *transoid* conformer *(30)*.



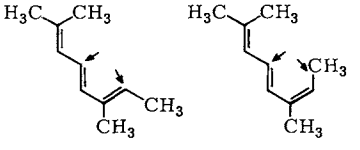
(29) *(30)* *(31)*

The reaction of *(29)*, R = CH_3, with maleic anhydride gives only a 4 % yield of the 1:1 adduct[30]; the reaction of the corresponding *trans* compound *(31)*, on the other hand, is quantitative and exothermic. The reactivities towards tetracyanoethylene differ by a factor of almost 10^5 (at 20 °C in CH_2Cl_2)[39,69]. The diene reactivity decreases further through *cis*-1-ethyl- and *cis*-1-isopropylbutadiene, and disappears completely with 1-t-butyl- and 1-phenylbutadiene[7,31]. The inability or reluctance of these *cis*-substituted dienes to add to dienophiles is explained in the literature by overlap of the spheres of influence of the substituent R on C-1 and of the hydrogen atom on C-4 of the diene chain. Coplanar arrangement, and hence Diels-Alder addition, becomes difficult or impossible, and the diene exists preferentially or completely in the *transoid* conformation *(30)*. The difference in the ease of addition of *(29)* and *(31)* can be utilized for the preparation of the pure, less reactive *cis* isomers *(29)*, R = C_6H_5[32], R = $CH{=}CH_2$[33], R = halogen[7,34].

However, the situation is not quite so clear as would appear from the above examples, as is shown by the systems *(32)* to *(36)* which, with the exception of *(35)*, contain reaction-inhibiting *cis*-1-substituents on the diene system. Compound *(32)* reacts with tetracyanoethylene at room temperature to



(32) *(33)* *(34)*



(35) *(36)*

give a mixture of the Diels-Alder adduct and the four-membered cycloaddition product[35]. Compound *(33)* reacts with maleic anhydride in boiling benzene to give a high yield of the expected 1:1 adduct[36]; the reaction of *(34)*, *e.g.* with TCNE, maleic anhydride, or *p*-benzoquinone, immediately

[28] *N. A. Belikova, V. G. Berezkin,* and *A. F. Platé*, J. gen. Chem. USSR (Engl. transl. of Ž. obšč. Chim. *32*, 2896 (1962).

[29] *L. Horner* and *W. Dürckheimer*, Chem. Ber. *95*, 1219 (1962).

[29a] *R. Hoffmann* and *R. B. Woodward*, J. Amer. chem. Soc. *87*, 4388 (1965).

[30] *E. H. Farmer* and *F. L. Warren*, J. chem. Soc. (London) *1931*, 3221; *D. Craig*, J. Amer. chem. Soc. *72*, 1678 (1950).

[31] *K. Alder* and *M. Schumacher* in *L. Zechmeister*: Fortschritte der Chemie Organischer Naturstoffe. Springer, Vienna 1953, Vol. X, p. 1.

[32] *O. Grummitt* and *F. J. Christoph*, J. Amer. chem. Soc. *73*, 3479 (1951).

[33] *J. C. H. Hwa, P. L. de Benneville,* and *H. J. Sims*, J. Amer. chem. Soc. *82*, 2537 (1960).

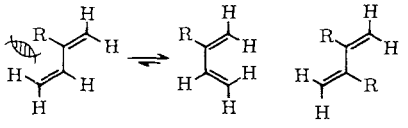
[34] *A. S. Onishchenko* and *N. J. Aronova*, Doklady Akad. Nauk SSSR *132*, 138 (1960); Chem. Abstr. *54*, 20916 (1960).

[35] *C. A. Stewart*, J. Amer. chem. Soc. *84*, 117 (1962).

[36] *N. L. Goldman*, Chem. and Ind. *1963*, 1036.

yields the diadduct [37]. The two isomeric alloocimenes *(35)* and *(36)* add on maleic anhydride in good yields in the positions indicated [38]. Kinetic measurements will probably provide more definite information on this behavior than preparative experiments, which are often difficult to compare [39].

In 2-substituted butadienes, on the other hand, bulky substituents promote the diene addition [40]. The k_2 value [*] for the addition of maleic anhydride (at 25 °C in benzene) is 50 times as great for 2-neopentylbutadiene than for butadiene.



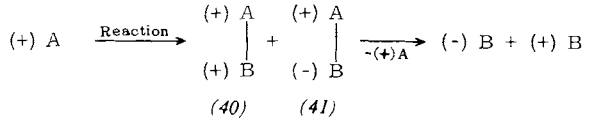
(37) *(38)* *(39)*

In contrast to the *cis*-1-substituted butadienes, a bulky group R displaces the conformational equilibrium *(37)* ⇌ *(38)* in favor of the strainless *cisoid* conformation *(38)* required for the reaction.

As expected, large substituents R in 2,3-disubstituted butadienes *(39)* prevent the molecule from assuming the planar *cisoid* conformation. 2,3-Dimethylbutadiene reacts rapidly with maleic anhydride (see Section D), whereas 2,3-dichloro- and 2,3-di-t-butylbutadiene [7,41] cannot be forced to undergo Diels-Alder additions with maleic anhydride. Surprisingly, 2,3-diiodobutadiene enters into diene additions under relatively mild conditions [42]. This is another case where a thorough kinetic investigation would be desirable in order to find an explanation for this behavior. Many apparent failures of the Diels-Alder reaction can possibly be explained by competition between the cycloaddition and a faster polymerization of the diene or by copolymerization of the diene and the dienophile.

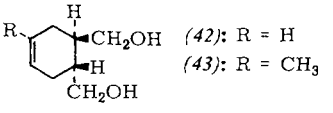
4. Partial Asymmetric Syntheses with Diels-Alder Reactions

The synthesis of asymmetric molecules, *e.g.* optically active compounds, from inactive material always leads to the racemate. If, on the other hand, the asymmetric center B is formed under the influence of an auxiliary asymmetric center [(+)A in the formula scheme] already present in the molecule, the possible diastereoisomers *(40)* and *(41)* are no longer formed in equal quantities, since the transition states leading to *(40)* and *(41)* are already diastereoisomeric in character (different energy contents), *i.e.* the rates of formation of *(40)* and *(41)* are different. If the auxiliary asymmetric center (+)A is now split off, one obtains a mixture (+)B/(−)B in which one of the two enantiomers predominates. This scheme of partial asymmetric syntheses [43] can be applied to many types of reactions; it sometimes gives an insight into the detailed reaction mechanism, and if the optical yield is sufficiently high, it may be of preparative interest, since it is then possible to avoid resolution of the racemate.

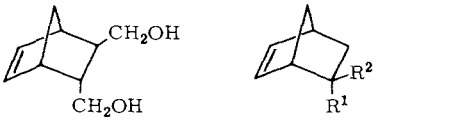


(40) *(41)*

Diels-Alder reactions were only recently studied for their suitability for partial asymmetric syntheses [44–46a,25]. The reaction of optically active menthyl fumarate with butadiene, isoprene, or cyclopentadiene followed by reduction of the 1:1 adduct with $LiAlH_4$ and removal of the auxiliary asymmetric center (−)-menthol (which corresponds to (+)A in the above scheme) gives optically active samples of the compounds *(42)–(44)* in optical yields of only 1–9 %. Under the same conditions, menthyl acrylate and cyclopentadiene give the compounds *(45)* and *(46)*, again in optical yields of 1–9 %.



(42): R = H
(43): R = CH_3



(44)

(45): R^1 = CH_2OH, R^2 = H
(46): R^1 = H, R^2 = CH_2OH

However, the optical yields can be increased to a maximum of 88 % by the addition of Lewis acids to the reaction mixture. The absolute configuration of the predominant enantiomer can be predicted from the known absolute configuration of the auxiliary asymmetric center in the cases studied [46,46a].

This offers a promising field for further investigations. The establishment of rules for the prediction of the predominant absolute configuration would seem to be a worthwhile objective; it would then be possible to produce a large number of optically active compounds of known absolute configuration, in high optical yields, by partial asymmetric syntheses using the versatile diene synthesis.

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[37] *H. Hopff* and *G. Kormany*, Helv. chim. Acta *46*, 2533 (1963).

[38] *J. E. Milks* and *J. E. Lancaster*, J. org. Chemistry *30*, 888 (1965).

[39] *C. Rücker*, unpublished.

[40] *D. Craig*, *J. J. Shipman*, and *R. B. Fowler*, J. Amer. chem. Soc. *83*, 2885 (1961).

[*] In this paper k_2 is the second-order rate constant: $-d[A]/dt = k_2[A][B]$.

[41] *H. J. Backer*, Recueil Trav. chim. Pays-Bas *58*, 643 (1939); *D. D. Coffman* and *W. H. Carothers*, J. Amer. chem. Soc. *55*, 2040 (1933); *H. Wynberg*, *A. De Groot*, and *D. W. Davies*, Tetrahedron Letters *1963*, 1083.

[42] *F. Wille*, *K. Dirr*, and *H. Kerber*, Liebigs Ann. Chem. *591*, 177 (1955).

[43] *E. L. Eliel*: Stereochemistry of Carbon Compounds. McGraw-Hill, New York 1962; *J. I. Klabunowsky*: Asymmetrische Synthese. Deutscher Verlag der Wissenschaften, Berlin 1963; *K. Mislow*: Introduction to Stereochemistry. W. A. Benjamin, New York 1965.

[44] *A. I. Korolev* and *V. I. Mur*, Doklady Akad. Nauk SSSR *59*, 251 (1948); Chem. Abstr. *42*, 6776 (1948); *A. I. Korolev*, *V. I. Mur*, and *V. G. Avaykyan*, J. gen. Chem. USSR (Engl. transl. of Ž. obšč. Chim. *34*, 713 (1964).

[45] *H. M. Walborsky*, *L. Barash*, and *T. C. Davis*, Tetrahedron *19*, 2333 (1963).

[46] *J. Kredel*, Diplom Thesis, Universität München 1965; *J. Sauer* and *J. Kredel*, Tetrahedron Letters *1966*, 6359.

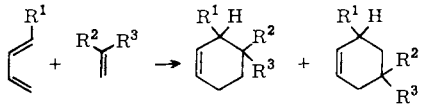
[46a] *R. F. Farmer* and *J. Hamer*, J. org. Chemistry *31*, 2418 (1966).

C. Orientation Phenomena in Reactions of Unsymmetrical Components

The relative amounts of structurally isomeric adducts formed in many reactions of unsymmetrical components cannot yet be explained on the basis of mechanism. Since comprehensive reviews exist on this subject [7,47], the present discussion can be confined to a few facts characteristic of orientation problems. The earlier view[31] that one of the possible structural isomers is often formed to the exclusion of all others had to be revised in most cases as a result of improvements in analytical methods. Since often the composition of the reaction product was not deduced from the primary Diels-Alder adducts, but from degradation products (numerous reaction steps), the accuracy of the numerical data in Tables 2 and 3 should not be overestimated. More recent investigations on the mixtures of primary adducts by analytical gas chromatography[48] cast some doubt on earlier results. However, the general trends evident in Tables 2 and 3 are probably real.

1. 1-Substituted Dienes

The discussion of *trans*-1-substituted butadienes[49] will be restricted to a reaction with acrylic acid derivatives. The electronic effect of the substituent R^1 in the diene *(47)* is reflected in the rate of diene additions (see Section D 2), but not in the orientation. The predominant product in every case is the 1,2-disubstituted cyclohexene derivative *(49)*, the 1,3-isomer *(50)* being formed only in small amounts.



(47) *(48)* *(49)* *(50)*

Table 2. Orientation in the reaction of *trans*-1-substituted dienes *(47)* with unsymmetrical dienophiles *(48)* [7,47].

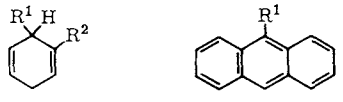
R^1	R^2	R^3	Temp. (°C)	Ratio *(49)*:*(50)*	Yield (%) of *(49)* + *(50)*
Electronic substituent effects					
$N(C_2H_5)_2$	H	$CO_2C_2H_5$	20	*cis-(49)* only	94
CH_3	H	CO_2CH_3	20	18:1	64
C_6H_5	H	CO_2CH_3	150	39:1	61
CO_2H	H	CO_2H	150	8.8:1	87
CO_2H	H	CO_2H	70–75	*cis-(49)* only	67
CO_2Na	H	CO_2Na	220	1:1	50–60
Steric effect of substituents in the diene					
CH_3	H	CO_2CH_3	200	6.8:1	85
$CH(CH_3)_2$	H	CO_2CH_3	200	5:1	60
$C(CH_3)_3$	H	CO_2CH_3	200	4.1:1	76
Steric effect of α-substituents in the dienophile					
$C(CH_3)_3$	H	CO_2CH_3	200	4.1:1	76
$C(CH_3)_3$	CH_3	CO_2CH_3	200	2.6:1	75
$C(CH_3)_3$	$CH(CH_3)_2$	CO_2CH_3	200	0.9:1	19

Since the combined yield of *(49)* and *(50)* is sometimes not much greater than 60%, these data seem rather uncertain.

The orientating forces are relatively weak, as is clearly shown by the influence of steric factors and of Coulomb repulsion. The anions of *trans*-butadiene-1-carboxylic acid and acrylic acid give equal amounts of *(49)* and *(50)*, whereas the free carboxylic acids give only *(49)*. The extent to which the difference in reaction temperature is responsible for the change in the isomer ratio was not studied in detail for the carboxylates. Branching in the substituents R^1 or R^3 also favors formation of the 1,3-disubstituted cyclohexene *(50)*.

As mentioned above the numerical values in Table 2 should be viewed with caution; the yields relate to the primary mixture of the 1:1 adducts, while the isomer ratios *(49)*:*(50)* in the examples of Sections 2 and 3 often were determined *via* degradations involving several steps. It was not rigorously established in every case whether the reactions in question were kinetically or thermodynamically controlled.

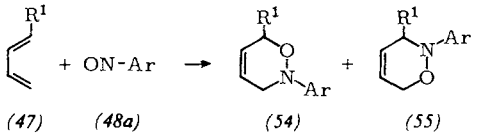
The reactions of 1-substituted dienes with dienophiles containing a carbon-carbon triple bond follow the same orientation rules as those with the double-bond analogues. Methyl propiolate and free propiolic acid react with 1-methyl- and 1-phenylbutadiene, respectively, to give the 1:1 adducts *(51)* and *(52)*, which correspond to *(49)* with one extra double bond.



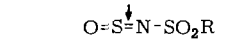
(51): $R^1 = CH_3$, $R^2 = CO_2CH_3$ (85%) *(53)*
(52): $R^1 = C_6H_5$, $R^2 = CO_2H$ (30%)

9-Substituted anthracenes *(53)* may be regarded formally as 1-substituted butadienes; however, the rules evident from Table 2 are not applicable to the diene reactions of *(53)* with unsymmetrical dienophiles. Depending on the nature of the substituent R^1 in *(53)* or in the dienophile, the reaction sometimes leads exclusively to the Diels-Alder adduct corresponding to *(49)* or to that corresponding to *(50)*, while in other cases mixtures are obtained[51,52]. It is not yet possible to give a clear mechanistic interpretation of the results.

In recent years, the orientation problems with nitroso compounds as heterodienophiles have been studied extensively by NMR methods[53,54,55]. In every case



(47) *(48a)* *(54)* *(55)*



(56)

[47] *J. A. Titov*, Russ. chem. Rev. (English transl. of Usp. Chim.) *1962*, 267.

[48] *H. E. Hennis*, J. org. Chemistry *28*, 2570 (1963).

[49] A review of the diene additions of this class of compounds was published by *I. I. Guseinov* and *G. S. Vasil'ev*, Russ. Chem. Rev. (English translation of Usp. Chim.) *1963*, 20.

[50] *J. S. Meek, B.T. Poon, R.T. Merrow*, and *S. J. Cristol*, J. Amer. chem. Soc. *74*, 2669 (1952); *E. G. Kataev* and *M. E. Mat'kova*, Uchenye Zapiski Kazan.Gos.Univ.im.V.I Ul'yanova Lenina, Chim. *115*, 21 (1955); Chem. Abstr. *52*, 1967 (1958).

[51] *J. S. Meek, D. R. Wilgus*, and *J. R. Dann*, J. Amer. chem. Soc. *82*, 2566 (1960); *J. S. Meek, P. A. Monroe*, and *C. J. Bouboulis*, J. org. Chemistry *28*, 2572 (1963); further literature cited there.

[52] *K. Alder* and *K. Heimbach*, Chem. Ber. *86*, 1312 (1953).

[53] The reactions of heterodienes and heterodienophiles are reviewed by *S. B. Needleman* and *M. C. Chang Kuo*, Chem. Reviews *62*, 405 (1962).

[54] *G. Kresze* and *J. Firl*, Tetrahedron *19*, 1329 (1963); *J. Firl*, Dissertation, Technische Hochschule München, 1965.

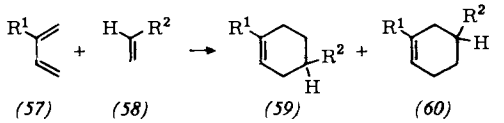
[55] *G. Kresze* and *J. Firl*, Tetrahedron Letters *1965*, 1163; *G. Kresze*, personal communication.

the reaction was found to be kinetically controlled. Compounds *(47)* and *(48a)* with $R^1 = CH_3$, $Ar = C_6H_5$ give a mixture of *(54)* and *(55)* in the ratio 58:42; on the other hand, with $R^1 = CH_3CO_2$, $(CH_3)_2N$, CH_3O_2C, $(CH_3)_3C$, or *p*-Z–C_6H_4 (Z = CH_3O, CH_3, Cl, NO_2), only the structural isomer *(54)* can be isolated. Studies are being carried out at present on the reactions with *N*-sulfinylamines *(56)* [55].

2. 2-Substituted Butadienes

Some of the results obtained with 2-substituted butadienes *(57)* are shown in Table 3. The numerical values must be regarded with the same caution as those of Table 2.

The electronic nature of the substituents in the diene *(57)* again has little effect on the isomer ratio *(59)*:*(60)*; the 1,4-disubstituted cyclohexene *(59)* always predominates. The dependence of the ratio *(59)*:*(60)* on steric factors probably is of little significance in view of the simultaneous decrease in the overall yields *(59)* + *(60)*.



(57) *(58)* *(59)* *(60)*

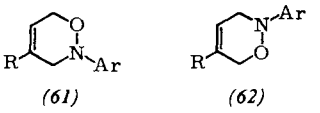
Table 3. Orientation in the reaction of 2-substituted dienes *(57)* with unsymmetrical dienophiles *(58)* [7, 47].

R^1	R^2	Temp. (°C)	Ratio *(59)*:*(60)*	Yield (%) of *(59)* + *(60)*
Electronic substituent effects				
OC_2H_5	CO_2CH_3	160	*(59)* only	50
CH_3	CO_2CH_3	20	5.4:1	54
C_6H_5	CO_2CH_3	150	4.5:1	73
Cl	CO_2CH_3	160	*(59)* only	60
CN	$COCH_3$	95	*(59)* only	86
Steric effect of substituents in the diene				
n-C_3H_7	CO_2CH_3	200	2.4:1	81
$CH(CH_3)_2$	CO_2CH_3	200	3.0:1	65
$C(CH_3)_3$	CO_2CH_3	200	3.5:1	47
Effect of temperature				
CH_3	CO_2CH_3	20	5,4:1	54
CH_3	CO_2CH_3	120	4.0:1	74
CH_3	CO_2CH_3	200	2.0:1	84
CH_3	CO_2CH_3	400	1.4:1	18
CH_3	CO_2CH_3	25–350	2.33:1 [48]	39–82

A distinct temperature effect was reported [56] for the system isoprene/methylacrylate (and also with acrylic acid and methyl methacrylate as dienophiles), the proportion of *(59)* in the mixture decreasing with rising temperature. The isomer ratio *(59)*:*(60)* was found in some cases by a series of degradation steps, and in others by gas chromatography. However, according to *Hennis* [48], who analysed the mixture of Diels-Alder adducts by capillary gas chromatography, the isomer ratio does not change in the temperature range studied (25–350 °C). This critical study casts doubt on the earlier results.

As with 1-substituted dienes, dienophiles containing triple bonds exhibit the same orientation behavior as their double-bond analogues [57].

The reaction of nitrosoaromatic compounds with 2-substituted butadienes generally leads to the adduct *(61)*, whereas the reaction of 2-arylbutadienes or 2-chlorobutadienes with α-chloronitrosocyclohexane yields a mixture of *(61)* and *(62)* or only *(62)* (with Ar = 1-Cl–C_6H_{10}) [55].



(61) *(62)*

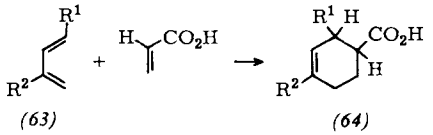
R = C_6H_5, *p*-Z–C_6H_4 (Z = CH_3O, CH_3, Cl); Ar = C_6H_5

R = C_6H_5; Ar = *p*-Z–C_6H_4 (Z = Cl, OCH_3)

R = CH_3, Cl, CF_3, CN; Ar = C_6H_5

3. Disubstituted Dienes

The problems arising in the Diels-Alder reactions of polysubstituted dienes will be illustrated with only two disubstituted dienes; for comprehensive reviews see [7, 47]. In 1,3-disubstituted dienes *(63)*, the directing effects of R^1 and R^2 are additive; the adduct contains the substituent of the dienophile in the preferred 1,2- and 1,4-arrangement in relation to R^1 and R^2, respectively [58]. It is reported that at 200 °C 1,3-dimethylbutadiene and



(63) *(64)*

$R^1 = CH_3$, $R^2 = C_6H_5$

$R^1 = C_6H_5$, $R^2 = CH_3$

methyl acrylate also give small quantities of the second possible isomer (methyl 3,5-dimethyl-3-cyclohexencarboxylate) [59].

In the case of 1,4-disubstituted butadienes *(65)*, it is possible in principle to obtain information about the relative orienting forces of various substituents from the relative yields of the isomers *(66)* and *(67)*. According to earlier work of *Alder*'s school [60], to which

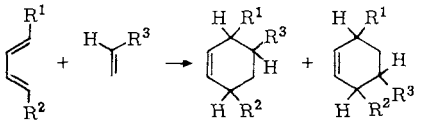
[56] *I. N. Nazarov, Y. A. Titov*, and *A. I. Kuznetsova*, Bull. Acad. Sci. USSR, Div. chem. Sci. (English transl. of Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk) *1959*, 1412; *I. N. Nazarov, A. I. Kuznetsova*, and *N. V. Kuznetsov*, Ž. obšč. Chim. *25*, 88 (1955); J. gen. Chem. USSR (English transl. of Ž. obšč. Chim.) *25*, 75 (1955); Chem. Abstr. *50*, 1623 (1956); *V. F. Kucherov, A. S. Onishchenko, B. A. Rudenko*, and *E. A. El'perina*, Doklady Akad. Nauk SSSR *158*, 397 (1964); Chem. Abstr. *62*, 7630c (1965).

[57] For example *S. Murahashi, Y. Shuto*, and *K. Kawasaki*, J. chem. Soc. Japan, Pure Chem. Sect. *78*, 327 (1957); Chem. Zbl. *1957*, 10167.

[58] *K. Alder, K. H. Decker*, and *R. Lienau*, Liebigs Ann. Chem. *570*, 214 (1950).

[59] *I. N. Nazarov, A. I. Kuznetsova, N. V. Kuznetsov*, and *Y. A. Titov*, Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1959*, 663; Chem. Abstr. *54*, 1408 (1960); *K. Alder* and *W. Vogt*, Liebigs Ann. Chem. *564*, 120 (1949).

[60] *K. Alder, M. Schumacher*, and *O. Wolff*, Liebigs Ann. Chem. *570*, 230 (1950).



(65) (66) (67)

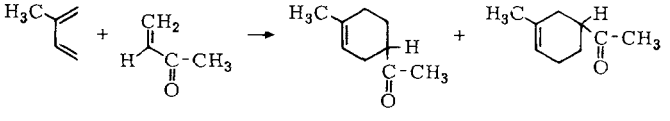
the previously mentioned reservations regarding analytical procedure apply, the orienting forces decrease in the order:

$C_6H_5 \gg CH_3 \geqslant CO_2H$.

More comprehensive and more reliable investigations with nitroso compounds as dienophiles [55] show that the direction of addition is influenced by the ability of the substituents R^1 and R^2 to attract electrons by an inductive effect.

4. Influence of Catalysts on Orientation Phenomena

As pointed out in Section B 2, Lewis acids can effect the relative yields of the stereoisomers formed in diene additions. Recently *Lutz* and *Bailey* [61] showed that they also change the relative amounts of structurally isomeric products.



Toluene, 120 °C, no catalyst	71	:	29
Toluene, 25 °C, $SnCl_4 \cdot 5\ H_2O$	93	:	7

Acrolein may also be used as the dienophile. The reaction rate increases and the product becomes more uniform, a fact that is important for preparative work. A systematic extension of these experiments would appear worthwhile; reactions at low temperatures in the presence of Lewis acids under mild conditions should lead to almost perfectly uniform Diels-Alder products.

As was shown by *Inukai* and *Kojima* [61a], the change in isomer ratio in the presence of a catalyst cannot be explained by steric factors (the catalyst is coordinately bonded to the carbonyl function in vinyl methyl ketone, and so increases the bulk of the acetyl group). Thus the overall reaction rate increases rapidly from butadiene *via* 2-methylbutadiene to the 2,3-dimethyl derivative.

D. Kinetic Studies of Diels-Alder Reactions

In addition to stereochemical aspects, rate measurements often give an insight into the mechanistic details of a reaction. The diene additions, many of which proceed quantitatively, are excellent subjects for a kinetic study. The characteristic chromophores in the diene and dienophile components disappear during the reactions, which can therefore be readily followed by spectrophotometry. Since diene additions are accompanied by a decrease in volume, dilatometry can also be used. Pioneering work on the kinetics of Diels-Alder reactions was carried out by *Wassermann* [27] and *Kistiakowsky* [62].

1. The "Alder Rule": Influence of Activating Substituents in the Dienophile

In preparative experiments *Alder* found that the reaction rate is often increased by electron-donating substituents [*e.g.* $N(CH_3)_2$, OCH_3, CH_3] in the diene and by electron-attracting substituents (*e.g.* CN, CO_2CH_3, CHO, NO) in the dienophile. This result was extended without question to all dienes and dienophiles, and appeared in the literature as the "Alder rule" [63]. That this generalization does not include every case is shown by the phenomenon of diene additions with "inverse" electron demand (see Section D 3).

Kinetic studies on the electron-rich dienes cyclopentadiene and 9,10-dimethylanthracene (Tables 4 and 5) prove the validity of the Alder rule for dienes of this type [5,64]. The difference in rates is particularly marked for the cyanoethylenes (Table 4). Table 5 contains quantitative data for a comparison of the reactivities with other activating substituents on the double bond of the dienophile.

Table 4. Kinetics of the reaction of dienophiles with cyclopentadiene and with 9,10-dimethylanthracene in dioxane at 20 °C [5,64].

Dienophile	Diene: Cyclopentadiene $10^5\ k_2$ (l mole^{-1} sec^{-1})	Diene: 9,10-Dimethylanthracene $10^6\ k_2$ (l mole^{-1} sec^{-1})
Cyano-substituted ethylenes		
Tetracyanoethylene	*ca.* 43000000	*ca.* 13000000000
Tricyanoethylene	*ca.* 480000	5900000
1,1-Dicyanoethylene	45500	127000
trans-1,2-Dicyanoethylene	81	139
cis-1,2-Dicyanoethylene	91	131
Acrylonitrile	1.04	0.89
Dienophiles with triple and double bonds		[a]
Dimethyl fumarate	74	2150
Dimethyl acetylenedicarboxylate	31	1400
Methyl acrylate	—	718
Methyl propiolate	—	113
α- and β-methylated dienophiles		
Acrylonitrile	—	1450
Methacrylonitrile	—	205
trans-Crotononitrile	—	11
Methyl acrylate	—	718
Methyl methacrylate	—	148
Methyl *trans*-crotonate	—	5.0

[a] Values refer to 130 °C.

[61] *E. F. Lutz* and *G. M. Bailey*, J. Amer. chem. Soc. *86*, 3899 (1964).

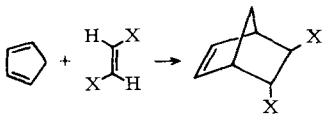
[61a] *T. Inukai* and *T. Kojima*, J. org. Chemistry *31*, 1121 (1966). See also *J. C. Soula, D. Lumbroso, M. Hellin*, and *F. Coussement*, Bull. Soc. chim. France *1966*, 2059, 2065.

[62] *G. B. Kistiakowsky* and *J. R. Lacher*, J. Amer. chem. Soc. *58*, 123 (1936); *G. B. Kistiakowsky* and *W. W. Ransom*, J. chem. Physics *7*, 725 (1939).

[63] *K. Alder*, Experientia Supplementum II, 86 (1955).

[64] *J. Sauer*, Habilitation Thesis, Universität München 1963. *J. Sauer, H. Wiest*, and *A. Mielert*, Chem. Ber. *97*, 3183 (1964).

Table 5. Kinetics of the reaction [a].



X	k_2 (relative)
COCl	*ca.* 6700
$SO_2-C_6H_5$	155
$CO-C_6H_5$	18
$CO-CH_3$	4.0
CN	1.1
CO_2CH_3	≡1.00

[a] Temperature 20 °C; solvent: dioxane.

Such dienophile activity series are of interest in the investigation of the reaction mechanism; they are also a guide to the rates of other Diels-Alder reactions. However, these activity series must not be applied indiscriminately to dienes that have not yet been investigated, since the purely electronic substituent effect is sometimes masked or even reversed by steric factors.

Important for preparative work are the higher reactivity of dienophiles containing double bonds relative to similarly substituted acetylene derivatives, the difference in the effects of methyl groups in the α or β position of acrylonitrile or methyl acrylate, and the much higher reactivity of some *trans* dienophiles relative to the *cis* isomers (Table 6) [65]. It is interesting that diethyl *cis*-azodicarboxylate reacts much more rapidly with cyclopentadiene than the *trans* form [65a]. Since all these

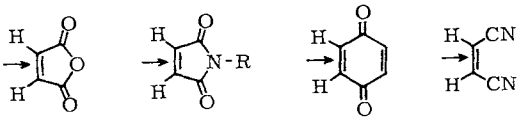
Table 6. Ratio k_{trans}/k_{cis} for the additions of *cis-trans* isomeric dienophiles in dioxane to
(a) cyclopentadiene (40 °C);
(b) 2,3-dimethylbutadiene (100 °C);
(c) 9,10-dimethylanthracene (130 °C).

Dienophile *cis-* and *trans-*	k_{trans}/k_{cis} (a)	(b)	(c)
$C_6H_5-CO-CH=CH-SO_2-C_6H_5$	282	187	—
$C_6H_5-CO-CH=CH-CO-C_6H_5$	149	740	—
$CH_3O_2C-CH=CH-CO_2CH_3$	82	—	105
$C_6H_5-SO_2-CH=CH-SO_2-C_6H_5$	44	83	—
$NC-CH=CH-CO_2CH_3$	—	—	2 00
$NC-CH=CH-CN$	1.03	1.15	1.04

phenomena can be explained substantially as for 1,3-dipolar additions (cycloadditions leading to five-membered heterocycles [1,5,66]), they will not be discussed here.

The high dienophile activity of tetracyanoethylene (TCNE) compared to other dienophiles can be seen from Table 4. However, TCNE is not the strongest dienophile.

A comparison of the k_2 values (towards cyclopentadiene at 20 °C in dioxane) in the series *(68)–(71)* shows that the double bond indicated is more strongly activated by the cyclic structural elements in the compounds *(68)* to *(70)* than by a *cis*-dinitrile arrangement in the dinitrile of maleic acid *(71)*. The replacement of one *cis*-dinitrile



(68) *(69)* *(70)* *(71)*

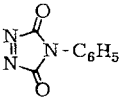
$k_2$rel. 61 43 (R=CH_3) 10 ≡1.00
77 (R=C_6H_5)

grouping in TCNE by the stronger activating groups in *(68)–(70)* should lead to very active dienophiles. This expectation is fulfilled by *p*-benzoquinone-2,3-dicarboxylic anhydride and by dicyanomaleimide, which sometimes add much more rapidly than TCNE to the dienes of Table 7 [67].

Table 7. Kinetics of the reaction of dienophiles with
(a) 2,3-dimethylbutadiene;
(b) anthracene;
(c) isoprene
at 20 °C in dichloromethane [67] (values of 10^2 k_2, in l mole^{-1}sec^{-1}).

Dienophile	(a)	(b)	(c)
p-Benzoquinonedicarboxylic anhydride	14900	8300	900
2,3-Dicyanomaleic anhydride	830	680	85
Tetracyanoethylene	240	390	7.7
2,3-Dicyano-*p*-benzoquinone	15	—	1.26

The strongest dienophile known, according to recent kinetic measurements [67], is the cyclic azo compound *(72)*, which was recently studied by *Cookson et al.* [68]. Dienophiles containing N=N double bonds, such as esters of azodicarboxylic acid, generally are more reactive than the C=C analogues [69].



(72)

2. Reactivity of Dienes towards Maleic Anhydride and Tetracyanoethylene

The "Alder rule" can be used also to estimate the rate of addition of electron-poor dienophiles with various dienes. This is illustrated in Table 8 for reactions with maleic anhydride and with TCNE. Cycloaddition is promoted by the electron-donating methyl or alkoxy group in the diene, and inhibited by the electron-attracting chlorine [1,40,69,70]. The reactions of phenylated butadienes (*trans*-1-,2-, or *trans,trans*-1,4-isomers) show different reactivity series, depending on the dienophile used (maleic anhydride, dicyanomaleimide, TCNE) [1,69] a phenomenon which cannot yet be explained.

[65] *J. Sauer, D. Lang*, and *H. Wiest*, Chem. Ber. *97*, 3208 (1964).

[65a] *G. O. Schenck, H. R. Kopp, B. Kim*, and *E. Koerner v. Gustorf*, Z. Naturforsch. *20b*, 637 (1965).

[66] *R. Huisgen*, Angew. Chem. *75*, 604, 742 (1963); Angew. Chem. internat. Edit. *2*, 565, 633 (1963).

[67] *B. Schröder*, Dissertation, Universität München 1965; *J. Sauer* and *B. Schröder*, Angew. Chem. *77*, 736 (1965); Angew. Chem. internat. Edit. *4*, 711 (1965).

[68] *R. C. Cookson, S. S. H. Gilani*, and *I. D. R. Stevens*, Tetrahedron Letters *14*, 615 (1962).

[69] *D. Lang*, Dissertation, Universität München 1963. Further kinetic data for the reaction of dienes with TCNE can be found in *C. A. Stewart*, J. org. Chemistry *28*, 3320 (1963), and [39].

[70] *J. Sauer, D. Lang*, and *A. Mielert*, Angew. Chem. *74*, 352 (1962); Angew. Chem. internat. Edit. *1*, 268 (1962).

Table 8. Kinetics of the reaction of (a) maleic anhydride and (b) tetracyanoethylene in dioxane with dienes.

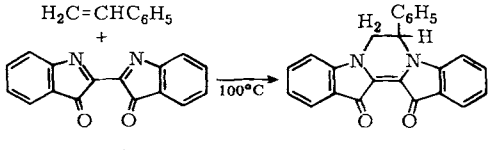
Diene	(a) $10^8\ k_2$ (at 30 °C) (l mole^{-1} sec^{-1})	(b) $10^5\ k_2$ (at 20 °C) (l mole^{-1} sec^{-1})
Cyclopentadiene	9210000	*ca.* 43000000
9,10-Dimethylanthracene	1600000	*ca.* 1300000000
1,3-Cyclohexadiene	13200	7290
Hexachlorocyclopentadiene	1.14	—
1,2-Dimethylenecyclohexane	755000	1230000
1,1'-Bicyclopentenyl	118000	1900000
1-Methoxybutadiene	84100	598000
2,3-Dimethylbutadiene	33600	24300
trans-1-Methylbutadiene	22700	2060
2-Methylbutadiene	15400	1130
Butadiene	6830	519
2-Chlorobutadiene	690	1.0

The reactivity of hexachlorocyclopentadiene is surprisingly low compared to that of cyclopentadiene itself; no Diels-Alder adduct could be obtained with TCNE even under forcing conditions[71]. However, hexachlorocyclopentadiene is often found to be a reactive diene component[1]; in fact, *Alder* classified perchlorocyclopentadiene as the "diene with the highest possible addition ability"[63]. This apparent contradiction of the rate data in Table 8 can be readily explained by the phenomenon of Diels-Alder reactions with "inverse" electron demand.

3. Diels-Alder Reactions with Inverse Electron Demand

The data in Tables 4 to 8 demonstrate the validity of the Alder rule in the reactions of electron-rich dienes and of electron-poor dienophiles: the reaction is accelerated by electron-donating substituents in the diene and by electron-attracting substituents in the dienophile. Cycloadditions with formation of six-membered rings are particularly fast when the components are very different in their electronic character, *e.g.* in the reaction of cyclopentadiene or 9,10-dimethylanthracene with TCNE.

Many reactions that can be described formally as Diels-Alder additions do not obey the Alder rule. α,β-Unsaturated carbonyl compounds and *o*-quinones combine preferentially with electron-rich dienophiles[2]; similar deviations are observed in the reactions of some substituted tetracyclones (tetraphenylcyclopentadienones)[72], thiophene 1,1-dioxides[73], hexafluorocyclopentadiene[73a], and of dehydroindigo *(73)*, which gives



(73)

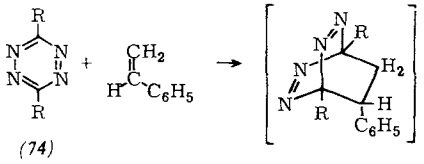
a 1:1 adduct with styrene, but not with the reactive dienophile maleic anhydride[74].

Bachmann and *Deno*[75] first proposed that the converse of the Alder rule should also hold, *i.e.* that electron *poor* dienes should react preferentially with electron-*rich* dienophiles; they termed this type of cycloaddition *Diels-Alder reactions with "inverse" electron demand*, but were unable to find a suitable model system. However, this postulated inversion of the diene activity scale was in fact observed in a kinetic study with the electron-poor hexachlorocyclopentadiene[71,76]. The data in Table 9 show this inversion in a comparison of hexachlorocyclopentadiene and the electron-rich compound 9,10-dimethylanthracene. This phenomenon becomes particularly striking in the reactions of the dienophiles cyclopentene and maleic anhydride or the *p*-substituted styrenes.

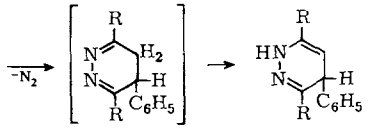
Table 9. Kinetics of the reaction of (a) hexachlorocyclopentadiene and (b) 9,10-dimethylanthracene with dienophiles in dioxane at 130 °C[71,76].

Dienophile	$10^6\ k_2$ (l mole^{-1} sec^{-1}) (a)	(b)
Cyclopentadiene	15200	—
p-Methoxystyrene	1580	50
Styrene	793	70
p-Nitrostyrene	538	602
2,3-Dihydrofuran	333	—
Norbornene	72	36
Cyclopentene	59	7.8
Maleic anhydride	29	1410000

The reactions of 1,2,4,5-tetrazines with olefins to form 1,4-dihydropyridazines *(76)*[77] are also diene additions with inverse electron demand, as has been established by kinetic measurements[78]. The addition of dienophile (formulated for styrene) to the diene system in *(74)*, R = aryl, CO_2CH_3, $CHF{-}CF_3$, *etc.*, is rate-determining; this is followed by rapid liberation of N_2 from the 1:1 adduct *(75)*, which cannot be isolated. Electron-attracting substituents R in the tetrazine *(74)* promote the reaction. The inversion of the dienophile scale in



(74) *(75)*



(76)

[71] *H. Wiest*, Dissertation, Universität München 1963.

[72] *M. G. Romanelli* and *E. I. Becker*, J. org. Chemistry *27*, 662 (1962); *E. I. Becker*, personal communication.

[73] *H. Bluestone*, *R. Bimber*, *R. Berkey*, and *Z. Mandel*, J. org. Chemistry *26*, 346 (1961); *R. M. Bimber*, US.-Pat. 3110739, Diamond Alkali Co. (12 Nov., 1963); Chem. Abstr. *60*, 2870b (1964).

[73a] *R. E. Banks*, *A. C. Harrison*, *R. N. Haszeldine*, and *K. G. Orrell*, Chem. Commun. *1965*, 41.

[74] *R. Pummerer* and *H. Fiesselmann*, Liebigs Ann. Chem. *544*, 206 (1940).

[75] *W. E. Bachmann* and *N. C. Deno*, J. Amer. chem. Soc. *71*, 3062 (1949).

[76] *J. Sauer* and *H. Wiest*, Angew. Chem. *74*, 353 (1962); Angew. Chem. internat. Edit. *1*, 269 (1962).

[77] *R. A. Carboni* and *R. V. Lindsey*, J. Amer. chem. Soc. *81*, 4342 (1959).

[78] *J. Sauer* and *D. Lang*, Angew. Chem. *76*, 603 (1964); cf. also [64,80].

this system was particularly clear with dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate *(74)*, R = CO_2CH_3 [79] (Table 10). Special mention should be made of the similar [76,80] activity of *p*-substituted styrenes in the reactions with hexachlorocyclopentadiene and dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate, as well as of the strong reaction-promoting effect of enamine groupings in the dienophile. The Diels-Alder reactions of these

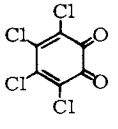
Table 10. Kinetics of the reaction of dimethyl 1,2,4,5-tetrazine-3,6-dicarboxylate with dienophiles in dioxane at 30 °C [78, 80].

Dienophile	$10^5\ k_2$ (l mole^{-1} sec^{-1})
Substituted styrenes	
α-Morpholinostyrene	*ca.* 470000
p-Methoxystyrene	25400
Styrene	6550
p-Nitrostyrene	872
α-Methylstyrene	600
trans-β-Methylstyrene	145
1,1-Diphenylethylene	*ca.* 3
Substituted ethylenes	
Ethylene	36300
Ethyl vinyl ether	21600
1-Hexene	5560
trans-4-Octene	330
Methyl acrylate	117
cis-4-Octene	48
Acrylonitrile	0.93

tetrazines with electron-rich dienophiles (enamines, enol ethers, enol esters) permit a one-step pyridazine synthesis and the preparation of diaza analogues of tropylidene and norcaradiene [81,82].

It is to be expected that other electron-poor diene systems will obey the principle of Diels-Alder reactions with inverse electron demand. For example, tetramethyl furantetracarboxylate or 6-*p*-nitrophenyl-1',2',3',4'-tetrachlorofulvene do not react with electron-poor dienophiles (*e.g.* maleic anhydride, esters of acetylenedicarboxylic acid) [83,84]; on the other hand, it cannot yet be decided from preparative studies whether tetrachlorofuran [85] and perchloro-α-pyrone [86] obey the Alder rule.

Kinetic studies by *Horner* and *Geyer* showed inversion of the dienophile activity for the carbocyclic diene system in perchloro-*o*-benzoquinone *(76a)*. The *p*-substituted styrenes approximately obey a Hammett relationship with a negative

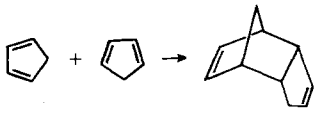

(76a)

ρ value ($k_{p\text{-}CH_3O\text{-styrene}}$: $k_{p\text{-}NO_2\text{-styrene}} \approx 40{:}1$ at 20 °C) [86a]. In the reaction of styrene with substituted *o*-benzoquinones, there is a linear relationship between the redox potentials of the latter and the logarithms of the rate constants for the Diels-Alder addition.

Kinetic data, solvent effects, and activation parameters show that the additions of hexachloropentadiene and of the 1,2,4,5-tetrazines are mechanistically of the same reaction type as the reactions in Tables 4 to 6.

4. Solvent Effects and Activation Parameters

The rate of diene additions is only slightly affected by a change of solvent. The dimerization of cyclopentadiene to dicyclopentadiene is only about three times as fast in nitrobenzene or ethanol as in benzene; this Diels-Alder reaction has a comparable rate in the gas phase [87].


(77)

This low solvent dependence is a general kinetic characteristic of cycloadditions leading to six-membered rings [88]; k_2 rarely increases by a factor of more than 10 on change to a solvent of higher solvating power, as can also be seen from Table 11 [64]. The solvent effect is of the same order of magnitude even for a combination

Table 11. Influence of the solvent on the rate of addition of fumaronitrile to 9,10-dimethylanthracene [64].

Solvent	$10^3\ k_2$ (l mole^{-1} sec^{-1})	Solvent	$10^3\ k_2$ (l mole^{-1} sec^{-1})
$HCBr_3$	*ca.* 21	CH_3—CN	9.0
$HCCl_3$	22	C_5H_5N	7.9
CH_3CO_2H	20	Dioxane	6.5
CH_3OH	*ca.* 19	CH_3—SO—CH_3	6.5
C_2H_5OH	16	$HCON(CH_3)_2$	4.2
CCl_4	15	$N(C_2H_5)_3$	*ca.* 4
CH_2Cl_2	14	CH_3—CO—CH_3	3.9
Cl—CH_2—CH_2—Cl	14	CH_3O-CH_2-CH_2-OCH_3	2.8
CH_3—NO_2	12		

of more strongly polar components (*e.g.* 9-methylanthracene + 1,1-dicyanoethylene) [64]. Diene additions with inverse substituent effects (see Section D 3) behave analogously (Table 12) [69].

Table 12. Influence of the solvent on the Diels-Alder reactions of styrene with (a) hexachlorocyclopentadiene (85 °C) and (b) 3,6-diphenyl-1,2,4,5-tetrazine (90 °C).

Solvent	(a) $10^5\ k_2$ (l mole^{-1} sec^{-1})	(b) $10^4\ k_2$ (l mole^{-1} sec^{-1})
$HCON(CH_3)_2$	11.1	10.6
C_6H_5—NO_2	10.2	10.6
C_6H_5—$CO_2C_2H_5$	9.5	7.8
Dioxane	6.8	4.9
C_6H_5—CH_3	6.6	4.4

[79] *M. Avram, I. G. Dinulescu, E. Marica,* and *C. D. Nenitzescu,* Chem. Ber. *95,* 2248 (1962).

[80] *J. Sauer* and *A. Mielert,* unpublished results.

[81] *J. Sauer, A. Mielert, D. Lang,* and *D. Peter,* Chem. Ber. *98,* 1435 (1965).

[82] *J. Sauer* and *G. Heinrichs,* Tetrahedron Letters *1966,* 4979.

[83] *E. C. Winslow, J. E. Masterson,* and *D. A. Campell,* J. org. Chemistry *23,* 1383 (1958).

[84] *J. S. Meek* and *P. Argabright,* J. org. Chemistry *22,* 1708 (1957).

[85] *H. Krzikalla* and *H. Linge,* Chem. Ber. *96,* 1751 (1963).

[86] *G. Märkl,* Chem. Ber. *96,* 1441 (1963).

[86a] *L. Horner,* personal communication.

[87] *H. Kaufmann* and *A. Wassermann,* J. chem. Soc. (London) *1939,* 870.

[88] For example, *A. Wassermann,* Trans. Faraday Soc. *34,* 182 (1938); *R. A. Fairclough* and *C. N. Hinshelwood,* J. chem. Soc. (London) *1938,* 236; *Y. Yukawa* and *A. Isohisa,* Mem. Inst. sci. ind. Res., Osaka Univ. *10,* 191 (1953); Chem. Abstr. *48,* 7598 (1954); *L. J. Andrews* and *R. M. Keefer,* J. Amer. chem. Soc. *77,* 6284 (1955). The effect of the solvent on the reaction of tetracyanoethylene with anthracene and bicyclo[2.2.1]hepta-2,5-diene was studied by *P. Brown* and *R. C. Cookson,* Tetrahedron *21,* 1977 (1965).

The small solvent effect on the rate of addition in Diels-Alder reactions and the fact that a number of cycloadditions leading to six-membered rings proceed at comparable rates in the gas phase and in solution may be taken as an indication that the rate-determining transition state is only slightly more polar than the ground state, or that in many cases it requires no stabilization by the solvent.

Important evidence for the establishment of a reaction mechanism is often provided by the activation parameters, *i.e.* the activation enthalpy $\Delta H^{\neq}$ and the activation entropy $\Delta S^{\neq}$; these values can be readily determined from experimental data by means of the Eyring equation. In practically every case examined it was found that, like the mechanistically related 1,3-dipolar additions[66], the Diels-Alder reactions require only a relatively small enthalpy of activation ($\Delta H^{\neq} < 25$ kcal/mole). The strongly negative entropies of activation, $\Delta S^{\neq}$, are remarkably constant; an average value of about −35 e.u. points to a highly ordered rate-determining transition state[1,5,27,64,88a]. There is no difference in the activation parameters of Diels-Alder reactions that obey the Alder rule and those with inverse electron demand. It should already be mentioned here that the strongly negative values of $\Delta S^{\neq}$ must be regarded as important evidence of synchronous bond formation.

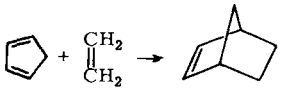
5. Acceleration of Diels-Alder Reactions by Catalysts and by Pressure

Many diene additions are reasonably fast at room temperature or on gentle heating. With less reactive systems, however, it would be interesting to accelerate the reaction with catalysts. Until recently it was thought that diene additions could be influenced only slightly by catalysts[89,90]. The dimerization of cyclopentadiene and the additions of *p*-benzoquinone[89] and fumarodinitrile[71] to dienes are only slightly accelerated by α-halogenated acetic acids.

Yates and *Eaton*[91] were the first to recognize that diene additions proceed much more rapidly in the presence of $AlCl_3$. It was subsequently found that these reactions are also catalysed by other Lewis acids (BF_3, $SnCl_4$, $TiCl_4$)[92]. As pointed out in Section B 2, the acceleration is considerable, and often the reaction temperature can be lowered by more than 100 °C with no decrease in rate.

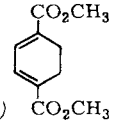
The catalytic action probably is due to complex formation between the Lewis acid and the polar groups of the activating substituents in the dienophile (*e.g.* in maleic anhydride, ethyl maleate and fumarate, and esters of acrylic acid) or in the diene (reaction of tetraphenylcyclopentadienone with ethylene). The complex formation has been confirmed by IR spectra[25,64]. In all the cases studied, *cis-trans* isomeric dienophiles give diastereoisomeric adducts in the presence of Lewis acids just as in the uncatalysed reaction, *i.e.* the catalysed reactions also are pure *cis* additions[65,91]. There is therefore no reason to believe that the catalysis by Lewis acids involves any change in mechanism of the Diels-Alder reaction; an ionic two-step mechanism is occasionally discussed[61a].

Schrauzer and *Glockner*[93] found that homo-Diels-Alder additions[2] are catalysed by Ni(0) complexes. It is not yet known whether the acceleration of the reaction of ethylene with cyclopentadiene (at 144 °C; catalyst: $CuCl/NH_4Cl$/activated charcoal) is due to formation of



a metal complex[94]. Rhodium on activated charcoal converts norbornadiene (bicyclo[2.2.1]hepta-2,5-diene) into a mixture of dimers and trimers, whose structures correspond to a cycloaddition with formation of a four-membered ring and to a homo-Diels-Alder reaction, respectively[94a]. No catalysis by Lewis acids has been observed in systems with no polar groups, *i.e.* with purely olefinic components. It may be possible in such cases to accelerate the diene additions by the addition of metal complexes[95].

The yield of Diels-Alder reactions is increased by an increase in pressure (*e.g.*[96–98]). This effect is particularly important for gaseous reactants; for example, ethylene adds smoothly to *(78)* at 165 °C/1000 atm[98]



(78)

The reaction of naphthalene with maleic anhydride at 10000 atm gives the 1:1 adduct in 78 % yield, whereas at 1 atm and under otherwise identical conditions the yield is only 1 %[97].

[88a] An exception in the system diphenylisobenzofuran + acrylonitrile has been reported by *M. Gillois* and *P. Rumpf*, Bull. Soc. chim. France *1959*, 1823. The values of log *A* in the Arrhenius equation vary with the solvent between 2.2 and 14.5; no product analysis was carried out.

[89] *A. Wassermann*, J. chem. Soc. (London) *1942*, 618; *W. Rubin*, *H. Steiner*, and *A. Wassermann*, *ibid. 1949*, 3046.

[90] *Y. Yukawa* and *A. Isohisa*, Mem. Inst. sci. ind. Res., Osaka Univ. *10*, 191 (1953); Chem. Abstr. *48*, 7598 (1954).

[91] *P. Yates* and *P. Eaton*, J. Amer. chem. Soc. *82*, 4436 (1960).

[92] For example, *G. I. Fray* and *R. Robinson*, J. Amer. chem. Soc. *83*, 249 (1961); US.-Pat. 3067244; Chem. Abstr. *58*, 13816h (1963); *H. Jahn* and *P. Goetzky*, Z. Chem. *2*, 311 (1962); Chem. Abstr. *58*, 5526g (1963); *C. F. H. Allen*, *R. W. Ryan*, and *J. A. van Allan*, J. org. Chemistry *27*, 778 (1962); *I. A. Favorskaya* and *E. M. Auvinen*, Žh. obšč. Chim. *33*, 2795 (1963); Chem. Abstr. *59*, 15191 (1963); *T. Inukai* and *M. Kasai*, J. org. Chemistry *30*, 3567 (1965).

[93] *G. N. Schrauzer* and *P. Glockner*, Chem. Ber. *97*, 2451 (1964).

[94] *T. Bota*, *C. Bucur*, *J. Drimus*, *L. Stanescu*, and *D. Sandulescu*, Rev. Chim. (Bukarest) *12*, 503 (1961); Chem. Abstr. *56*, 5848g (1962).

[94a] *J. J. Mrowca* and *T. J. Katz*, J. Amer. chem. Soc. *88*, 4012 (1966).

[95] See, for example, *R. L. Pruett* and *W. R. Myers*, Brit. Pat. 923462 (10 April ,1963); Chem. Abstr. *59*, 11291b (1963).

[96] *B. Raistrick*, *R. H. Sapiro*, and *D. M. Newitt*, J. chem. Soc. (London) *1939*, 1761, 1770.

[97] *W. H. Jones*, *D. Mangold*, and *H. Plieninger*, Tetrahedron *18*, 267 (1962).

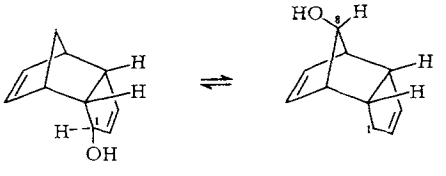
[98] *J. C. Kauer*, *R. E. Benson*, and *G. W. Parshall*, J. org. Chemistry *30*, 1431 (1965).

E. On the Mechanism of Diels-Alder Reactions

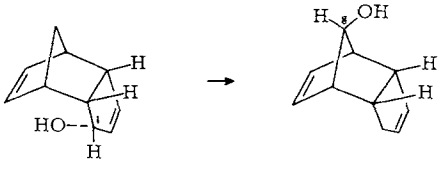
The possible mechanisms for diene additions were described in Section A. Numerous recent publications testify to the interest shown in a final elucidation of the course of this cycloaddition [99].

1. Rearrangements of Diels-Alder Adducts

A stereoselective intramolecular rearrangement takes place when α-(1-hydroxy)dicyclopentadiene *(79)* is heated; at 140 °C, *(79)* exists in equilibrium with about 50 % of the 8-*syn* isomer *(80)* [100]. Similarly, the epimeric β-alcohol *(81)* is converted into the 8-*trans* form *(82)*. Using optically active compounds, *Woodward* and *Katz* [100] showed that this reaction does not

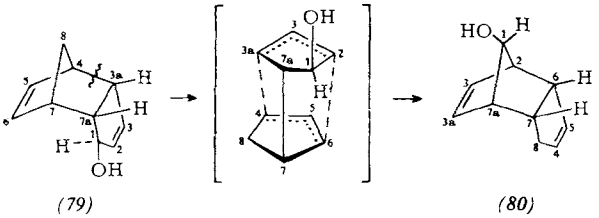


(79) *(80)*



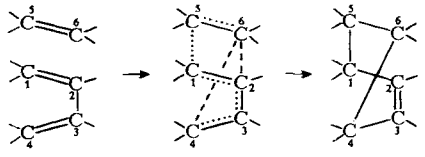
(81) *(82)*

involve dissociation into the fragments cyclopentadiene and cyclopentadienol, but is intramolecular. The results could be explained by the assumption that only the bond between C-3a and C-4 is broken. Decomposition into cyclopentadiene and its 1-hydroxy derivative, *i.e.* breakage of the second bond, (C-7)–(C-7a), in the Diels-Alder adduct, occurs only above 140 °C.



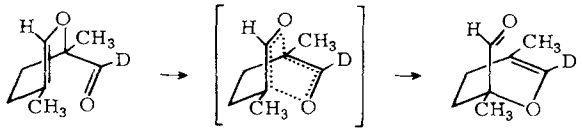
(79) *(80)*

On the basis of the principle of microscopic reversibility, the authors assumed that Diels-Alder reactions in general must proceed by a two-stage mechanism, in which the bonds between the components are formed in succession. The diene and the dienophile are first oriented in parallel planes; in the rate-determining step, only one bond, *i.e.* that between C-1 and C-5, is formed; "secondary attractive forces (attractive electrostatic, electrodynamic, and even to some extent exchange forces)" between the centers C-6, C-4, and C-2, which are not directly involved in the primary bond formation, are assumed to be responsible for the observed stereospecific *cis* addition by preventing rotation about C-C single bonds.



(83)

Several authors have questioned this mechanistic generalization [101,102]. There is as yet no conclusive experimental evidence that the Woodward-Katz rearrangement is not a special case of the Cope rearrangement, in which no intermediate has so far been detected [103]. The Woodward-Katz rearrangement appears to be confined to adducts in which both components possess diene character, and so is not of general validity [104]. The stereospecific rearrangement of the deuterated methacrolein dimer *(84)* fits into this scheme [105].



(84)

On the other hand, the rearrangements *(85)* ⇌ *(86)* [102], *(87)*→*(88)* [106], *(89)* ⇌ *(90)* [107], and *(77)* ⇌ *(77a)* [107a] definitely proceed by a retro-Diels-Alder reaction, *i.e.* the two bonds between the components are broken in the course of the rearrangement (see also [108]).

The Woodward-Katz scheme (two-stage mechanism) has another consequence, which is amenable to experimental test. In *(83)*, "secondary attractive forces" operate from C-6 to C-2 and C-4; it might be expected that cycloadditions leading to four-membered rings and

[99] Numerous references are also given by *B. Capon* and *C. W. Rees*, Annual Rep. Progr. Chem. (Chem. Soc., London) *61*, 266 (1964); *60*, 269 (1963); *59*, 227 (1962). *B. Capon, M. J. Perkins*, and *C. W. Rees* in Organic Reaction Mechanisms – 1965. Interscience, New York 1966, p. 123.

[100] *R. B. Woodward* and *T. J. Katz*, Tetrahedron *5*, 70 (1959); Tetrahedron Letters *5*, 19 (1959).

[101] *M. J. S. Dewar*, Tetrahedron Letters *4*, 16 (1959).

[102] *J. A. Berson* and *A. Remanick*, J. Amer. chem. Soc. *83*, 4947 (1961).

[103] *E. Vogel*, Angew. Chem. *74*, 829 (1962); *W. v. E. Doering* and *W. R. Roth*, Angew. Chem. *75*, 27 (1963); Angew. Chem. internat. Edit. *2*, 115 (1963). On the Oxy-Cope rearrangement, see *J. A. Berson* and *M. Jones*, J. Amer. chem. Soc. *86*, 5017 (1964).

[104] Further examples were contributed by *R. C. Cookson, J. Hudec*, and *R. O. Williams*, Tetrahedron Letters *22*, 29 (1960); *P. Yates* and *P. Eaton*, Tetrahedron *12*, 13 (1961); *E. Vogel* and *E. G. Wyes*, Angew. Chem. *74*, 489 (1962); Angew. Chem. internat. Edit. *1*, 404 (1962); *M. Livar, P. Klucho*, and *M. Paldan*, Tetrahedron Letters *1963*, 141; *J. E. Baldwin, ibid. 1964*, 2029.

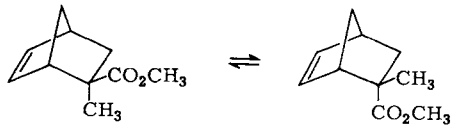
[105] *R. P. Lutz* and *J. D. Roberts*, J. Amer. chem. Soc. *83*, 2198 (1961).

[106] *C. Ganter, U. Scheidegger*, and *J. D. Roberts*, J. Amer. chem. Soc. *87*, 2771 (1965).

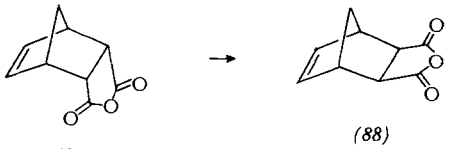
[107] *J. A. Berson* and *W. A. Mueller*, J. Amer. chem. Soc. *83*, 4940 (1961).

[107a] *J. E. Baldwin*, J. org. Chemistry *31*, 2441 (1966).

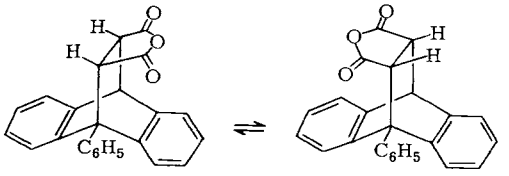
[108] *K. Alder* and *H. J. Ache*, Chem. Ber. *95*, 511 (1962).



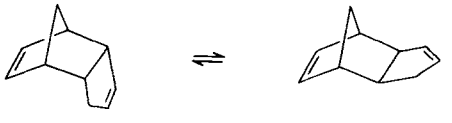
(85) (86)



(87) (88)

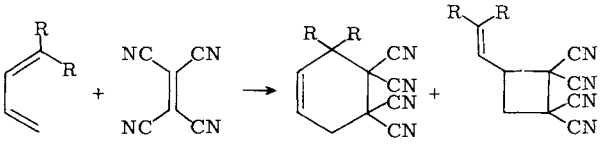


(89) (90)



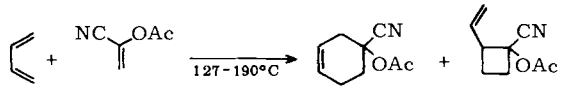
(77) (77a)

those leading to six-membered rings would involve the same intermediate. According to *Stewart*[35], 1,1-dimethylbutadiene reacts with TCNE to give both the cyclohexene derivative *(91a)* and the cyclobutane derivative *(92a)*. The use of a different solvent leads to



(91) a: R = CH_3 (92)
b: R = C_6H_5

a marked change in rate only for the cycloaddition leading to *(92)*. Thus *(91a)* and *(92a)* cannot be formed *via* the same intermediate[35]. 1,1-Diphenylbutadiene gives mainly *(92b)* together with a little *(91b)*; when heated in solution, however, *(92b)* rearranges to the thermodynamically more stable *(91b)*[108a]. On the other hand, the product ratio *(93)*:*(94)* obtained from butadiene and 1-cyanovinyl acetate (α-acetoxyacrylonitrile) is relatively insensitive to changes of solvent (cyclohexane, toluene, acetonitrile, nitromethane) and temperature[109]; *Little* prefers to interpret his results



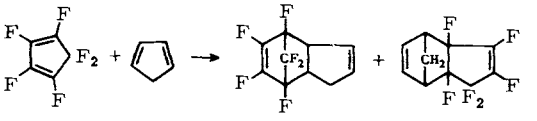
(93) (94)

[108a] *J. J. Eisch* and *G. R. Husk*, J. org. Chemistry *31*, 589 (1966).

[109] *J. C. Little*, J. Amer. chem. Soc. *87*, 4020 (1965).

by a two-step mechanism and rejects the alternative explanation that the competing cycloadditions leading to the fourmembered ring and to the six-membered ring have comparable activation enthalpies and similar polar transition states.

The reaction of equimolar amounts of hexafluorocyclopentadiene with cyclopentadiene always yields a mixture of the adducts *(94a)* and *(94b)* in the constant yield ratio of 16:84, irrespective of the temperature (20–120 °C) or of the solvent (n-hexane, nitrobenzene)[109a]. Neither *(94a)* nor *(94b)* rearranges to the other under these conditions. The best interpretation in



(94a) (94b)

this case appears to be formation of *(94a)* and *(94b)* *via* a common intermediate, *i.e.* that the reaction proceeds by a two-step mechanism, probably by way of a biradical intermediate.

2. Kinetic Isotope Effects

Primary and secondary kinetic isotope effects have been used as mechanistic criteria in many reactions[110,110a]. A number of recent investigations using this method provide information about the hybridization of the transition states of Diels-Alder additions and of the redissociation of diene adducts[111–114] (Table 13). Since the addition step involves the conversion of sp^2

Table 13. Secondary isotope effects in Diels-Alder additions (at 25 °C).

System	k_D/k_H per D atom	Ref.
With deuterated dienes		
[9,10-D_2]Anthracene + maleic anhydride	1.06	[111]
[9,10-D_2]Anthracene + tetracyanoethylene	1.06	[114]
[1,1,4,4-D_4]Butadiene + maleic anhydride	1.07	[111]
With deuterated dienophiles		
[D_2]Maleic anhydride + butadiene	1.01	[111]
[D_2]Maleic anhydride + cyclopentadiene	1.03	[111]
[D_2]Maleic anhydride + anthracene	1.05	[111]

[109a] *R. E. Banks*, *A. C. Harrison*, and *R. N. Haszeldine*, Chem. Commun. *1966*, 338.

[110] Reviews are to be found in *K. B. Wiberg*, Chem. Reviews *55*, 713 (1955); *F. H. Westheimer*, *ibid. 61*, 265 (1961); *L. Melander*: Isotope Effects on Reaction Rates. Ronald Press, New York 1960; *W. H. Saunders* in *A. Weissberger*: Technique of Organic Chemistry. 2nd Edition, Interscience, New York 1961. Vol. 8, Part 1, p. 389.

[110a] *E. A. Halevi* in *S. G. Cohen*, *A. Streitwieser*, and *R. W. Taft*: Progress in Physical Organic Chemistry. Interscience, New York 1963, Vol. I, p. 109.

[111] *D. E. Van Sickle* and *J. O. Rodin*, J. Amer. chem. Soc. *86* 3091 (1964).

[112] *S. Seltzer*, J. Amer. chem. Soc. *87*, 1534 (1965).

[113] *M. J. Goldstein* and *G. L. Thayer*, J. Amer. chem. Soc. *87*, 1925, 1933 (1965).

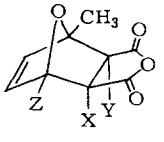
[114] *P. Brown* and *R. C. Cookson*, Tetrahedron *21*, 1977, 1993 (1965).

into sp^3 centers, it is found, in agreement with theoretical considerations[115,110a], that $k_D:k_H > 1$, *i.e.* that there is an inverse secondary isotope effect.

The low magnitudes of the inverse secondary isotope effects are taken as evidence that the hybridization of the reaction centers in the transition state has changed only very slightly. Thus the rate-determining energy threshold occurs very early on the reaction coordinate, so that the transition state is structurally similar to the original diene and dienophile. According to the authors, the magnitude of the secondary isotope effect agrees with a multicenter mechanism, *i.e.* with synchronous bond formation. Results on the systems [9-D]anthracene + acrylonitrile, 1,1-dicyanoethylene, tricyanoethylene, and chlorotricyanoethylene[114] can be explained by the assumption that, with highly unsymmetrical dienophiles, bond formation at the four centers probably begins simultaneously, but has proceeded to different extents in the transition state (see the similar discussion for 1,3-dipolar additions[11]); with acrylonitrile and 1,1-dicyanoethylene, it should be most advanced at the electrophilic end of the double bond in the dienophile.

It should be mentioned that unlike the primary isotope effect the small magnitude of the secondary isotope effect makes high experimental accuracy essential. The numerical values cannot yet be fully explained. Thus it is difficult to understand why the hybridization changes in the diene (larger isotope effect) should be more marked in the transition state than those in the dienophile. It is also surprising that the secondary isotope effect is independent of the reactivity of the dienophile used. The dienophile activities differ by many orders of magnitude between TCNE and maleic anhydride and between acrylonitrile and 1,1-dicyanoethylene; the inverse secondary isotope effects observed are equal within the limits of error.

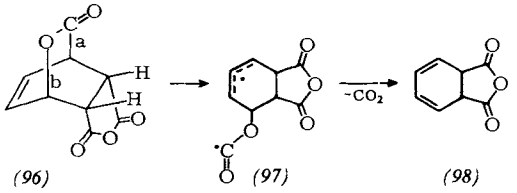
Many Diels-Alder additions can be reversed even under mild conditions. The cleavage of a number of adducts has been studied with the aid of labeled compounds[112,113]. The 2-methylfuran/maleic anhydride adduct *(95a)* in the form of its partially deuterated derivatives is particularly suitable for such investigations. According to *Seltzer*[112], the secondary isotope effects observed indicate synchronous breakage of the bonds in the cleavage step; on the basis of the principle of microscopic reversibility, the author postulates a one-step multicenter mechanism for the addition.



(95a): X = Y = Z = H
(95b): X = Y = D; Z = H
(95c): X = Y = H; Z = D
(95d): X = D; Y = Z = H
(95e): X = Z = H; Y = D

$k_{(95a)}: k_{(95b)} = 1.16$
$k_{(95a)}: k_{(95c)} = 1.08$
$k_{(95d)}: k_{(95e)} = 1.00$

In contrast, *Goldstein* and *Thayer*[113] conclude from the primary carbon and oxygen isotope effects ($k_{12C}/k_{13C} = 1.030$; $k_{16O}/k_{18C} = 1.014$) that the elimination of CO_2 from the α-pyrone/maleic anhydride adduct *(96)* proceeds in two steps, the first involving the breakage of the bond *a* to the carbonyl carbon, while the C–O bond *b* is still practically unaffected. These



(96) *(97)* *(98)*

authors assume that the addition of CO_2 as a dienophile to *(98)* (which has not yet been achieved experimentally) would proceed by a two-step mechanism involving the intermediate *(97)*. It would seem premature, however, to assume from this one result that *all* Diels-Alder additions are two-step reactions.

3. One-Step or Two-Step Reaction?

The data discussed in Sections B to E can at present be most easily explained by a multicenter mechanism, the two new σ bonds (Section A) between the diene and the dienophile being formed simultaneously. However, the formation of these σ bonds will not have reached exactly the same extent at the peak of the activation barrier, except in the extreme case. In general, though the bonds begin to form at the same time, they will not both be equally pronounced in the transition state. If the bond formation is rather faster at one center than at the other, the dienophile will necessarily assume a partial positive or negative charge (or a partial free-radical character). These partial charges will be small, and will depend on the nature of the reacting components.

The practically universal stereospecific *cis* addition is a necessary result of synchronous bond formation between the reactants; the experimental results would agree with a two-step mechanism only on the basis of the additional hypothesis, mentioned in Section A, that rotation about C–C single bonds in the intermediate is impossible, *i.e.* that ring closure to form the adduct is very fast. No biradical intermediates[10], such as occur in cycloadditions leading to four-membered rings, have been detected[11].

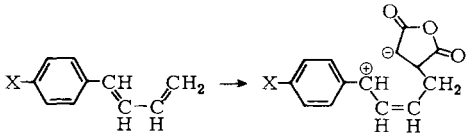
No satisfactory explanation can be given for the orientation phenomena (Section C)[116]. The relative yields of the structural isomers are largely independent of the electronic nature of the substituents in the dienes; this rules out the possibility of a zwitterion intermediate, but could be compatible with a biradical intermediate.

The kinetic results discussed in Section D also indicate a synchronous mechanism. The effects of substituents in the diene and in the dienophile on the rate of the reaction are very large in absolute terms, but are much too small for a rate-determining transition state that corresponds closely to a zwitterion intermediate. Thus

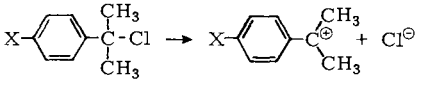
[115] *A. Streitwieser, R. H. Jagow, R. C. Fahey,* and *S. Suzuki,* J. Amer. chem. Soc. *80*, 2326 (1958).

[116] Cf. also *A. Streitwieser*: Molecular Orbital Theory for Organic Chemists. Wiley, New York 1961, p. 432.

when CH_3O is replaced by NO_2 in the reaction of *p*-substituted 1-phenylbutadienes *(99)* with maleic anhydride, the k_2 value decreases by only a factor of 10[117]; on the other hand, the rate of solvolysis of *p*-substituted α,α-dimethylbenzyl chlorides *(101)* to give the ion pair decreases to 7×10^{-9} of the original value when the *p*-NO_2 compound is used instead of the *p*-CH_3O compound[118]. Thus it is unlikely that the



(99) *(100)*



(101) *(102)*

reaction proceeds *via* a zwitterion intermediate *(100)* similar in structure to the carbonium ion in *(102)*. The partial charges are small in other diene additions also, as shown by the fact that the ρ values are always low[119]. The k_2 values for diene additions of arylated dienes or dienophiles can be better interpreted by a σ^+ relationship as described by *H. C. Brown*[118]. In reactions of tetraphenylcyclopentadienone with esters of substituted phenylpropiolic acid the effect of substituents in the nucleus can be better described by σ^- values ($\rho \approx 0.3$)[119a].

The small positive solvent effect on the reaction rate and the fact that diene additions also proceed at comparable rates in the gas phase show that the transition states in all the cases studied are only slightly more polar than the ground states, and often (in gas reactions) do not require solvation, and are therefore essentially nonpolar. These facts also oppose a zwitterionic two-step mechanism.

The synchronous mechanism imposes high steric demands on the rate-determining step, since four centers must come together in a favorable arrangement in order that a collision may be successful. The highly negative activation entropies characteristic for such multicenter mechanisms are found in nearly all the systems studied. The fact that the values of $\Delta S^{\neq}$ are relatively constant, irrespective of the absolute rate of the Diels-Alder reaction, points to a common mechanism, *i.e.* synchronous bond formation, in all the systems studied. Diene additions with inverse electron demand are no exception.

Recent attempts to obtain more detailed insight into the mechanism of cycloadditions and mechanistically related valence isomerizations with the aid of MO calculations and symmetry considerations appear promising [120–122]. A multicenter mechanism is possible for the thermal 4 + 2 cycloadditions, but impossible for the photochemical reactions; photochemical Diels-Alder reactions probably proceed by a two-step mechanism. As pointed out in Section B 2, a quantitative description of *Alder*'s *endo* rule could be possible on the basis of MO considerations. Earlier calculations[123], which were based on the assumption of synchronous bond formation between the diene and the dienophile, had already led to correct predictions of the reactive positions in polycycles and of the relative reactivities of various dienes; however, steric factors, which play a considerable part in Diels-Alder reactions in general, were not taken into account.

The pressure-dependence of the rate of a reaction permits the determination of the activation volume $\Delta V^{\neq}$, *i.e.* the volume difference between the reactants and the transition state. The fact that $\Delta V^{\neq}$ for the dimerization of isoprene is equal to half of the total volume decrease led *Walling* and *Peisach*[124] to assume a two-step mechanism for this reaction involving a biradical intermediate. A similar relationship was found for the reaction of butyl acrylate with 2,3-dimethylbutadiene, but not for the dimerization of cyclopentadiene[125]. It was concluded from the $\Delta V^{\neq}$ values that the Woodward-Katz rearrangement and retro-Diels-Alder reactions have the same energy profile, and have a different mechanism from Cope rearrangements[126]. Experimental difficulties and the theoretical interpretation of these experiments[127,128] are still under discussion.

A biradical triplet intermediate has been fairly definitely ruled out. Compounds that catalyse singlet-triplet transitions have no effect on Diels-Alder reactions[102]. The entropies of activation for the cleavage of the adducts are "normal", so that a change in multiplicity can be excluded; consequently, from the principle of microscopic reversibility, such a change can also be ruled out for the addition step. The fact that photochemically induced (photosensitized) diene additions that definitely pass through a triplet state give more

[117] *E. J. De Witt, C. T. Lester,* and *G. A. Ropp,* J. Amer. chem. Soc. *78,* 2101 (1956).

[118] *H. C. Brown* and *Y. Okamoto,* J. Amer. chem. Soc. *79,* 1913 (1957); *Y. Okamoto* and *H. C. Brown,* J. org. Chemistry *22,* 485 (1957).

[119] For example *I. Benghiat* and *E. I. Becker,* J. org. Chemistry *23,* 885 (1958); *G. Kresze, J. Firl, H. Zimmer,* and *U. Wollnick,* Tetrahedron *20,* 1605 (1964); *J. Hamer, M. Ahmad,* and *R. E. Holiday,* J. org. Chemistry *28,* 3034 (1963); *M. Ahmad* and *J. Hamer, ibid. 31,* 2829, 2831 (1966). For a critical discussion of the Hammett equation applied to Diels-Alder reactions see *M. Charton,* J. org. Chemistry *31,* 3745 (1966).

[119a] *D. N. Matthews* and *E. J. Becker,* J. org. Chemistry *31,* 1135 (1966).

[120] *K. Fukui,* Tetrahedron Letters *1965,* 2009; further literature cited there.

[121] *R. B. Woodward* and *R. Hoffmann,* J. Amer. chem. Soc. *87,* 395, 4388 (1965).

[122] *H. C. Longuet-Higgins* and *E. W. Abrahamson,* J. Amer. chem. Soc. *87,* 2045 (1965).

[123] *R. D. Brown,* J. chem. Soc. (London) *1950,* 691, 2730; *1951,* 1612.

[124] *C. Walling* and *J. Peisach,* J. Amer. chem. Soc. *80,* 5819 (1958).

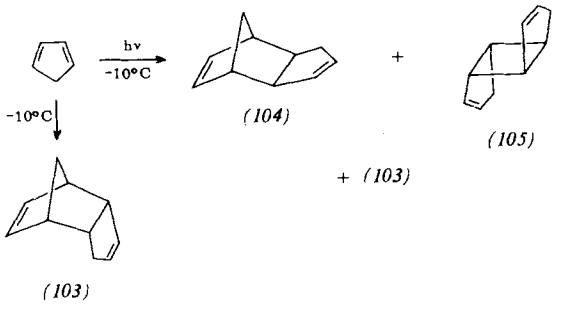
[125] *C. Walling* and *H. J. Schugar,* J. Amer. chem. Soc. *85,* 607 (1963).

[126] *C. Walling* and *M. Naiman,* J. Amer. chem. Soc. *84,* 2628 (1962).

[127] *S. W. Benson* and *J. A. Berson,* J. Amer. chem. Soc. *84,* 152 (1962); *86,* 259 (1964).

[128] *C. Walling* and *D. D. Tanner,* J. Amer. chem. Soc. *85,* 612 (1963).

products than thermal diene additions is a further argument against a triplet intermediate[129]. In the photosensitized dimerization of cyclopentadiene, for instance, the products *(103)* to *(105)* of cycloadditions



leading to six-membered rings and those leading to four-membered rings are formed in equal amounts. Similar results were obtained with cyclohexadiene and isoprene the diene components[129]. The reaction of cyclopentadiene with its hexafluoro derivative (see Section E 1), on the other hand, shows that a biradical singlet intermediate must be seriously considered.

In conclusion, a still unsolved problem may be mentioned. In 1942, *Woodward*[130] suggested that the actual Diels-Alder reaction is preceded by formation of an intermediate charge-transfer complex. *Andrews* and *Keefer*[131] showed that it is impossible to distinguish between the alternative mechanisms A and B by kinetic measurements alone:

$$\text{A: diene} + \text{dienophile} \underset{}{\overset{\text{fast}}{\rightleftharpoons}} \text{complex} \xrightarrow{\text{slow}} \text{adduct}$$

$$\text{B: complex} \overset{\text{fast}}{\rightleftharpoons} \text{diene} + \text{dienophile} \xrightarrow{\text{slow}} \text{adduct}$$

The mathematical development leads to the same formal kinetics for both possibilities. Abundant experimental data show qualitatively that both the formation of the charge-transfer complexes and the Diels-Alder reactions are favored by increasing donor stength of the diene and by increasing acceptor strength of the dienophile.

However, no definite quantitative relationship could be found for a number of model systems in which steric factors were practically eliminated[67]. Whereas the reactivities of the dienophiles in Table 7 change in the same order for various dienes, no such clear relationship is found for the formation of charge-transfer complexes with the same dienophiles (acceptors); dicyano-*p*-benzoquinone, although having the lowest dienophile activity, is relatively "too strong" as an acceptor, while the relative acceptor strength of TCNE is a function of the donor used (hexamethylbenzene, durene, pyrene, naphthalene, anisole). In view of the fact that the same sandwich structure is proposed for the transition state of the diene additions and the charge-transfer complexes, the above possibility A appears more probable.

F. Conclusion

Almost four decades have passed since *Diels* and *Alder* recognized the general applicability of these cycloadditions with formation of six-membered rings. As in many other fields the mechanistic interpretation of these reactions has also lagged behind the accumulation of experimental data. However, it is to be hoped that all the details of the mechanism of Diels-Alder reactions will be fully elucidated in the near future, thereby stimulating new investigations that will bring new preparative possibilities.

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Spin Density Distribution in 2,4,6-Triphenylphenoxyl

BY K. DIMROTH, A. BERNDT, F. BÄR, A. SCHWEIG, AND R. VOLLAND[*]

The distribution of the unpaired electron over the oxygen and the 24 carbon atoms in the free 2,4,6-triphenylphenoxy radical was determined by electron spin resonance spectroscopy and quantum-mechanical approximation methods. The hyperfine splitting was evaluated with the aid of the spectra of triphenylphenoxyls deuterated in some or all of the substituent phenyl groups. The results of the quantum-mechanical approximations were checked by recording the ESR spectra of triphenylphenoxyls labeled with ^{13}C in positions 1, 2, 3, or 4 of the central ring. The spin density distribution permits a first discussion of the ^{17}O-coupling constants of correspondingly labeled triphenylphenoxyl and other organic free radicals.

The dehydrogenation of 2,4,6-triphenylphenol[1] and many other 2,4,6-triarylphenols[2] in an alkaline or a neutral medium leads to phenoxy radicals, which are unusually stable: they do not react with oxygen and, despite their high oxidation potentials[3], they can be kept in organic solvents for a long time without any change. As in the case of 2,4,6-tri-t-butylphenoxyl[4], blocking of the reactive 2, 4, and 6 positions with aryl groups suppresses the susceptibility of the ring to further addition and substitution. Since the steric hindrance with phenyl groups is less than with t-butyl groups another factor must be present in 2,4,6-triphenylphenoxyl to compensate for the decrease in steric hindrance. This effect is due to the participation of the phenyl groups in the π-electron system thus enabling the unpaired electron to occupy 25 positions, as compared to only seven in phenoxyl or trialkylphenoxyls.

The distribution of the unpaired electrons over the various atoms can be determined from the ESR spectra[5], and in particular from the resulting coupling constants and empirical relations between the latter and the spin densities. The development of special syntheses of triphenylphenoxyl isotopically labeled in distinct positions[6] was also an essential requirement for the determination of the spin density distribution.

ESR spectra with proton hyperfine structure can be used to determine the spin densities only on carbon atoms carrying hydrogens, and, for the other ("blind"[7]) atoms, one can use quantum-mechanical approximations in such a way that the calculated results agree with the experimental values for the hydrogen-carrying carbons. However, it has been shown on *p*-benzosemiquinone[7], that this technique may lead to incorrect values for the blind atoms. We have therefore checked the calculated spin densities of the blind atoms with triphenylphenoxyl labeled in known positions with ^{13}C. From the experimental spin density distribution and the ^{17}O-coupling constant[8], we could make an inference concerning the connection between the ^{17}O-coupling constant and the spin density on oxygen.

1. The Proton Hyperfine Structure of the ESR Spectrum of 2,4,6-Triphenylphenoxyl

The ESR spectrum of 2,4,6-triphenylphenoxyl *(1)* consists of about 100 proton hyperfine structure lines having approximately equal separation (Fig. 1)[a].

No grouping of the proton hyperfine structure lines exists that would permit analysis of the spectrum on the basis of the characteristic intensity ratios[9].

[*] Prof. Dr. K. Dimroth
Dr. A. Berndt
Dr. F. Bär
Dipl.-Chem. R. Volland
Institut für Organische Chemie der Universität
Bahnhofstr. 7
355 Marburg (Germany)

Dr. A. Schweig
Physikalisch-Chemisches Institut der Universität
Biegenstr. 12
335 Marburg (Germany)

[1] *K. Dimroth, F. Kalk,* and *G. Neubauer,* Chem. Ber. *90,* 2058 (1957); *K. Dimroth, F. Kalk, R. Sell,* and *K. Schlömer,* Liebigs Ann. Chem. *624,* 51 (1959); *K. Dimroth* and *A. Berndt,* Angew. Chem. *76,* 434 (1964); Angew. Chem. internat. Edit. *3,* 385 (1964).

[2] *K. Dimroth,* Angew. Chem., in preparation.

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[4a] *C. D. Cook,* J. org. Chemistry *18,* 261 (1953).

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[4c] *E. Müller* and *K. Ley,* Chemiker-Ztg. *80,* 618 (1956).

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[a] This degree of resolution of the proton hyperfine structure was first achieved by *K. H. Hausser* (Z. Elektrochem., Ber. Bunsenges. physik. Chem. *65,* 636 (1961). Owing presumably to the presence of oxygen during measurements, only a single line was obtained by *B. A. Arbusov, L. M. Kataeva, E. G. Kataev,* and *A. V. Ilyasov,* Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1962,* 360; Chem. Abstr. *57,* 11079 (1962).

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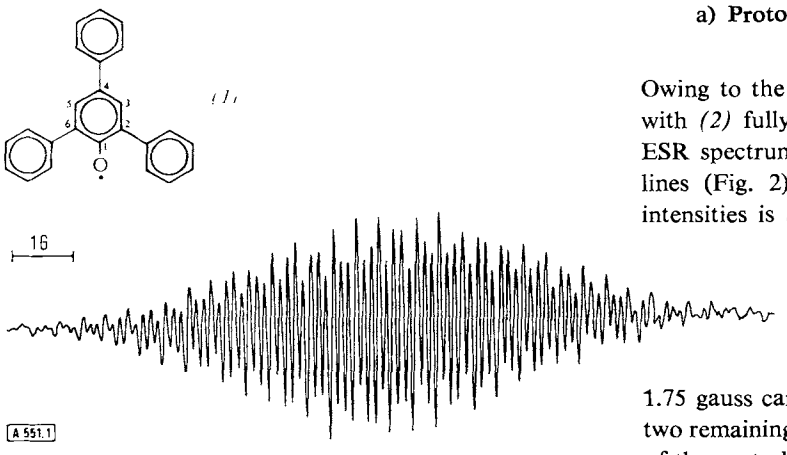
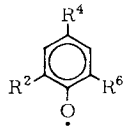


Fig. 1. The ESR spectrum of 2,4,6-triphenylphenoxyl in benzene at 50 °C.

Furthermore, the coupling constants cannot be assigned from the ESR spectrum of 2,4,6-triphenylphenoxyl alone, since there are several groups present with the same number of equivalent protons. Examination of a spectrum with an expanded abscissa has given the value of 0.37 gauss for the smallest coupling constant.

The deuterated compounds *(2)* to *(5)* were prepared to find the other coupling constants and to assign them to the hydrogens of *(1)* [b].



		R^2	R^4	R^6
[c]	*(2)*	C_6D_5	C_6D_5	C_6D_5
	(3)	C_6D_5	C_6H_5	C_6D_5
	(4)	C_6D_5	C_6H_5	C_6H_5
	(5)	C_6H_5	C_6D_5	C_6H_5

The coupling constant a_k of a nucleus k is proportional to μ_k/I_k, eq. (I)[12] (μ_k = magnetic moment, I_k = nuclear spin

$$a_k = (8\pi\mu_k/3\,I_k)\,\rho_k(o) \qquad (I)$$

and $\rho_k(0)$ = net spin density of all the electrons on nucleus k). Furthermore, since deuterium has a smaller magnetic moment and larger nuclear spin ($\mu_{k.D}$ = 0.85738 $\mu_{k.B}$, $I_{k.D}$ = 1; $\mu_{k.B}$ is the nuclear Bohr magneton), the coupling constant of deuterium is smaller than that of hydrogen ($\mu_{k.H}$ = 2.79267 $\mu_{k.B}$, $I_{k.H}$ = 1/2) by a factor of 6.514. The spectrum may therefore be simplified by the substitution of D for H on carbons with a small spin density, since the hyperfine lines of the remaining hydrogens may then appear in groups.

a) Proton Coupling Constant of the Central Ring

Owing to the absence of deuterium hyperfine splitting with *(2)* fully deuterated in the substituent rings, the ESR spectrum of this radical shows only three broad lines (Fig. 2). Since the ratio of the corresponding intensities is about 1:2:1, the coupling constant a = 1.75 gauss can be assigned unambiguously to the only two remaining hydrogens, *i.e.* those in positions 3 and 5 of the central ring.

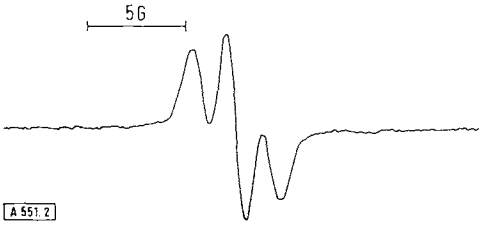


Fig. 2. The ESR spectrum of 2,4 6-tris(pentadeuteriophenyl)phenoxyl in benzene at 50 °C.

The coupling constant is seen to differ only slightly from that of the unsubstituted phenoxy radical (1.8 gauss[13]; 1.9 gauss[14]), in agreement with the more general observation that phenyl substituents affect only slightly the spin densities on carbons adjacent to the substituted positions[4b,4d,15,16].

b) Coupling Constants of Hydrogens in the 4-Phenyl Group

Fig. 3 shows that the ESR spectrum of 2,6-bis(pentadeuterophenyl)-4-phenylphenoxyl *(3)* consists of a sextet with the approximate intensity ratio of 1:5:10:10:5:1, and is assignable to five protons with $|a|$ = 1.75 gauss [d].



Fig. 3. The ESR spectrum of 2,6-bis(pentadeuterophenyl)-4-phenylphenoxyl in benzene at 60 °C.

[b] Some of these results were included in a lecture at the EUCHEM Conference on ESR Spectroscopy in Cirencester (England), March 28th to April 2nd, 1965.

[c] *I. S. Hyde* (Varian Ass., Palo Alto, California) has found from the ENDOR spectrum [10] that the 2-phenyl and the 6-phenyl groups in *(2)* are not fully deuterated. Deuterium analysis has also given a decrease in deuterium content of about 22%. Thus, some D must have been replaced by H during the synthesis [11] from 2,4,6-triiodophenol and hexadeuteriobenzene (>99 atom-% D).

[10] *J. S. Hyde*, J. chem. Physics *43*, 1806 (1965).

[11] *N. Kharasch, W. Wolf, T. J. Erpelding, P. G. Naylor*, and *L. Tokes*, Chem. and Ind. *1962*, 1720.

[12] *E. Fermi*, Z. Physik *60*, 320 (1930); *A. Abragam* and *M. H. L. Pryce*, Proc. Roy. Soc. (London) A *205*, 135 (1951).

[13] *T. J. Stone* and *W. A. Waters*, J. chem. Soc. (London) *1964*, 213.

[14] *W. T. Dixon* and *R. O. C. Norman*, J. chem. Soc. (London) *1964*, 4857.

[15] *E. W. Stone* and *A. H. Maki*, J. chem. Physics *41*, 284 (1964).

[16a] *P. B. Ayscough, F. P. Sargent*, and *R. Wilson*, J. chem. Soc. (London) *1963*, 5418.

[16b] *E. A. C. Lucken*, J. chem. Soc. (London) *1963*, 5123.

[d] The range of deviation can here be up to a fourth of the bandwidth of 0.88 gauss [9]. *J. S. Hyde* (cf. note [c]) has made a more accurate determination of the coupling constants of *(1)* by the ENDOR method [10] with the aid of these and other deuterated 2,4,6-triphenylphenoxyls (personal communication).

Two of these have appeared before as 3- and 5-hydrogens, and the other three must belong to the 4-substituent. They are assigned to the *p*- and the two *o*-positions, since with all known phenyl-substituted radicals [15, 16a, 17], the coupling constants of the *o*- and the *p*-protons in substituent rings are 2–3 times as great as those of the *m*-protons.

The spectrum of *(3)* contains no hyperfine lines corresponding to coupling with the *m*-protons of the 4-phenyl group. It follows from the band-width of 0.88 gauss that the splitting constant must be smaller than 0.7 gauss.

Using the SESRS computer program [18], one can compute theoretical spectra from the coupling constants and the experimental band-widths. In the present case, we assumed 1.75 gauss for five coupling constants and varied the coupling constant a_m of the two *m*-protons in the 4-phenyl group between 0.50 and 0.80 gauss in steps of 0.05 gauss and then between 0.62 and 0.68 gauss in steps of 0.02 gauss. The best agreement between the theoretical and the observed spectra was obtained at $a_m = 0.64$ gauss.

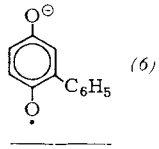
c) Coupling Constants of Protons in the 2- and the 6-Phenyl Groups

Only these are now required for a full elucidation of the ESR spectrum of *(1)*, and they can be estimated from a comparison between the following approximate ranges of the various spectra: 13, 8, 12, 12, and 8 gauss for *(1)–(5)*, respectively [no resolved hyperfine lines appeared for *(4)* and *(5)*]. The decrease in the coupling constants caused by deuteration is correlated as follows with the decrease ΔA in the spectral range:

$$\Delta A = \sum_{i=1}^{n} (1-1/6.514)\,|\,a^{H}{}_i\,| \qquad \text{(II)}$$

where n is the number of hydrogens replaced by deuterium. From the experimental coupling constants given in Fig. 4, the value of ΔA is estimated at 5.5 gauss for the 4-phenyl group, *i.e.* the spectral ranges of *(2)* and and *(5)* should be shorter by 5.5 gauss than those of *(3)* and *(1)* respectively. This is in a fairly good agreement with the observed values (4–5 gauss).

Since the spectral range of *(1)* differs from that of *(3)* and *(4)* only by 1 gauss, the coupling constants of the 2- and the 6-phenyl groups must be considerably smaller than that of the 4-phenyl group. This indeed is to be expected on account of the fact that the steric effect of the oxygen atom must twist these adjacent phenyl groups well out of the central plane.



(6)

[17] See, *e.g.*, *D. C. Reitz*, J. chem. Physics *30*, 1364 (1959); *34*, 701 (1961); *H. Ueda*, J. physic. Chem. *68*, 1304 (1964).

[18] *E. W. Stone* and *A. H. Maki*, J. chem. Physics *38*, 1999 (1963).

Analogously to all known phenyl-substituted radicals [15, 16a, 17], the smallest coupling constant of *(1)* (0.37 gauss) can be assigned to the *m*-protons of the 2- and the 6-phenyl groups. Furthermore, since generally $a_o \approx a_p \approx 2a_m$, we can estimate a value of 0.7–0.8 gauss for the coupling constants of the *o*- and the *p*-protons.

Of all radicals containing a phenyl substituent, phenyl-*p*-benzosemiquinone [15] is best comparable with *(1)*, because the phenyl group is *ortho* to the oxygen. The coupling constants of protons in the phenyl substituent of this radical are as follows: $a_o = a_p = 0.29$ gauss and $a_m = 0.16$ gauss. On account of the similarity between this radical and *(1)* as regards the twisting of the phenyl substituents, one may assume that the *o,p*:*m* ratio of the coupling constants is the same for *(1)* as for this radical. This leads to $a_o = a_p = 0.7$ gauss for the 2- and the 6-phenyl groups in *(1)* (cf. note [d]). The coupling constants thus obtained are mapped in Fig. 4.

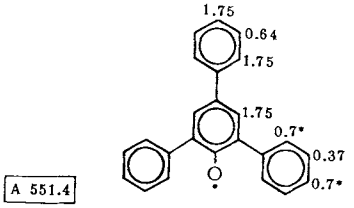


Fig. 4. Proton coupling constants in 2,4,6-triphenylphenoxyl *(1)* Asterisks denote estimated values.

2. Spin Density Distribution on Carbons Carrying Hydrogen Atoms

According to *McConnell* [19], the proton coupling constant a^H is proportional to the spin density ρ_C on the carbon atom to which it is bonded:

$$a^H = Q_{C\text{-}H}{}^H \rho_C \qquad \text{(III)}$$

The value of −27 gauss was adopted for the proportionality constant $Q_{C\text{-}H}{}^H$, because recent investigations had shown it to be better than the previous values of −23 to −24 [7, 20] [e]. As the sign of a^H is difficult to determine, one must generally be content with the magnitude of the spin densities. These are mapped below for the 17 hydrogen-bearing carbons in *(1)*.

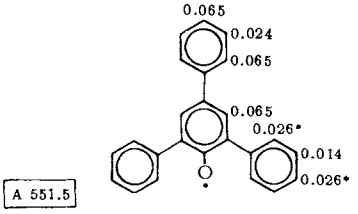


Fig. 5. Spin densities on the hydrogen-bearing carbon atoms in 2,4,6-triphenylphenoxyl *(1)*. Asterisks denote estimated values.

[19] *H. M. McConnell*, J. chem. Physics *24*, 764 (1956).

[20] *L. C. Snyder* and *T. Amos*, J. chem. Physics *42*, 3670 (1965); *K. Möbius*, Z. Naturforsch. *20a*, 1102 (1965).

[e] Furthermore the σ-π parameters of *Das* and *Fraenkel* [7] also involve $Q_{C\text{-}H}{}^H = -27$ gauss. These parameters are used in the calculation of the ^{13}C-coupling constants from the spin densities (see Section 4).

3. Calculation of the Spin Density Distribution by McLachlan's Method

In order to obtain the spin densities on carbon atoms carrying no hydrogens calculations were carried out using *McLachlan*'s SCF–MO method [21]. By taking into account electronic interactions, *McLachlan*'s method leads to spin density distributions that are in better agreement with experiments than are the results of the Hückel MO method [22]. It also gives negative spin densities, which have been clearly observed in experiments [23].

The common value of $\lambda = 1.2$ for *McLachlan*'s parameter was used and the values for the Coulomb integral of the oxygen atom ($\alpha_O = \alpha_C + h\beta_{CC}$), the resonance integral for the C–O bond ($\beta_{CO} = k\beta_{CC}$), and the angle of twist of the 4-phenyl group (φ_4) and the 2- and 6-phenyl groups ($\varphi_{2,6}$) were chosen so as to ensure the best possible agreement between the resulting spin densities on the hydrogen-bearing carbon atoms and the experimental values in Fig. 5. As usual, the effect of twisting was taken into account by using the expression $\beta_{C-C}(\varphi) = \beta_{C-C} \cos\varphi$ to calculate the resonance integrals of bonds between the central ring and the phenyl substituents [22]. In order to avoid arbitrary variation of the parameters and to minimize the computational work (quite considerable if all the parameters are varied simultaneously), the parameters h and k as well as φ_4 were first determined on simpler systems, namely on phenoxyl [13,14] and on 2,6-di-t-butyl-4-phenylphenoxyl [4b,4d].

a) Spin Density Distribution in Phenoxyl

The parameters k and h were varied in steps of 0.1 within the range generally considered [7,24] with radicals containing C–O bonds, *i.e.* $k = 0.8$ to 1.6 and $h = 1.0$ to 2.0. The best agreement with the spin densities obtained from the coupling constants of phenoxyl [13,14] and with $Q_{C\text{-}H}{}^{H} = -27$ gauss was found at $k = 1.6$ and $h = 1.9$ [f]. The spin densities in phenoxyl calculated by various authors are listed in Table 1.

b) Spin Density Distribution in 4-Phenyl-2,6-di-t-butylphenoxyl

In this calculation, the value of k was kept constant at 1.6 and the influence of the t-butyl groups was neglected. The angle of twist φ_4 of the 4-phenyl group was varied between 0 and 50° in steps of 5°, and between 0 and 20° in steps of 2°, whilst the value of h was varied between 1.0 and 1.9.

The use of different h values for phenoxyl and the radical in question is justifiable, since the coupling constants were determined in water for phenoxyl and in benzene for the other radical. The effect of the solvent on the spin distribution of the radicals [30] can be taken into account in the calculations by changing the Coulomb integral of the heteroatom, which reflects the change in the electronegativity caused by the solvation [7,31]. The solvation of 2,4,6-triphenylphenoxyl and 4-phenyl-2,6-di-t-butylphenoxyl may be influenced by the steric effect of the 2- and the 6-substituents.

Table 1. Spin densities in phenoxyl.

	O	C^1	C^2 and C^6	C^3 and C^5	C^4	Ref.
exp.	—	—	0.255	0.070	0.374	[13]
	—	—	0.246	0.066	0.374	[14]
Method of calculation						
McLachlan	0.198	0.125	0.253	−0.071	0.315	
HMO	0.183	0.135	0.193	0.018	0.261	[*]
Extended VB	—	—	0.323	−0.212	0.283	[25]
HMO	0.147	0.228	0.138	0.039	0.271	[26]
CI	0.170	0.227	0.154	−0.022	0.338	[26]
SCF	0.556	−0.006	0.211	−0.092	0.223	[27]
VB	—	—	0.19	−0.135	0.35 [**]	[28]
semi empirical	0.50	−0.06	0.176	−0.071	0.352	[29] [g]

[*] $h = 1.9$, $k = 1.6$; [**] adjusted for positions 2, 6, and 4.

Table 2 Spin densities of 4-phenyl-2,6-di-t-butylphenoxyl.

Position	exp. [4b]	exp. [4d]	*McLachlan*'s method (for 4-phenylphenoxyl)
Phenoxyl:			
O	—	—	0.289
1	—	—	0.029
2/6	—	—	0.242
3/5	0.066	0.067	−0.064
4	—	—	0.241
4-Phenyl:			
1′	—	—	−0.035
2′/6′	0.066	0.067	0.062
3′/5′	0.033	0.022	−0.030
4′	0.066	0.067	0.056

[21] *A. D. McLachlan*, Molecular Physics *3*, 233 (1960).

[22] *A. Streitwieser, jr.*: Molecular Orbital Theory. Wiley, New York 1961.

[23] *H. S. Gutowsky, H. Kasumoto, T. H. Brown*, and *D. H. Anderson*, J. chem. Physics *30*, 860 (1959).

[f] Only the experimental spin density on C-1 (determined by the ^{13}C labeling of C-1 or C-2) or on the oxygen can confirm whether these are in fact the best parameters.

[24] *O. H. Griffith*, J. chem. Physics *42*, 2651 (1965); *G. P. Rabold, K. H. Bar-Eli, E. Reid*, and *K. Weiss, ibid. 42*, 2438 (1965); *R. Gerdil* and *E. A. C. Lucken*, J. Amer. chem. Soc. *87*, 213 (1965).

[25] *J. C. Schug, Th. H. Brown*, and *M Karplus*, J. chem. Physics *37*, 330 (1962).

[26] *N. M. Atherton, E. J. Land*, and *G. Porter*, Trans. Faraday Soc. *59*, 818 (1963).

[27] *G. Berthier* and *J. Baudet*, J. chem. Physics *61*, 1598 (1964).

[28] *J. K. Becconsall, S. Clough*, and *G. Scott*, Trans. Faraday Soc. *56*, 459 (1960).

[29] *E. Müller, A. Rieker*, and *K. Scheffler*, Liebigs Ann. Chem. *465*, 92 (1961).

[g] The spin density distribution obtained with 2,4,6-tris(diphenylmethyl)phenoxyl, which is supposed to be essentially unaffected by substitution of the aroxyl and therefore to hold also for the phenoxy radical, must be viewed with reserve as regards the spin densities on C-1, C-2, and O. The assumption that the bulky diphenylmethyl groups next to the oxygen rotate freely seems as untenable as the assumption that the electron distribution is essentially left unchanged by the replacement of the oxyl oxygen by the azyl group, –N–H. In fact, as we go from benzyl to phenoxyl [14], the change in the electronegativity χ (from 2.5 for C to 3.5 for O) causes an appreciable change in the spin densities on the benzene ring, as a result of which the spin densities on the methylene group and the oxygen will also differ considerably. The spin distribution in the phenylamino radical, $C_6H_5HN\cdot$ ($\chi_N = 3.0$), is expected to lie between that of benzyl and that of phenoxyl. If we assume as a first approximation a linear relationship between electronegativity and spin density on the exocyclic atom, we then find by extrapolation $\rho_O = 0.27$ for the spin density on the oxygen in phenoxyl by the use of $\rho_{CH_2} = 0.61$ and $\rho_N = 0.44$ (with $Q_{N\text{-}H}{}^{H} = 27$gauss).

[30] See, *e.g., J. Gendell, J. H. Freed*, and *G. K. Fraenkel*, J. chem. Physics *37*, 2832 (1962); *E. W. Stone* and *A. H. Maki*, J. Amer. chem. Soc. *87*, 454 (1965).

[31] For example *P. H. Rieger* and *G. K. Fraenkel*, J. chem. Physics *30*, 609 (1963).

The best agreement with the experimental spin densities obtained from the coupling constants [4b,4d] and $Q_{C\text{-}H}{}^{H}$ = −27 gauss (Table 2) was obtained at $\varphi_4 = 0°$ and $h = 1.2$.

c) Spin Density Distribution of 2,4,6-Triphenylphenoxyl

In this calculation, we kept constant $k = 1.6$, $h = 1.2$, and $\varphi_4 = 0$ and varied $\varphi_{2,6}$ between 40 and 70 ° in steps of 10 °, and then between 42 and 48 ° in steps of 2 °. The best agreement with the experimental spin density distribution of the hydrogen-bearing carbon atoms shown in Fig. 5 was obtained at $\varphi_{2,6} = 46°$ (Table 3). The calculations show therefore that, in accordance with expectations, the 2- and the 6-phenyl groups are twisted by the oxygen out of the plane of the central ring much more than is the 4-phenyl group.

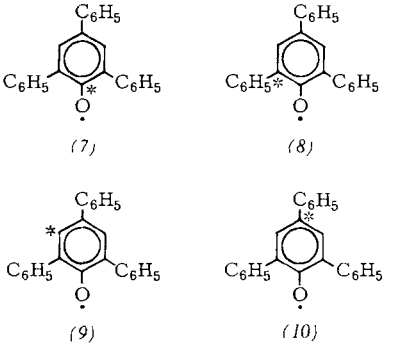
Table 3. Spin densities in 2,4,6-triphenylphenoxyl.

Position	Spin density	
	exp.	calc.
Phenoxyl:		
O	—	0.256
1	—	0.030
2/6 (C^2 and C^4)	—	0.211
3/5 (C^3 and C^5)	0.065	−0.055
4 (C^4)	—	0.218
4-Phenyl:		
1	—	−0.026
2/6	0.065	0.058
3/5	0.024	−0.024
4	0.065	0.056
2,6-Phenyls:		
1	—	−0.013
2/6	0.026 [*]	0.026
3/5	0.014	−0.010
4	0.026 [*]	0.024

[*] See Section 1c.

4. Use of ^{13}C-Labeled 2,4,6-Triphenylphenoxyl to Check the Calculated Spin Densities

To test the calculated spin densities at the blind atoms (Table 3), we prepared the labeled radicals *(7)* to *(10)* with an enrichment of 55 atom-% of ^{13}C.



The corresponding ESR spectra are shown in Fig. 6.

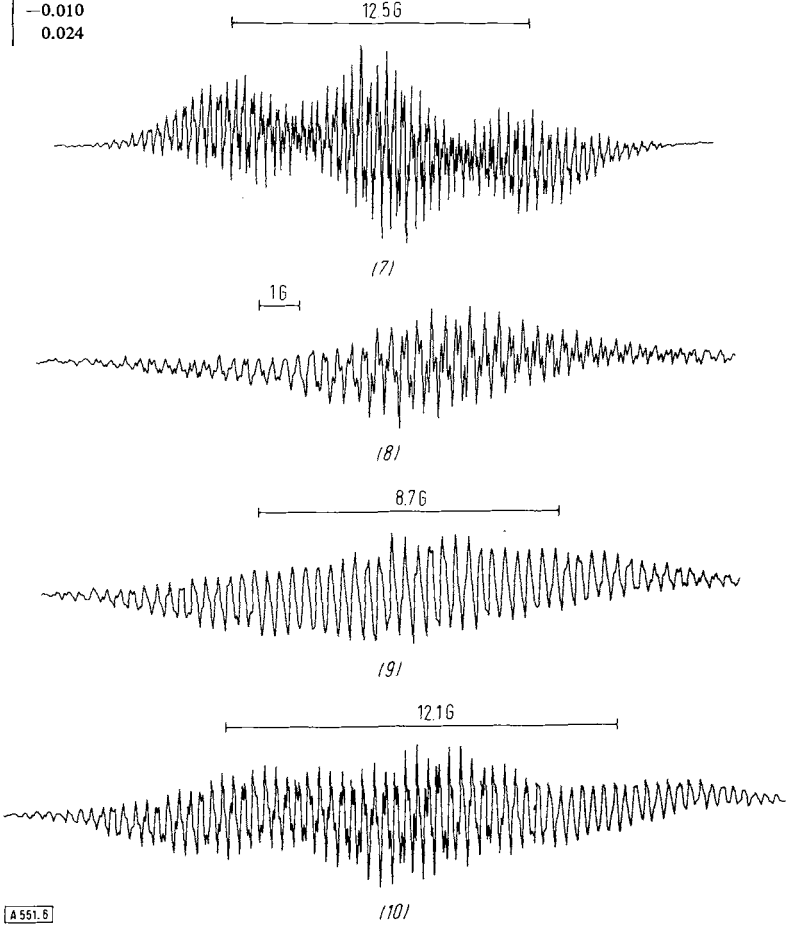


Fig. 6.
The ESR spectra of 2,4,6-triphenylphenoxyls labeled with ^{13}C.

The ^{13}C-coupling constant $a_{^{13}C}$ depends both on the spin density ρ_i of the labeled atom, i, and on the spin densities of all the adjacent atoms ρ_j[32]:

$$a_{^{13}C} = (-12.7 + \sum_{j=1}^{3} Q_{ij})\rho_i + \sum_{j=1}^{3} Q_{ji}\rho_j \qquad \text{(IV)}$$

The following values were used for the $\sigma-\pi$ parameters Q_{ij} and Q_{ji} belonging to the adjacent hydrogen, carbon, and oxygen atoms[7, 32]:

Q_{ij}: $Q_{^{13}C\text{-}H}C = 19.5$; $Q_{^{13}C\text{-}C}C = 14.4$ [h]; $Q_{^{13}C\text{-}O}C = 17.7$

Q_{ji}: $Q_{H\text{-}^{13}C}C = 0$; $Q_{C\text{-}^{13}C}C = -13.9$ [h]; $Q_{O\text{-}^{13}C}C = -27.1$

Using eq. (IV) and the calculated spin densities in Table 3, one can calculate the ^{13}C-coupling constants for the radicals *(7)* to *(10)*. The results are compared in Table 4 with the experimental values.

Table 4. ^{13}C-coupling constants of *(7)* to *(10)*, $a_{^{13}C}$ (in gauss)

Radical	calc. *McLachlan*	($\varphi_4 = 0°$) ρ_3 (exp.) considered	exp	calc. ($\varphi_4 = 30°$) ρ_3 (exp.) considered
(7)	−11.8	—	±12.5	−12.4
(8)	+ 7.0	+7.1	± 4.7 [*]	+ 7.4
(9)	− 7.9	−8.3	± 8.7	− 8.6
(10) [**]	+ 8.5	±8.8	±12.1	+ 9.1

[*] This coupling constant could not be obtained unambigously from the spectra, since the ^{13}C content was not sufficiently high. Therefore, we calculated the theoretical spectrum of *(8)* for various values of the ^{13}C-coupling constant, on the basis of the experimental spectrum of unlabeled 2,4,6-triphenylphenoxyl and a ^{13}C enrichment of 55 atom-%. The best agreement with the experimental spectrum was obtained with the values given here.

[**] *Note added in proof* (Nov. 1st, 1966): By synthesis of 2,6-diphenyl-4-[1−^{13}C]phenylphenoxyl the ^{13}C-coupling constant for the junction of the phenylsubstituted in the 4-position of 2,4,6-triphenylphenoxyl has been determined. It is 6 gauss, to be compared with the value of 5.4 gauss calculated according to *McLachlan*.

In comparison with the results for other ^{13}C-labeled radicals[33–35], there is a good agreement between the experimental and the theoretical ^{13}C-coupling constants of *(7)* and *(9)*, and the agreement is still better when we use $\varphi_4 \neq 0°$. The last column in Table 4 gives ^{13}C-coupling constants derived from spin densities obtained with $\varphi_4 = 30°$. In the case of radical *(8)*, on the other hand, the agreement with the experiment is less good. Such deviations with the radicals *(8)* and *(10)* carrying phenyl substituents on labeled carbon atoms may be due to the unjustifiability of using the specified $\sigma-\pi$ parameters $Q_{^{13}C\text{-}C}C$ and $Q_{C\text{-}^{13}C}C$ for the bond between the central ring and the substituent, caused by the fact that the length of this bond differs from that of aromatic sp^2 C–C bonds[32]. This is supported by the poor agreement between the calculated and the experimental ^{13}C-coupling constants of triphenylmethyl[32] [i] [j] [37a].

The improvement in the agreement in the ^{13}C-coupling constants of *(7)* and *(9)* by increasing φ_4 is accompanied by a deterioration in the agreement between calculated and experimental spin densities at hydrogen-bearing carbon atoms in the 4-phenyl substituent.

5. Spin Density on the Oxygen Atom

On the basis of the general theory of *Karplus* and *Fraenkel*[32], which has been applied to the coupling constants of ^{13}C[7, 33–35], ^{14}N[31, 36], ^{19}F[37b], and ^{17}O[38], we can use eq. (V) to express the correlation between the ^{17}O-coupling constants and the spin density ρ_O on the oxygen in radicals whose oxygen is linked only to one atom:

$$a_{^{17}O} = Q_1\rho_O + Q_2\rho_n \qquad \text{(V)}$$

where ρ_n is the spin density on the atom adjacent to the oxygen.

The parameters Q_1 and Q_2, which may depend on the nature of the neighboring atom, are not known, and the available experimental results are insufficient for their exact determination. However, it seems permissible for the interpretation of the results to assume a direct proportionality between the ^{17}O-coupling constant and the spin density on the oxygen[k]:

$$a_{^{17}O} = Q^O\rho_O \qquad \text{(VI)}$$

On the basis of the following arguments, we propose the value of $Q^O = 40 \pm 4$ gauss:

a) We obtain $\rho_O = 0.26$ from the value of calculated spin density distribution of *(1)* which agrees the best with the experimental H- and ^{13}C-coupling constants. On the basis of this and $a_{^{17}O} = 9.7$ gauss [8], eq. (VI) gives $Q^O = 37$ gauss.

[i] Although the ^{13}C-coupling constant calculated by the VB method agrees well with the experimental value, the corresponding spin densities on hydrogen-bearing carbons differ considerably from observed data.

[j] Neglect of the deviation in the bond length from that in aromatic sp^2 C–C bonds may perhaps also account for the discrepancy between experimental and theoretical coupling constants in the 7,7,8,8-tetracyanoquinodimethane radical anion [35].

[k] A direct proportionality between the ^{14}N-coupling constants and the spin density at the nitrogen has been assumed for some nitrogen radicals [36].

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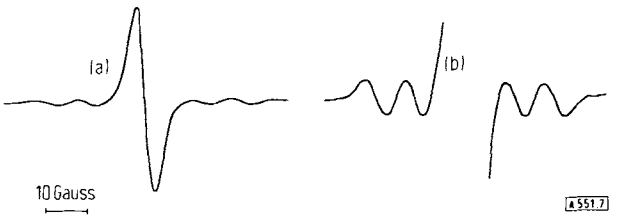


Fig. 7. ESR-Spectrum of ^{17}O-labeled 2,4,6-triphenylphenoxyls. (b) corresponds to (a) enlarged 10 ×.

b) *McLachlan*-type SCF calculations for 2,4,6-tri-t-butylphenoxyl[1] ($a_{^{17}O}$ = 10.23 gauss[39]) have led to ρ_O = 0.261. Substitution in eq. (VI) gives Q^O = 39.2 gauss[39a].

c) The^{14}N- and the^{13}C-spectra of di-t-butylnitroxyl(t-Bu_2NO) recorded in various solvents show that the ^{14}N-coupling constant does not depend on the spin density on the oxygen atom[42]. On the basis of an LCAO calculation[43] and in agreement with results for other radicals[36a–36c], the proportionality constant can be taken as Q_N = 26 gauss. This has given ρ_N = 0.515 for di-s-butylnitroxyl (s-Bu_2NO), the first ^{17}O-labeled organic radical to be described[44]. Therefore, the spin density on the oxygen is ρ_O = 0.485. With an ^{17}O-coupling constant of 19.71 gauss, we obtain Q^O = 40.7 gauss.

Rieger and *Fraenkel*[31] have obtained ρ_O = 0.199 for the oxygen atoms in the nitrobenzene radical anion by adjusting the parameters to the experimental spin densities of the phenyl-ring carbon atoms. The ^{17}O-coupling constants of 8.86 gauss for acetonitrile and 8.84 gauss for dimethylformamide[38] lead to Q^O = 44.5 gauss. However, since these authors used $Q_{C\text{-}H}{}^H$ = −23.7 gauss instead of the more recent value of −27 to −28 gauss, their spin density on the benzene ring is probably too high and that on the nitro group and hence on the oxygen probably too low, in which case the value of Q^O should be less than 44.5 gauss.

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[1] The calculations were carried out with k = 1.6 and the usual auxiliary parameter accounting for the inductive effect of the alkyl groups ($\Delta\alpha = -0.3\ \beta_{C-C}$ [40]). To account for the effect of solvation of phenoxyl in water and 2,4,6-tri-t-butylphenoxyl in benzene, the value of h was varied between 1.1 and 1.9 and then between 1.59 and 1.55. The best agreement with the experimental spin concentration in the 3- and 5-positions (0.067) and with the experimental ^{13}C-coupling constant for C-1 (9.6 gauss [41] was obtained at h = 1.56. The spin densities are then as follows: ρ_0 = 0.261, ρ_1 = 0.127, $\rho_{2,6}$ = 0.247, $\rho_{3,5}$ = 0.067, and ρ_4 = 0.253. These values lead to 9.6 gauss for the ^{13}C-coupling constant of C-1.

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Chemistry of Stable α-Halogenoorganolithium Compounds and the Mechanism of Carbenoid Reactions[1]

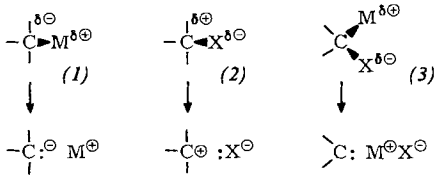
BY G. KÖBRICH [*]

IN COLLABORATION WITH A. AKHTAR, F. ANSARI, W. E. BRECKOFF, H. BÜTTNER, W. DRISCHEL, R. H. FISCHER, K. FLORY, H. FRÖHLICH, W. GOYERT, H. HEINEMANN, I. HORNKE, H. R. MERKLE, H. TRAPP, AND W. ZÜNDORF

Some years ago we found that α-halogenoorganolithium compounds (carbenoids) previously postulated as transient intermediates in organolithium-initiated α-eliminations can be obtained in a stable form. The present paper is a review of the methods for their preparation and of their reactivity. They possess both nucleophilic and electrophilic properties, which can be utilized singly or combined for the synthesis of substances of very different types. Their thermolability, which is considerably reduced (with only one known exception) by the solvent tetrahydrofuran, is due to electrophilic secondary reactions, in which carbenes evidently do not occur as intermediates. A mechanism is proposed which fits the experimental data for various carbenoid reactions.

1. Introduction

Carbon is often connected with ligands of lower (*e.g.* the alkali metals M) or higher electronegativity (*e.g.* the halogens X). The result in both cases is a polarization of the bond (though in opposite directions), *i.e.* the bond has ionic character. In one case [formula *(1)*] the carbon assumes a negative charge, which explains its nucleophilic reactivity; in the other [formula *(2)*] it carries a positive charge, and therefore undergoes electrophilic reactions. The extreme is the ionization of the polar bonds with liberation of carbanions or carbonium ions, respectively.



When M and X are attached to the same carbon atom, the polarization of the bonds may be represented as in formula *(3)*; owing to the mutual interaction of M and X, this polarization should be even more pronounced than in *(1)* or *(2)*. Compounds of this type are extremely unstable. When $M^{\oplus}$ and $X^{\ominus}$ are released from the common carbon atom to form MX, this leaves a molecular "residue" with an electron sextet on carbon. This carbene contains both the lone pair that characterizes carbanions and the unoccupied p orbital typical of carbonium ions; it can therefore, in particular, undergo electrophilic reactions.

One need not emphasize the value of this carbene concept[3], developed by *Hine* for the alkali hydrolysis of haloforms, as a heuristic principle in organic chemistry. On the other hand, it can be seen that the formation of a carbene, like that of carbonium ions or carbanions, evidently depends on favorable conditions (*e.g.* solvent and substituent effects). One may therefore ask whether many of the typical electrophilic carbene or "carbenoid"[4] reactions, particularly in the organometallic reactions discussed here, which are always carried out in solvents of low polarity, might not be due to the organometallic species *(3)* instead of to carbenes.

"Amphophilic" or "ambiphilic" (both nucleophilic and electrophilic) behavior would be plausible for the compounds *(3)*, in view of their relationship with the substrates *(1)* and *(2)*. In fact, there is evidence that the free-carbene stage may be by-passed in α-eliminations in ethereal media[4]. In reactions that proceed *via* the same (carbene) intermediate, one would expect the same products to be formed in the same ratios from different substrates and by different reaction paths. However, this is not the case in two typical carbene reactions, *i.e.* addition to olefins[4] and intramolecular insertion in C–H bonds in the γ position[5], both of which give cyclopropanes. Moreover, a number of stable α-halogenoorganyls of zinc[6,7] and aluminum[8]

[*] Doz. Dr. G. Köbrich
Institut für Organische Chemie der Universität
Tiergartenstrasse
69 Heidelberg (Germany)

[1] Stable Carbenoids XXIII. Part XXII: [2]. Based on various lectures delivered between April 1964 and June 1966.

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(3) (M = Zn/2 or Al/3) can react with olefins to form cyclopropanes evidently without first undergoing α-elimination. For this reason carbene mechanisms for α-eliminations from organometallic compounds of alkali metals are nowadays generally advanced only with reservations.

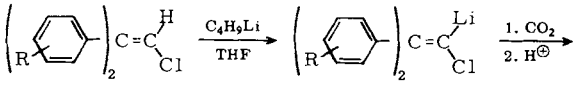
The study of the postulated intermediates *(3)*[9] in these reactions, which have been detected indirectly in many cases, should provide more accurate information. Until recently, however, such studies were impossible because of the instability of these compounds.

The present paper is a review of our preparative work and of the associated investigations on the reaction behavior of α-halogenoorganolithium compounds *(3)* (M = Li). In anticipation of the subsequent discussion these compounds are termed carbenoids.

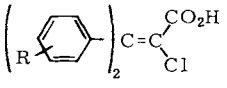
2. Preparation

In α-eliminations in ethereal media, use is made of *Wittig*'s observation[10] that the α-hydrogen of many chlorinated hydrocarbons is acidified by the halogen to such an extent that it can be replaced readily by lithium on reaction with organolithium reagents. However, this metalation is generally followed by fast secondary reactions characterized by the elimination of lithium chloride. To avoid these, it would *a priori* be desirable to carry out the metalation at low temperatures and to use substrates whose α-carbon is relatively stable in the anionized state and whose α-halogen is relatively firmly bound. The most favorable conditions are offered by olefinic carbon atoms, which are more electronegative than saturated carbon atoms.

Our experiments based on these considerations, and starting from 1-chloro-2,2-diarylethylenes, led in 1963 to the first, and so far the simplest, method for the preparation of carbenoids[11]. The action of n-butyl-lithium on the substrates *(4)* in tetrahydrofuran at a low temperature gives the stable lithium derivatives *(5)*, as is shown by the formation of the carboxylic acids *(6)*, generally in excellent yields, on subsequent carboxylation.



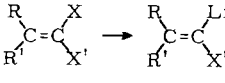
(4) *(5)*



(6)

The reaction can be carried out with numerous olefins having, instead of aryl groups[12], H or Cl, alkyl, or vinyl ligands in one or in both β positions[13–17] (see Table 1). The lower limit of the optimum reaction temperature depends on the rate of metalation and its upper limit on the thermal stability of the resulting carbenoids.

When metalation is slow the lithium may be introduced by halogen-metal interconversion on a geminal dihalide, which, for bromine derivatives, is faster than an H/Li

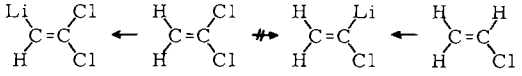


X, X' = Cl, Br

(7) *(8)*

exchange[10]. In this way one obtains the bromine or chlorine derivative *(8)* from the dibromide *(7)*, X = X' = Br, and chlorobromo derivatives (X = Br, X' = Cl) respectively. A less obvious reaction is the smooth Cl/Li exchange often observed with geminal dichlorides *(7)*, X = X' = Cl, which can be used for the preparation of carbenoids *(5)*[18,19]. The reaction with geminal dichloroolefins is slower than the metalation of the corresponding monochloroolefins.

Thus trichlorovinyl-lithium is formed only at a moderate rate from tetrachloroethylene at –110 °C, whereas the metalation of trichloroethylene proceeds violently under the same conditions. Further, the reaction of 1,1-dichloroethylene with butyl-lithium does not lead to α-chlorovinyl-lithium *(10)*, which can be obtained by metalation of vinyl chloride at –110 °C as a stable compound, but instead of a Cl/Li interconversion, metalation of the β position occurs to give the unstable product *(9)*[20].



(9) *(10)*

On the other hand, the Cl/Li exchange with dichlorides of saturated hydrocarbons can be faster than the metalation. Thus 7,7-dichloronorcarane can be used to prepare the carbenoids *(11)* and *(13)*, which cannot be obtained by metalation of the stereoisomeric 7-chloronorcaranes. This reaction leads to a mixture of stereoisomers, but the ratio of the components, which are characterized as the carboxylic acids *(12)*, m.p. 92 to 92.5 °C, and *(14)*, m.p. 108–108.5 °C, can be controlled by variation of the conditions. The principal product

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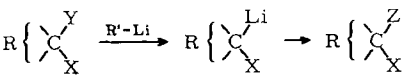
[17] *G. Köbrich* and *F. Ansari*, Chem. Ber., in press.

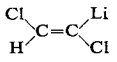
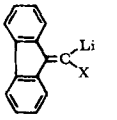
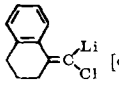
[18] *G. Köbrich*, *H. Trapp*, *K. Flory*, and *W. Drischel*, Chem. Ber. *99*, 689 (1966).

[19] *G. Köbrich*, *H. Trapp*, and *I. Hornke*, Chem. Ber., in press.

[20] *G. Köbrich* and *K. Flory*, Chem. Ber. *99*, 1773 (1966).

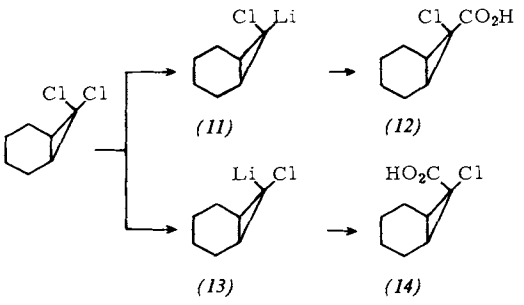
Table 1. Preparation and reaction products of carbenoids.



Carbenoid	Y	R′	Z	Yield (%)	Temp. (°C)	Ref.
$H_2C{=}CLiCl$	H	C_4H_9	CO_2H	100	110	[20]
	H	C_4H_9	CO_2H	99	−110	[20]
$Cl_2C{=}CLiCl$	H	C_4H_9	CO_2H	81	−110	[20]
$Cl_2C{=}CLiCl$	Br [a]	C_4H_9	CO_2H	92	−110	[20]
(5), R = H, *p*-Cl, *p*-CH_3, *p*-CH_3O, *o*-Cl, *o*-CH_3, or *o*-CH_3O	H, Br or Cl	C_4H_9	CO_2H, Br or I	⩽ 97	−45 to −110	[45]
(*p*-CH_3O-C_6H_4)$_2$C=CLiBr	Br	C_4H_9	CO_2H	69	−110	[15]
(C_6H_5)$_2$C=CLiBr	Br	C_4H_9	CO_2H	85	−100	[27]
(C_6H_5)$_2$C=CLiBr	H	$CHCl_2$	CO_2H	29	−85	[27]
 X = Br	Br	C_6H_5	CO_2H	99	−70	[28]
X = Cl	H	C_6H_5	CO_2H	99	−70	[28]
p-R-C_6H_4-C(R′)=CLiCl [b], R′ = C_6H_5; R = Cl, CH_3, or C_6H_5	H	C_4H_9	CO_2H	⩽ 91	−70 to −110	[19]
p-R-C_6H_4-C(R′)=CLiCl [b], R′ = CH_3; R=H or CH_3	H	C_4H_9	CO_2H	⩽ 93	−70 to −110	[17]
(C_6H_5-CH_2)$_2$C=CLiCl	H	C_4H_9	CO_2H or I	97	−108	[49]
(CH_3)$_2$C=CLiBr	Br	C_4H_9	CO_2H	94	−110	[50]
 [c]	H	C_4H_9	CO_2H	86	−110	[16]
(23)	H	C_4H_9	CO_2CH_3	87	−105	[25]
(31b) + *(32b)* [c]	H	C_4H_9	CO_2H	82	−100	[15, 16]
(31a) + *(32a)* [c]	H	C_4H_9	CO_2H	24	−100	[15, 16]
(11) + *(13)* [c]	Cl	C_4H_9	CO_2H	70	−110	[21]
Li-$CHCl_2$	H	C_4H_9	1/2 Hg	93	−74	[18]
Li-$CHBr_2$	H	$CHCl_2$	CO_2CH_3	54	−100	[27]
C_6H_5-CCl_2Li	H	C_4H_9	CO_2H	61	−100	[41]
Li-CCl_3	H	C_4H_9	1/2 Hg	96	−100	[41]
Li-CBr_3	Br	C_4H_9	CO_2H	81	−110	[27]
Li-CBr_3	H	$CHCl_2$	CO_2H	65	−100	[27]

[a] In diethyl ether. [b] *cis* and *trans* Forms. [c] Mixture of stereoisomers.

at −110 °C is *(11)*, since the *exo* chlorine atom is exchanged 3 to 4 times as rapidly, probably on steric grounds. The reaction at −80 °C leads mainly to the isomer *(13)*, because of decomposition and partial isomerization of the less stable *(11)* [21].



[21] *W. Goyert*, Diploma Thesis, Universität Heidelberg, 1966.

As can be seen from Table 1, the methods described can also be used for the preparation of carbenoids with a saturated carbon atom. Thus dichloromethane is completely converted into the stable dichloromethyllithium by the action of butyl-lithium in tetrahydrofuran at −70 °C [22], the less thermostable trichloromethyllithium can be prepared quantitatively in a similar manner from chloroform at temperatures below −100 °C [22]. The same compound can be obtained by halogen-metal interconversion from bromotrichloromethane in ether [23] or from carbon tetrachloride [24, 25].

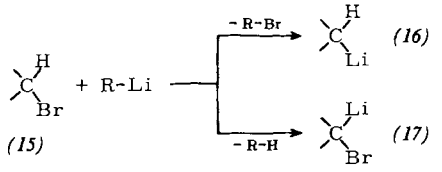
[22] *G. Köbrich, K. Flory*, and *W. Drischel*, Angew. Chem. *76*, 536 (1964); Angew. Chem. internat. Edit. *3*, 513 (1964).

[23] *W.T. Miller* and *D. M. Whalen*, J. Amer. chem. Soc. *86*, 2089 (1964).

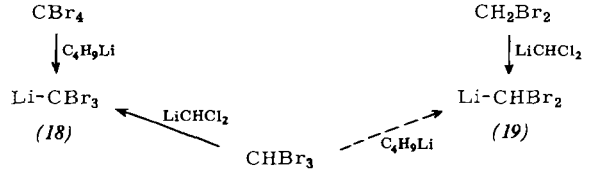
[24] *D. F. Hoeg, D. I. Lusk*, and *A. L. Crumbliss*, J. Amer. chem. Soc. *87*, 4147 (1965).

[25] *H. Büttner*, unpublished.

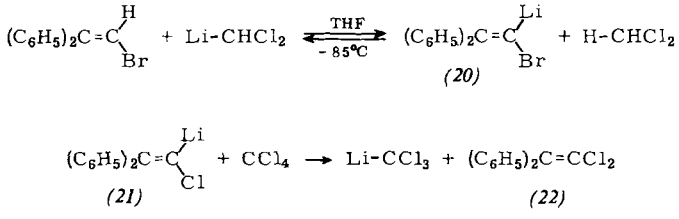
Since the Br/Li exchange is much faster than metalation, the action of organolithium reagents on substrates of the type *(15)* always leads predominantly to the halogen-free compound *(16)* at the expense of the carbenoid *(17)*. However, the observation that the action of *(5)* (R = H) on dibromomethane leads almost exclusively to H/Li exchange [26] forms the basis of a method favoring the metalation *(15)* → *(17)*. This is achieved by the use of carbenoids that are more basic than the



desired compound *(17)* [27]. Thus tribromomethyl-lithium *(18)* can be obtained not only by the reaction of tetrabromomethane with butyl-lithium, but also by transmetalation of bromoform with dichloromethyl-lithium (together with a little dibromomethyl-lithium). Similarly, the reaction of dibromomethane with dichloromethyl-lithium leads to dibromomethyl-lithium *(19)*, which was formerly also unknown, while the Br/Li interconversion between bromoform and butyl-lithium, which might be considered as an alternative route, is preparatively unproductive owing to side reactions [27].

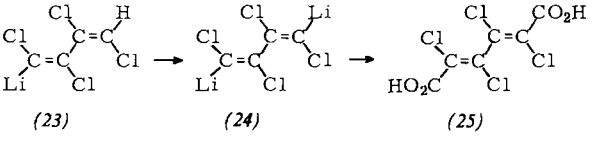


For carbenoids of similar basicities the metalation can be shown to be reversible, and equilibrium mixtures are conceivable. Thus the reaction of dichloromethyl-lithium with 1,1-diphenylbromoethylene in tetrahydrofuran at −85 °C gives about 30 % of the carbenoid *(20)*, which is identified as the carboxylic acid. On the other hand, when *(20)*, prepared by another route, is added to dichloromethane under the same conditions, dichloromethyl-lithium is formed [27].



In principle, carbenoids can also undergo halogen-metal exchange. Thus the action of tetrachloromethane on *(21)* at −85 °C gives the dichloro compound *(22)*, which is isolated in 91 % yield, together with trichloro-methyl-lithium [25]. This smooth reaction reflects the unusual readiness with which the anionized haloform is formed.

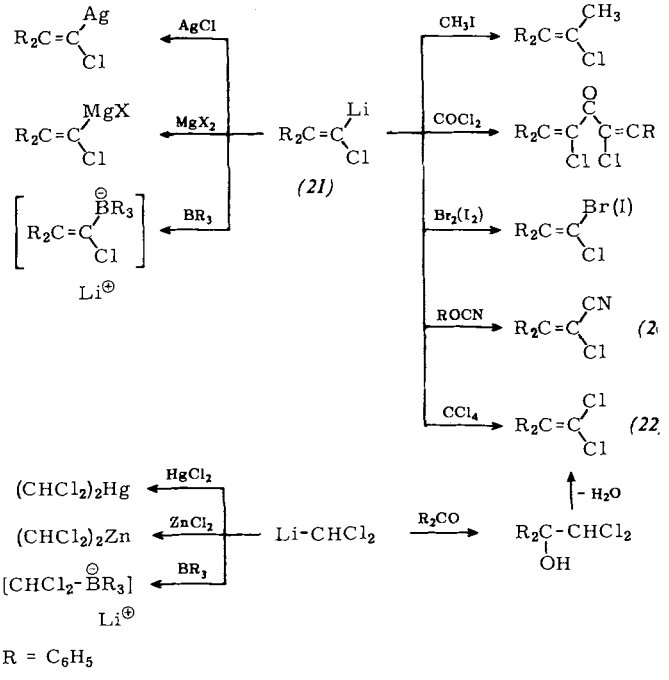
The "active" role in the anionization of other substrates is in contrast to the remarkable case in which a carbenoid is itself metalated. The compound *(23)*, which can be prepared from 1,2,3,4-tetrachlorobutadiene and butyl-lithium at −110 °C, reacts with a second mole of butyl-lithium to form *(24)*, which is isolated in high yield as the dicarboxylic acid *(25)*, m.p. 207–208 °C [25].



3. Nucleophilic Reactions

The stable carbenoids prepared by the methods discussed can undergo the nucleophilic reactions of "normal" organolithium compounds.

The formation of carboxylic acids is generally the best method of characterization, since the carboxylation proceeds to completion. A number of other reactions, all of which are probably generally applicable, are indicated in Scheme 1. These include alkylations, acylations, and halogenations [26]. Corresponding to the reaction of phenylmagnesium bromide with esters of cyanic acid [29], *(21)* reacts with naphthyl cyanate to give the nitrile *(26)* [30]. The reaction of dichloromethyl-lithium with diaryl ketones yields alcohols, which can be readily dehydrated to form diaryldichloroethylenes



Scheme 1. Nucleophilic reactions of carbenoids.

[26] *G. Köbrich* and *H. Trapp*, Chem. Ber. *99*, 670 (1966).

[27] *R. H. Fischer*, unpublished.

[28] *A. Akhtar*, unpublished.

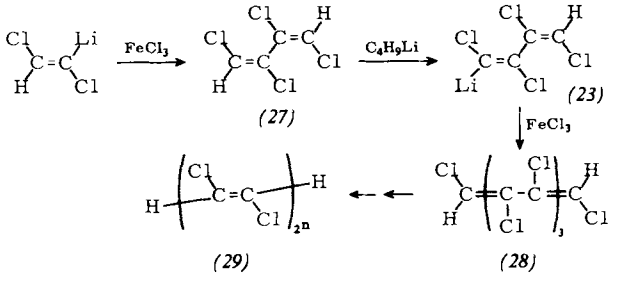
[29] *E. Grigat*, *R. Pütter*, and *E. Mühlbauer*, Chem. Ber. *98*, 3777 (1965); *D. Martin* and *S. Rachow*, ibid. *98*, 3662 (1965).

[30] *H. Trapp*, unpublished.

(22) [18,19] providing a convenient route to these compounds.

Special mention should be made of the reaction with derivatives of other metals which yields new α-halogeno-organometallic compounds [18,22,26,31–33]. Because of the well-known metathesis of the alkali metal compounds with salts of less electropositive metals [34], this reaction offers a route to a wide range of compounds having potential carbenoid character, starting from the lithium compounds.

The metal compounds of Scheme 1 are thermally more stable than the corresponding lithium derivatives. Others decompose immediately on formation. For example, *trans*-dichlorovinyl-lithium and iron(III) chloride react stereospecifically, presumably *via* an organo-iron intermediate that decomposes by a radical mechanism, to give the hitherto unknown isomer *(27)* of 1,2,3,4-tetrachlorobutadiene in good yield. This compound, which exhibits strong steric hindrance, dimerizes to 1,2,3,4,5,6,7,8-octachloro-1,3,5,7-octatetraene *(28)*, m.p. 54.5–55.5 °C, on reaction first with butyl-lithium and then with iron(III) chloride.

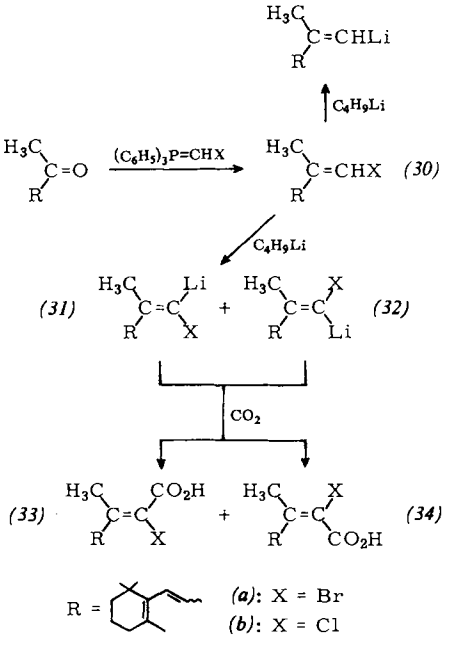


Longer-chain chloropolyenes of the general structure *(29)* can be synthesized by the same method [25].

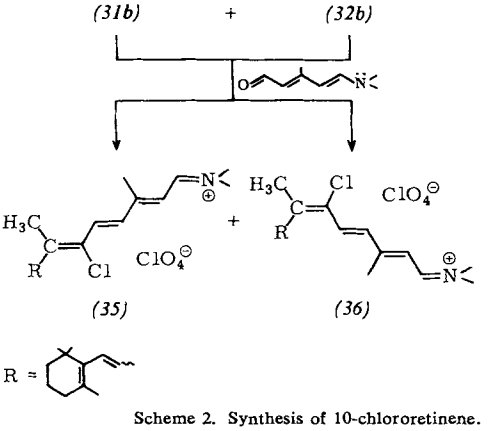
The nucleophilic reactions indicated in Scheme 1 are, in principle, typical organometallic reactions. The higher rate of these reactions in tetrahydrofuran (compared to diethyl ether), largely compensate for the very low reaction temperature.

If α-elimination is prevented by the use of sufficiently low temperatures, the stabilizing effect of the α-halogen on the C–Li bond becomes evident, as shown by the following example.

Ionylidenebromomethane *(30a)* and -chloromethane *(30b)* are readily obtainable [16,18] by Wittig halogeno-olefination [35]. When *(30a)* is treated with butyl-lithium in tetrahydrofuran at –95 °C, the principal product should be ionylidenemethyl-lithium, resulting from a Br/Li exchange. Owing to its tendency to polymerize, however, this product cannot be isolated, whereas the α-bromo compounds *(31a)* and *(32a)* formed by metalation can be detected by carboxylation to form *(33a)* and *(34a)* [15]. In the same way, the stereoisomeric α-chloroionylideneacetic acids *(33b)*, m.p. 124 °C, and *(34b)*, m.p. 99–100 °C, can be obtained from the chloro compound *(30b)* in a total yield of 82 % [16].



The stability of these carbenoids provides a basis for a new, simple synthesis of compounds of the vitamin A series [16,36]. The reaction of *(31b)* and *(32b)* with 3-methyl-5-dimethylaminopentadienal [37] followed by the action of perchloric acid gives a 68 % yield of the dimethylimonium perchlorates of all-*trans*- and 9-*cis*-10-chlororetinene *(35)* and *(36)* (Scheme 2), which can be readily converted into other derivatives whose structures have been verified by spectroscopic methods.



Scheme 2. Synthesis of 10-chlororetinene.

4. Solvent Effect and Thermal Stability

Some carbenoids, *e.g.* trichlorovinyl-lithium, α-chlorovinyl-lithium, and the norcarane derivative *(11)*, decompose more or less rapidly in tetrahydrofuran even

[31] *H. R. Merkle*, unpublished.

[32] *G. Köbrich, H. Fröhlich*, and *W. Drischel*, J. organometallic Chem. *6*, 194 (1966).

[33] *G. Köbrich* and *H. R. Merkle*, Chem. Ber. *99*, 1782 (1966).

[34] *H. Gilman* and *J. M. Straley*, Recueil Trav. chim. Pays-Bas *55*, 821 (1936).

[35] *G. Wittig* and *M. Schlosser*, Chem. Ber. *94*, 1373 (1961); *G. Köbrich*, Angew. Chem. *74*, 33 (1962); Angew. Chem. internat. Edit. *1*, 51 (1962).

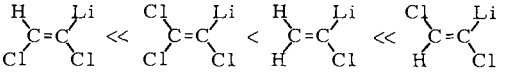
[36] *W. E. Breckoff*, Dissertation, Universität Heidelberg, 1964.

[37] *G. Köbrich*, Liebigs Ann. Chem. *648*, 114 (1961).

at temperatures below −100 °C. Others, such as dichloromethyl-lithium and 1,2-*trans*-dichlorovinyl-lithium, decompose only at a moderate rate at −30 °C. The most stable carbenoid is fluorenylidenebromomethyl-lithium, which can be detected as the carboxylic acid even at room temperature.

The stability is determined by the nature of the α-halogen, the nature of the α- and possibly β-substituents, and the solvent. No accurate comparative measurements on the influence of the α-halogen have been made. However, chloro derivatives are generally more stable than the corresponding bromo compounds.

Statements about substituent effects are naturally possible and meaningful only if the compounds in question decompose by the same mechanism. This is the case for carbenoids of the type *(5)*; these compounds are increasingly destabilized by electron-donating substituents in the β-aryl groups. On the other hand, the order of stability of the compounds as determined in tetrahydrofuran, *i.e.*:

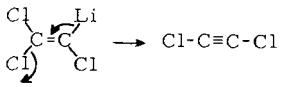


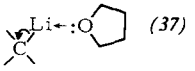
suggests that in spite of their structural similarity, they decompose by different routes [20] (see below).

A decisive factor with regard to the easy accessibility of the carbenoids is the use of tetrahydrofuran as the solvent. This substance fulfils two functions. Comparison with diethyl ether shows that tetrahydrofuran enables or accelerates the formation of the carbenoids, and particularly the metalation at low temperature. A more important point, however, is the fact that the carbenoids formed are much more stable in tetrahydrofuran than in ether, as has been shown by direct comparison in numerous cases [15,26,33,38].

The stabilizing influence persists even in admixture with other solvents. Thus dichloromethyl-lithium is stable at −74 °C in pure tetrahydrofuran and in tetrahydrofuran/ether mixtures containing up to 80 vol-% of ether, but cannot be detected in pure ether [33,38]. Consequently, in reactions carried out at temperatures below −100 °C, it is advantageous to use, instead of pure tetrahydrofuran, the "Trapp mixture" of tetrahydrofuran, ether, and light petroleum ether or hexane (4:4:1), which has a low viscosity and still exhibits the favorable influence of tetrahydrofuran.

There is no causal relation between the greater ease of formation of the carbenoids and their greater stability in tetrahydrofuran, so that one does not follow from the other. This is shown by the fact that trichlorovinyl-lithium, which is formed more rapidly in tetrahydrofuran than in ether, also decomposes more rapidly (contrary to the rule) in this solvent [20]. The decomposition mechanism is obviously different from that of the other compounds. The chlorine atoms in the β position and the greater stability of *trans*-dichlorovinyl-lithium point to a *trans*-β-elimination of LiCl [20]





(37)

As in the formation of the carbenoids, the activating influence of tetrahydrofuran on the C–metal bond in organolithium compounds (*e.g.* butyl-lithium) is noticeable [39]. This activation can be explained by the more effective complexing of the lithium atom with the relatively polar tetrahydrofuran, which leads to stronger polarization of the C–Li bond and so strengthens the carbanion character and thereby the nucleophilicity of the molecule [formula *(37)*].



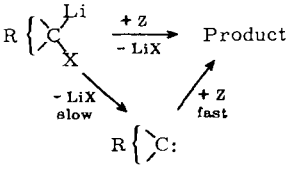
(3)

The nucleophilic character of the carbenoids is, in principle, weaker than that of the other organolithium compounds, owing to the interaction of the C–Li bond with the halogen in the α-position; however, it is also strengthened by tetrahydrofuran, so that if this were the factor determining the stability, the carbenoids should decompose more rapidly. However, the thermal decomposition is due to electrophilic reactions of the carbenoid carbon, as shown in the next section, and the retardation of these reactions by tetrahydrofuran is the reason for the thermal stability of the substrates in this solvent.

5. Electrophilic Reactions

Most of the reactions in which the carbenoid carbon behaves electrophilically are known as secondary reactions of organometallic α-eliminations [9,40], so that the question of primary interest is whether this behavior is due to the carbenoids themselves or perhaps to carbenes formed from them by elimination of lithium halide.

A carbene formed in a preliminary step would react rapidly with a nucleophile Z. The rate of formation of the end product would thus be determined by the slow carbene-formation step, and unlike the rate of a direct reaction of the carbenoid with Z, it should be affected neither by the nature nor by the concentration of the nucleophile Z [eq. (1)].



(1)

[38] *G. Köbrich, H. R. Merkle,* and *H. Trapp,* Tetrahedron Letters *1965,* 969.

[39] See, *e.g., H. Gilman* and *R. D. Gorsich,* J. Amer. chem. Soc. *79,* 2625 (1957); *G. Wittig,* Angew. Chem. *70,* 65 (1958); *H. D. Zook* and *T. J. Russo,* J. Amer. chem. Soc. *82,* 1258 (1960); *L. I. Zakharkin, O. Yu. Okhlobystin,* and *K. A. Bilevitch,* Tetrahedron *21,* 881 (1965).

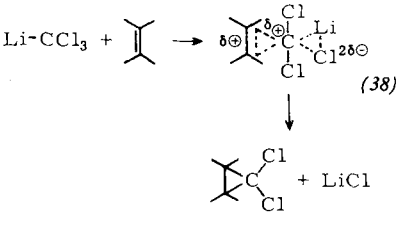
[40] *G. Köbrich,* Angew. Chem. *77,* 75 (1965); Angew. Chem. internat. Edit. *4,* 49 (1965).

A carbene (and also an intermediate in which the C-halogen bond is merely ionized) has an unoccupied p-orbital, and so has a higher symmetry than the substrate. Consequently, the stereochemistry of suitable carbenoid reactions provides a second criterion of the mechanism.

a) Formation of Dichlorocyclopropanes from Trichloromethyl-lithium and Olefins

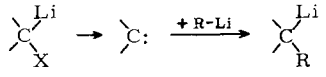
This reaction, which has also been studied by two American research groups [23,24], is more complex than was originally thought. The trichloromethyl-lithium produced from bromotrichloromethane in diethyl ether undergoes several secondary reactions even at temperatures below −100 °C. It is therefore difficult to decide whether the formation of 7,7-dichloronorcarane observed under these conditions with cyclohexene [23] is due to a reaction of trichloromethyl-lithium itself or of an initially formed cleavage product [41]. Trichloromethyl-lithium is stable in tetrahydrofuran at −100 °C, but it is also inert towards cyclohexene under these conditions. However, its slow decomposition in this solvent at −72 °C is accelerated by cyclohexene and other olefins. Moreover, the difference between the amount of decomposition with and without cyclohexene roughly corresponds to the yield of 7,7-dichloronorcarane. In view of these results it is probable that trichloromethyl-lithium can react with olefins without first decomposing to dichlorocarbene, and that this cyclopropane formation competes successfully with other reactions of the carbenoid [41].

From the fact that dimethyl-2-butene reacts more rapidly than *cis*- or *trans*-2-butene, each giving only one cyclopropane, it may be concluded that the reaction with the olefin is electrophilic and stereospecific. A cyclic transition state *(38)* offers a plausible interpretation of these observations. It differs from that formulated for the cyclopropane formation from dichlorocarbene in that lithium halide is also present.

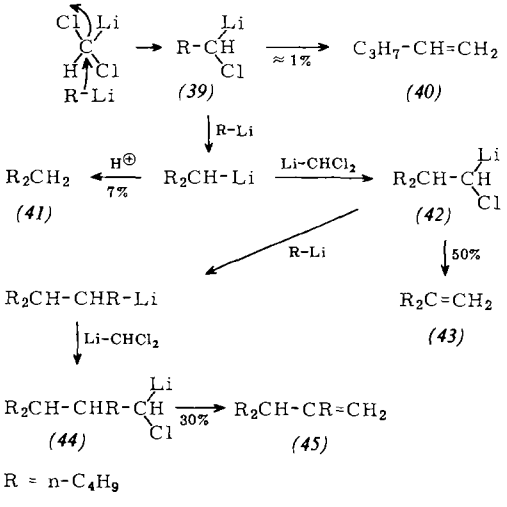


b) Reaction of Dichloromethyl-lithium with n-Butyl-lithium

The α-elimination from halohydrocarbons with organolithium compounds frequently leads to products in which the organic residue of the organolithium is attached to the carbenoid carbon [9]. This type of reaction leads *e.g.* to the formation of trityl-lithium from chloroform and excess of phenyl-lithium [10] or to 1-pentene from dichloromethane and butyl-lithium [42]. It was originally formulated as a direct substitution of halogen in the metalated halogenohydrocarbon [10], but after development of the carbene concept it was regarded as an insertion of the initially formed carbene in the C–Li bond of the organometallic compound.



We found [33] that dichloromethyl-lithium enters into a smooth multistep reaction with n-butyl-lithium in tetrahydrofuran at −74 °C to give the hydrocarbons *(40)*, *(41)*, *(43)*, and *(45)*. According to Scheme 3, the first step is the replacement of a halogen by butyl to form α-chloropentyl-lithium *(39)*. This reaction takes place under conditions in which dichloromethyl-lithium is thermally stable, and so does not proceed *via* chlorocarbene. The second halogen in the intermediate *(39)* is also preferentially replaced by butyl in a fast reaction; elimination of LiCl and hydrogen shift with formation of 1-pentene *(40)*, which is the principal reaction path in ether [42], is almost completely suppressed in tetrahydrofuran. This can be explained by the lower electrophilicity of *(39)* and the greater nucleophilicity of butyllithium in tetrahydrofuran. It is only in the higher condensation products *(42)* and *(44)* that the hydrogen, owing to its position on a tertiary carbon atom, is sufficiently mobile to be able to compete successfully with the intermolecular chloride substitution.



Scheme 3. Course of the reaction of dichloromethyllithium with n-butyl-lithium.

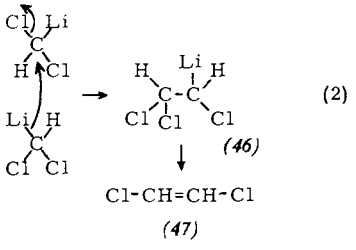
c) Dimerizing α-Elimination

The formation of carbene dimers is well known from a variety of carbene or carbenoid reactions, and is also observed during the thermal decomposition of several carbenoids in tetrahydrofuran. For example, dichloromethyl-lithium gives 1,2-dichloroethylene (which then

[41] *G. Köbrich, K. Flory*, and *R. H. Fischer*, Chem. Ber. *99*, 1793 (1966); *G. Köbrich, K. Flory*, and *H. R. Merkle*, Tetrahedron Letters *1965*, 973.

[42] *G. L. Closs* and *L. E. Closs*, J. Amer. chem. Soc. *81*, 4996 (1959); *84*, 809 (1962).

reacts further)[33]. Possibly chlorocarbene is formed and inserted in the C–Li bond of a second molecule of dichloromethyl-lithium (the dimerization of two carbenes need not be considered). According to eq. (1), this reaction should be of the first order. However, dichloromethyl-lithium decomposes with a shorter half-life at higher concentrations than in dilute solution. Thus the dimerizing α-elimination is better considered as a kind of Wurtz-Fittig reaction in which one carbenoid molecule acts as nucleophile, the other as electrophile, followed by a rapid β-elimination of lithium halide[33].



(2)

(46)

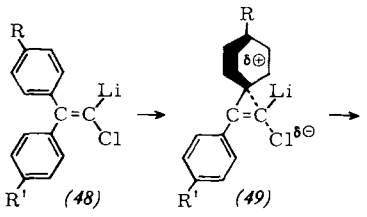
(47)

As expected, the replacement of α-halogen in the carbenoid by the more reactive butyl-lithium takes place at lower temperatures than the dimerizing α-elimination, in which the less nucleophilic carbenoid assumes the role of the nucleophile.

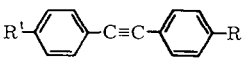
d) Fritsch-Buttenberg-Wiechell Rearrangement

The Fritsch-Buttenberg-Wiechell rearrangement is generally observed during the action of bases on diarylhalogenoethylenes, and involves α-elimination of hydrogen halide and migration of an aryl group to give diarylacetylenes[40]. It was recognized by its discoverer as a sextet rearrangement. However, experiments with labeled *cis-trans*-isomeric starting compounds (as shown in Scheme 4 for another case) have shown that both in alcohols and in ether, migration of the aryl group *trans* to the vinyl halogen to the neighboring carbon atom always predominates[43,44]. This rules out the carbene as a common intermediate, and indicates that the migration of the aryl group and the elimination of halogen takes place simultaneously. On the basis of the analogy to the isoelectronic Beckmann rearrangement, *Bothner-By*[43] postulated that the aryl group undergoes electrophilic attack by the α-carbon atom, so that a transition state *(49)* should occur [eq. (3)]. Thus the rearrangement was the first case in which a distinction was made between a carbene and (in current terminology) a carbenoid mechanism and the latter accepted as correct.

This view has been confirmed by the study of the stable carbenoids *(48)* (R = R')[45]. On thermolysis, these compounds are quantitatively converted into diarylacetylenes *(50)*, the ease of this conversion increasing in



(48) *(49)*

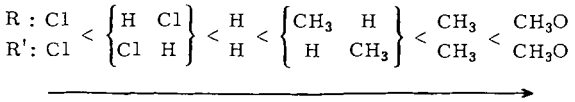


(3)

(50)

the order Cl < H < CH_3 < CH_3O; this corresponds to the order of stabilization of the partial positive charge on the migrating aryl group in the transition state by these groups. The importance of steric factors can be seen from the acceleration of the rearrangement when the *p*-substituent is (formally) moved to the *o*-position.

Surprisingly, the substituent in the stationary aryl group in eq. (3) has approximately the same effect, from the point of view of both direction and magnitude, as that in the migrating group. Thus the ease of rearrangement of a compound in which only one aryl group carries a substituent is intermediate between that of the unsubstituted compound and that of the compound with two substituents of the type in question, and differs only slightly for the two possible pairs of isomers[19]; schematically:



Increasing tendency of *(48)* to rearrange

Thus the greater ease of removal of the α-halogen [formula *(51)*] expected when the stationary aryl Ar' group contains electron-donating substituents is also of



(51)

decisive importance to the rate of rearrangement. Control experiments show that this substituent effect is not due to a rapid *cis-trans* isomerization of the carbenoids.

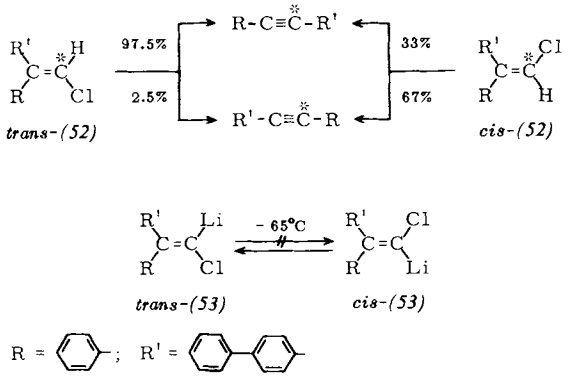
In other cases isomerization of carbenoids is observed, particularly with longer reaction times. This is surprising, since vinyl-lithium compounds without α-halogen are configuratively stable. For example, on slow thermolysis of the carbenoids *(53)* obtained from the two isomeric α-^{14}C-labeled chloroolefins *(52)*, the distribution of radioactivity between the two carbon atoms of the resulting acetylene shows that in the case of *trans-(52)*, the migrating group is almost exclusively the biphenylyl group; in *cis-(52)*, both aryl residues migrate in the statistical ratio of 2:1, the *trans* group (phenyl) again having the advantage. It has been shown that under the experimental conditions, *cis-(53)* is irreversibly converted into *trans-(53)*. The ratio of the rates of the Fritsch-Buttenberg-Wiechell rearrangement and the

[43] *A. A. Bothner-By*, J. Amer. chem. Soc. *77*, 3293 (1955).

[44] *D.Y.Curtin, E.W. Flynn*, and *R. F. Nystrom*, J. Amer. chem. Soc. *80*, 4599 (1958).

[45] *G. Köbrich* and *H.Trapp*, Chem. Ber. *99*, 680 (1966).

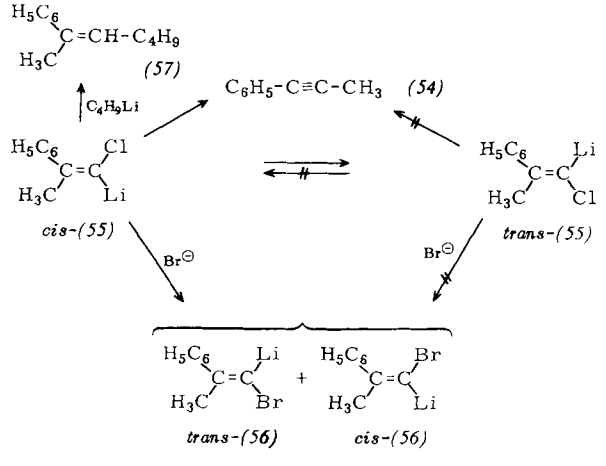
isomerization is approximately 2:1. It must therefore be concluded that the rearrangement step for both carbenoids *(53)* is highly stereoselective or even stereospecific, and that the apparent non-stereospecificity is due to a previous *cis-trans* rearrangement [19].



Scheme 4. Stereochemistry of the rearrangement of labeled chloroolefins.

e) Isomerization and Halogen/Halogen Exchange

Additional information on the stereochemistry of the Fritsch-Buttenberg-Wiechell rearrangement and its relationship with other carbenoid reactions is provided by a study of the two isomeric carbenoids *(55)*, which are obtained quantitatively [17] by metalation of the chloroolefins at −110 °C [46]. At −85 °C, the less stable *cis* compound decomposes slowly with formation of phenylmethylacetylene *(54)*; rearrangement to *trans-(55)* occurs simultaneously. The presence of lithium bromide during this reaction leads by halogen exchange to the formation of both isomers of the bromine compound *(56)*; the coupling product *(57)* is also obtained with butyl-lithium (after hydrolysis).



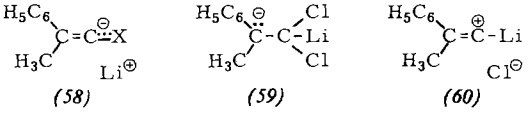
Scheme 5. Carbenoid reactions of *(55)* at −85 °C.

Since migration of a methyl group does not occur under these conditions (see below), and since *trans-(55)* is practically inert at −85 °C, *(54)* must have been formed from *cis-(55)* by *cis*-phenyl migration.

[46] The steric assignment of the substrates is confirmed by UV and NMR spectra.

The activation energy of the "*trans*-migration" that predominates in the β,β-diaryl compounds *(53)* evidently differs only slightly from that of the "*cis*-migration", which was first observed with *cis-(55)*; obviously, even small additional factors can lead to another mechanism. The greater ease of decomposition of *cis-(55)* may be due to a steric effect. It is conceivable that the interaction of the bulkier phenyl group with the chlorine atom facilitates the release of the halogen.

In the isomerization *cis-(55)* → *trans-(55)*, possible intermediates such as *(58)* and *(59)* are shown to be unlikely by solvent and substituent effects. On the other hand, a common intermediate with an ionized C–halogen bond could be responsible both for the isomerization

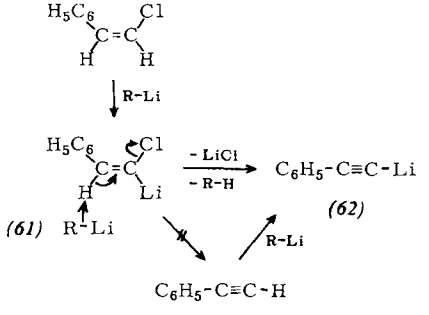


and for the other reactions in Scheme 5. However, this suggestion conflicts with the fact that no products resulting from interception by olefins or tetrahydrofuran can be detected (see below). Moreover, we have seen that isomerization is possible also in the carbenoid *cis-(53)*, in which an intermediate with an unoccupied p orbital, corresponding to *(60)*, is impossible on grounds of symmetry, owing to the stereospecificity of the Fritsch-Buttenberg-Wiechell rearrangement.

f) E2cb Mechanism

Schlosser's investigation of the organolithium-induced elimination of hydrogen chloride from *cis-* and *trans-*styryl chloride provided evidence for a previously unknown type of elimination, which would be described in *Ingold*'s system as an E2cb mechanism [47,48].

Fast metalation of styryl chloride at the chlorinated vinyl carbon atom occurs at the expense of a "classical" β-elimination, as can be shown by kinetic experiments at 0 °C in ether and by the synthesis of the metalated compounds [*e.g. (61)*] in tetrahydrofuran at lower temperatures. However, the decomposition of *(61)* to lithium acetylide *(62)* does not proceed *via* phenylacetylene (with elimination of lithium chloride and hydride shift), as might be assumed by analogy with the



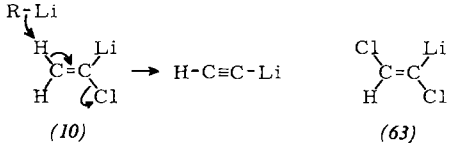
[47] *M. Schlosser* and *V. Ladenberger*, Tetrahedron Letters *1964*, 1945.

[48] *M. Schlosser*, Habilitation Thesis, Universität Heidelberg 1966.

Fritsch-Buttenberg-Wiechell rearrangement or with the H shift that can take place in aliphatic compounds [*e.g.* as in *(42)* → *(43)*]. Instead, the attack of the organolithium base on *(61)* initiates a β-elimination of HCl, which leads directly to the final product.

In the thermal decomposition of *(61)* at −110 °C, a second molecule of *(61)* assumes the function of the base R−Li. Added butyl-lithium or phenyl-lithium accelerate the formation of *(62)*, since these stronger bases can attack the hydrogen of *(61)* more readily. The slower elimination of DCl from the deuterated substrate *(61)* (with D instead of H) also indicates that the rate-determining step is the rupture of the C−H bond.

The fact that *trans*-β-elimination from *trans-(61)* occurs more readily than the *cis*-elimination from the *cis* isomer also explains the greater ease of decomposition of α-chlorovinyl-lithium *(10)* (which is further increased by the presence of butyl-lithium) in comparison with *trans*-dichlorovinyllithium *(63)* (cf. Section 4)[13,20]. Thus, though *(63)* contains a more acidic hydrogen, it does not offer the possibility of *trans*-elimination of HCl.



(10) *(63)*

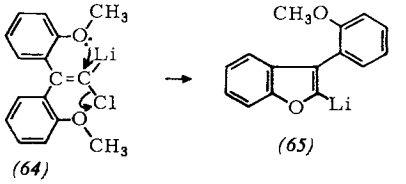
As in the other reactions discussed here, a pair of electrons is supplied to the carbenoid carbon in the step *(61)* → *(62)*, with formation of a new C−C bond and elimination of halogen.

g) Competition Phenomena

Some of the carbenoid reactions described are extremely selective, and in particular those in which the formally underlying carbene is only slightly stabilized by electron-donating substituents, *i.e.* in which the selectivity should be particularly low if the carbene actually occurred as an intermediate. Thus, in the decomposition of *(10)* to lithium acetylide in the presence of an excess of methyl-lithium, no replacement of the α-chlorine atom by methyl [corresponding *e.g.* to the formation of *(57)* from *cis-(55)*] is observed[20]. The thermal decomposition of dichloromethyl-lithium in tetrahydrofuran to 1,2-dichloroethylene (see Section 5c) is so strongly favored that no cyclopropane is formed with added olefins (which are only weakly basic in comparison to organolithium compounds). The reaction of dichloromethyl-lithium with the more nucleophilic butyl-lithium, on the other hand, takes place at −74 °C, and no dimerizing α-elimination occurs. The α-chloropentyl-lithium formed in this reaction (Scheme 3) also reacts selectively with further butyl-lithium; neither the possible reaction with dichloromethyl-lithium nor the intramolecular hydride shift takes place to any appreciable extent[33].

Conversely, reactions in which a relatively "stable" carbene might be expected are surprisingly unselective. Thus in the thermal decomposition of trichloromethyl-lithium or of the norcarane derivatives *(11)* and *(13)*, one observes the dimerizing α-elimination, reaction with olefins and with butyl-lithium, and insertion in the α-C−H bond of the solvent tetrahydrofuran[21,41].

The thermolysis of the carbenoids *(48)* to diarylacetylenes is accompanied by a side reaction only in the case of the methoxy derivative *(64)*; the steric position of the ether oxygen is such that it can replace the α-halogen at −70 °C, as can be deduced from the lithium compound *(65)*, characterized as the corresponding



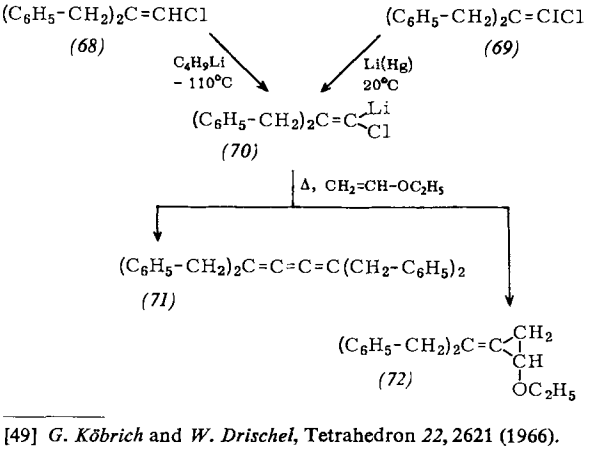
(64) *(65)*

carboxylic acid[45]. Competing intermolecular reactions, such as the dimerizing α-elimination or the reaction with added olefins, do not occur.

On the other hand, the thermal decomposition of the α-chloro silver compounds leads not only to diarylacetylenes, but also to tetraarylbutatrienes [about 30 % of *(67)* from *(66)*][32]. Dimerization actually becomes the main reaction with carbenoids in which the β-positions are occupied by alkyl groups, which cannot rearrange under these conditions. This fact can be utilized for the preparation of tetraalkylcumulenes, which were formerly difficult to obtain.

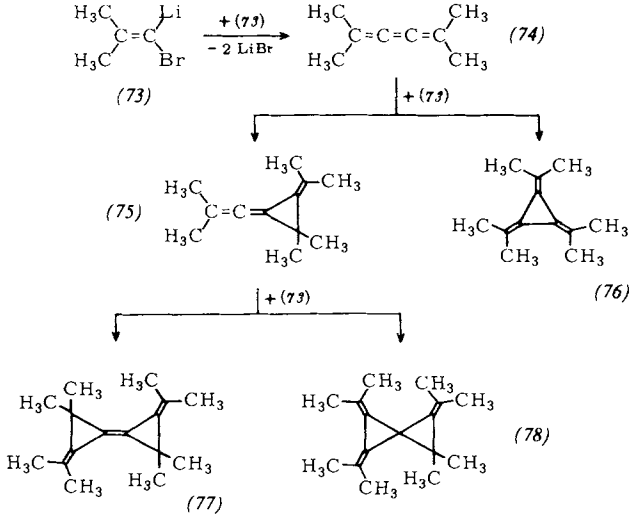
$$(C_6H_5)_2C{=}CAgCl \quad (66)$$
$$\longrightarrow C_6H_5{-}C{\equiv}C{-}C_6H_5 + (C_6H_5)_2C{=}C{=}C{=}C(C_6H_5)_2$$
$$(67)$$

Thus the thermolysis of the carbenoid *(70)*, obtained from *(68)* at −110 °C, leads to tetrabenzylbutatriene *(71)* in good yield. The cyclopropane derivative *(72)* is formed to only a small extent (about 15 %) even in the presence of a 30-fold excess of ethyl vinyl ether. If the carbenoid is produced from the dihalide *(69)* with lithium amalgam at room temperature, the reaction in ether again yields *(71)*, but the reaction in ethyl vinyl ether leads predominantly to *(72)*. Thus in this case the reaction can be made to proceed in one direction or the other by a suitable choice of conditions[22,49].



[49] *G. Köbrich* and *W. Drischel*, Tetrahedron *22*, 2621 (1966).

In the decomposition of the more reactive carbenoid *(73)*, even the initially formed cumulene *(74)* can act as an olefin with *(73)* if the latter is produced under conditions such that it is sufficiently reactive. Of the resulting oligomers *(75)–(78)* of "isopropylidenecarbene", triisopropylidenecyclopropane *(76)* is particularly interesting as the first and very stable [3]-radialene [50].



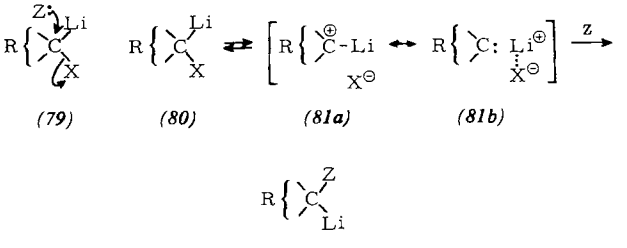
h) Mechanism

All the results indicate that no carbene intermediates are formed in the reactions discussed. Two extreme cases are conceivable for the substitution of the α-halogen in a carbenoid by a nucleophile Z:

1. The reaction proceeds by a synchronous mechanism as in "normal" S_N2 reactions [formula *(79)*].

2. Compound *(80)* first undergoes a fast, reversible reaction to give an intermediate [*(81a)*, *(81b)*], which then reacts with the nucleophile Z. This two-step process would be formally comparable with "normal" S_N1 reactions *via* carbonium ions.

Formulae *(81a)* and *(81b)* differ only in the bonding between the lithium and the carbon. They are best regarded as canonical structures of a single species. The intermediate *(81)* differs from the substrate *(80)* in that the C–halogen bond is ionized, and from a carbene in the inclusion of lithium halide in the same solvent cage. Structure *(81)* seems to be a logical formulation for the "carbene complex" sometimes discussed in the literature [51].



(79) *(80)* *(81a)* *(81b)*

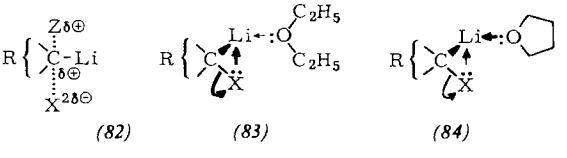
However, neither of the two extremes [*(79)* and *(81)*] can explain all the experimental results. The contradiction is that in substrates in which a build-up of negative charge occurs on the carbenoid reaction center owing to electron-donating substituents, the approach of the nucleophile Z should be difficult and reactions of the S_N2 type should therefore be hindered. On the other hand, the stability of the intermediate *(81)* in a carbenoid reaction of S_N1 type, and hence also its selectivity in secondary reactions, should increase with increasing compensation of the positive charge by electron-donating substituents. Neither of these expectations is confirmed by experiment. Further, in the Fritsch-Buttenberg-Wiechell rearrangement, in which the substituent effects point to the S_N1 type, the intermediate *(81)* can be ruled out on stereochemical grounds.

This leads us to assume that the carbenoid reactions discussed take place somewhere between the extremes indicated by the formulae *(79)* and *(81)*; this assumption is readily compatible with the experimental results:

In the reaction of a carbenoid with a nucleophile Z, the rupture of the C–halogen bond is faster than the formation of the bond between C and Z. Thus in the transition state *(82)*, the carbon carries a partial positive charge (if we assume for the moment that partial negative charge due to the lithium atom is constant). The later the energy-supplying bond between C and Z is formed, *i.e.* the weaker the nucleophilic character of Z, the greater will be the positive charge, and hence the energy of the transition state.

If there are no electron-donating substituents available to stabilize the partial charge on the carbon, the nucleophilicity of Z becomes the dominant factor. Thus the reaction with a strong nucleophile Z (*e.g.* butyllithium), which approaches the S_N2 extreme, is possible under conditions such that the reaction with a weaker nucleophile, which involves a higher positive charge on the carbenoid carbon (*e.g.* the insertion in the α-C–H bond of tetrahydrofuran or the formation of cyclopropanes with olefins), does not yet take place. These reactions are therefore very selective.

With increasing stabilization of the positive charge on the carbenoid carbon by (inductively or mesomerically) electron-donating substituents R (and possibly also by their steric interaction with the α-halogen), the release of the halogen becomes easier and the energy requirement of the transition state *(82)* is reduced. Carbenoid reactions, even with weaker nucleophiles, are then possible under relatively mild conditions. The reaction then approaches the S_N1 extreme, for which the selectivity should be lower, since the nucleophilic strength of Z is



(82) *(83)* *(84)*

[50] *G. Köbrich* and *H. Heinemann*, Angew.Chem.77, 590 (1965); Angew. Chem. internat. Edit. *4*, 594 (1965); *G. Köbrich, H. Heinemann*, and *W. Zündorf*, Tetrahedron, in press.

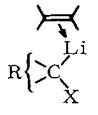
[51] The dissociation of one of the two ligands, lithium or halogen, can probably be ruled out in view of the low polarity of the solvent.

less important in this case. This type probably includes in particular the reactions of those carbenoids which can insert in the α-C–H bond of tetrahydrofuran, such as trichloromethyl-lithium and the norcarane derivatives *(11)* and *(13)*.

So far we have ascribed only a minor role (which is certainly inadmissible) to the C–Li bond. It was assumed as early as 26 years ago that the high polarity of this bond (*i.e.* the carbanion character of the carbenoid carbon) is responsible for the easy release of the α-halogen [10]. An increase in the s character of the metal-bonding electron pair evidently leads to an increase in the p character of the halogen-bonding orbital.

It may be assumed that the metal-bonding electron pair already interacts with the subsequent bond partner in the transition state of the cyclopropane formation from olefins (and possibly also in the Fritsch-Buttenberg-Wiechell rearrangement). A more important and more general role is evidently assumed by the lithium atom itself. Owing to its (potential) cationic and hence Lewis-acid character, it interacts with the lone pairs of the α-halogen and so withdraws the halogen from the carbenoid carbon. Thus the push provided by Z is supplemented by the pull of the lithium. The pull effect decreases when the Lewis-acid character of the lithium atom is reduced by solvation with a more polar medium [formulae *(83)* and *(84)*]. This explains why the thermal stability of carbenoids is greater in tetrahydrofuran than in the less polar ether [38,41]. The smooth formation of cyclopropanes from olefins in non-polar solvents [9] also agrees with this view. The strong pull of the lithium atom on the α-halogen provides the high positive charge on the carbenoid carbon required for the attack of the weakly nucleophilic olefin.

Presumably, nucleophilic substances such as olefins [c.f. (85)] are first attached to the lithium atom before



(85)

reacting with the carbon atom of the carbenoid. The displacement of a solvent molecule thus entailed is no doubt more difficult in the case of tetrahydrofuran than for less powerful solvating media. This is a further possible reason for the apparent reluctance of carbenoid reactions to take place in tetrahydrofuran. It is by no means the sole reason, as can be seen from the fact that the intramolecular Fritsch-Buttenberg-Wiechell rearrangement is subject to the same solvent effects.

6. Future Prospects

It appears that the synthesis of stable carbenoids offers attractive possibilities for preparative organic chemistry and makes available new methods for the study of reaction mechanisms. However, it would be wrong to consider the class of compounds described here in isolation. It is to be expected, and has been proved in several cases, that analogous chemical behavior will be found with substrates *(3)* containing metals other than lithium and leaving groups other than halogen. For example, the α-halogenoorganozinc compounds [*(3)*, M = Zn/2], which have been extensively studied, can enter into typical carbenoid reactions such as cyclopropane formation with olefins (Simmons-Smith reaction), dimerizing α-elimination, and intramolecular C–H insertion [6,7]. However, in view of the differences in valence and bonding, the relative importance of the various factors discussed can scarcely be expected to be the same as for the lithium compounds.

Many other metal derivatives are obtainable directly [52] and now also indirectly. Thus paths are indicated for the further development of this field.

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Trifluorophosphine Complexes of Transition Metals[**]

BY TH. KRUCK[*]

The present paper deals with a new class of inorganic coordination compounds, the first member of which, tetrakis(trifluorophosphine)nickel(0), was discovered in 1951. Not only have the neutral metal(0) trifluorophosphines been prepared, but also a number of their derivatives (trifluorophosphinemetal hydrides and trifluorophosphinemetallates, as well as nitrosyl, carbonyl, halogeno, and aromatic trifluorophosphine complexes). These compounds have been characterized by their chemical behavior and by spectroscopic and magnetochemical studies. Trifluorophosphine has the strongest π-acceptor properties of all neutral ligands, and is therefore particularly suitable for the stabilization of unusually low oxidation states (zero and negative) of transition metals.

I. Introduction and Statement of Problem

Until about 1951, the metal carbonyls occupied a special place in coordination chemistry by virtue of their stoichiometric composition and their physical and chemical properties. The discovery of ferrocene, however, then led to a rapid development of organometallic chemistry, in which other unsaturated carbon compounds displaced carbon monoxide from its special position. It is well known that aromatic compounds and olefins, as well as isonitriles and acetylenide and cyanide ions, can stabilize the oxidation state zero in transition metal compounds.

It was recognized that an important condition for the stability of complexes M^0L_n is the possibility of formation of double bonds between the central transition metal atom M and the ligand L. However, it appeared unlikely that this ability should be confined to unsaturated carbon compounds, as was shown *inter alia* by the existence of nitrosyl[1] and bipyridyl complexes[3] and of carbonyl derivatives containing organo-substituted or chloro-substituted ligands of trivalent phosphorus and its homologues[2]. No purely inorganic ligand had been found that, like carbon monoxide, forms a system of homogeneous inner-orbital complexes with a large number of transition metals in the oxidation state zero.

The insight gained, mainly in the last two decades, into bonding, *e.g.* in metal carbonyls, indicated that a neutral inorganic molecule would have to satisfy the following further requirements if it were to be capable of stabilizing the lowest oxidation states of transition metals:

a) The molecule L must possess a lone pair in order to form a coordinate L→M σ bond (donor function);

b) the molecule must also have available unoccupied π orbitals of suitable energy and symmetry to accept the electronic back-donation (M→L), which relieves the metal of the negative charge placed on it by the σ bond (acceptor function); and

c) its steric structure must favor the establishment of a coordination number *n* that satisfies the "inert gas rule".

The question immediately arises of the extent to which the simultaneous donor and acceptor properties of a ligand affect its ability to form complexes. One extreme, that of pure donor ligands (*e.g.* amines NR_3), has been extensively studied. Tertiary amines are particularly suitable for complex formation with transition metals in medium positive oxidation states. Carbon monoxide, the donor and acceptor properties of which are almost equal, forms homogeneous coordination compounds with metals in the (formal) oxidation states +1, 0, −1, and −2, but the complexes with the oxidation states −1 and −2 in particular, *i.e.* the carbonylmetallates, are extremely sensitive to oxidation. Even of the metal carbonyls and the metal carbonyl cations, only a few are stable to about 150 °C. On the other hand, ligands whose bonding to the transition metal depends mainly on their acceptor properties have not so far been considered.

In view of the requirements a) to c), the most electronegative carrier of a lone pair of electrons is trivalent phosphorus. Not only are the donor properties of this atom most effectively weakened by fluorine, but the acceptor properties of its 3d orbitals are also most strongly enhanced. Thus trifluorophosphine, as a typical π acceptor, should stabilize the lowest oxidation states (zero and negative) of transition elements to a greater extent than any of the usual ligands; on the other hand, the preparation of homogeneous cationic trifluorophosphine complexes seems problematical.

These arguments were supported by the existence of tetrakis(trifluorophosphine)nickel, $Ni(PF_3)_4$, which is more stable than the analogous tetracarbonylnickel[4]. For the past three years, therefore, we have been studying the ability of trifluorophosphine to form complexes with numerous transition metals. These investigations, which have led to the discovery of a new class of coordi-

[*] Prof. Dr. Th. Kruck
Anorganisch-Chemisches Institut
der Technischen Hochschule München
New address:
Anorganisch-Chemisches Institut der Universität
Zülpicher Straße 47
5 Köln (Germany)

[**] Based on lectures delivered in 1965 at Erlangen, Köln, and Düsseldorf.

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[2] For a review, see: *G. Booth*, Advances inorg. Chem. Radiochem. *6*, 1 (1964).

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nation compounds, have already shown that this molecule fulfils our highest expectations. The metal compounds of trifluorophosphine that are known at present are therefore reviewed in this article.

II. General Remarks

Trifluorophosphine has a trigonal-pyramidal structure (P–F distance = 1.535 Å), and the F–P–F angle is 104 ° [5], *i.e.* almost tetrahedral, owing to a high component of sp^3 hybridization. PF_3 is a poisonous gas, which burns in air in the presence of nitric oxide as a catalyst [7]. Like carbon monoxide, PF_3 forms a complex with the hemoglobin of human blood [6], but this complex is destroyed by hydrolysis within a few minutes. Some of the most important properties of trifluorophosphine are compared with those of carbon monoxide in Table 1.

Table 1. Properties of trifluorophosphine and carbon monoxide.

	PF_3	CO
Color	colorless	colorless
Odor	odorless	odorless
Melting point (°C)	−151.5	−199
Boiling point (°C)	−101.8	−191.5
Critical temperature (°C)	− 2.1	−140.2
Critical pressure (atm)	42.7	34.5
ΔH (kcal/mole)	− 71 (OPF_3)	− 67.6 (CO_2)
Dipole moment (D)	1.025	0.10
Flame color	yellowish	blue

The expansion of the preparative chemistry of trifluorophosphinemetals was made possible only by the development of a special high-pressure technique [14]. Since large quantities of pure trifluorophosphine were required, an economical laboratory preparation of PF_3 was developed at the same time [8]. This method is based on the fluorination of phosphorus trichloride with zinc fluoride [9]:

$$2\ PCl_3 + 3\ ZnF_2 \rightarrow 2\ PF_3 + 3\ ZnCl_2$$

The preparation is carried out in a modified Kipp's apparatus connected to washing and drying apparatus, and permits the generation of 150 to 200 ml of pure liquid trifluorophosphine per day with a single charge of reactants and without supervision

Trifluorophosphine can also be prepared by fluorination of PCl_3 with AsF_3 [10], HF [11], or benzoyl fluoride [12], by cleavage of $P(OC_6H_5)_3$ with benzoyl fluoride [12a], and by the reaction of red phosphorus with HF at 500 °C [13].

The high-pressure reactions are carried out as described earlier [14] in copper- or silver-coated electrically heated rotating autoclaves. Since the P–F bonds of trifluorophosphine and its metal compounds are slowly hydrolysed in moist air, the investigations are carried out in an atmosphere of dry nitrogen.

III. Metal(0) Trifluorophosphines [15]

The structure of the metal trifluorophosphines $[M(PF_3)_n]_x$ ($x = 1$ or 2 in all compounds known at present) is substantially identical with that of the metal carbonyls. Their stoichiometric composition can therefore be explained by *Sidgwick*'s "effective atomic number rule" [16], according to which stable complexes with trifluorophosphine must exist if the central metal atom can achieve an effective electronic configuration corresponding to that of the next inert gas in the periodic system by accepting the electron pairs from the phosphorus atoms of n PF_3 groups.

Metals with even atomic numbers should therefore give mononuclear metal trifluorophosphines, as was in fact found for all the metals of Group 6 B and Group 8 (see Table 2). These mononuclear complexes are diamagnetic and coordinatively saturated. The trifluorophosphine complexes of metals having odd atomic numbers (Groups 5 and 7, and some of Group 8), according to this structural principle, must be at least binuclear (*e.g.* by formation of a metal-metal bond as in the formula $(PF_3)_nM–M(PF_3)_n$ [17]) for the central metal atom to achieve the inert gas configuration. For reasons of time alone, however, only three crystalline diamagnetic trifluorophosphine complexes of such metals have so far been prepared; these are the violet, highly volatile cobalt compound $[Co(PF_3)_4]_x$ [18], the orange-red tetrakis(trifluorophosphine)rhodium(0), which is binuclear [19a, 19b], and the colorless pentakis(trifluorophosphine)rhenium(0), which is also dimeric [19c] (see Table 2). The cobalt and rhenium complexes have not yet been so thoroughly characterized as the rhodium compound, but studies on these complexes are in progress.

Though there are still some gaps among the trifluorophosphines of metals having odd atomic numbers, it can already be seen that the transition metals that form trifluorophosphine complexes occupy a closed field in the periodic system.

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[15] The complexes of trifluorophosphine are referred to as "metal trifluorophosphines", and this is the basis of the nomenclature used for their derivatives in the following discussion.

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Table 2. Metal(0) trifluorphosphines.

$Cr(PF_3)_6$ Colorless crystals M.p. 193 °C Subl. 30 °C/10^{-3} mm Decomp. above 300 °C [a]		$Fe(PF_3)_5$ Yellow crystals M.p. 45 °C Subl. 30 °C/10^{-3} mm Decomp. above 270 °C	$[Co(PF_3)_4]_x$ Violet crystals	$Ni(PF_3)_4$ Colorless liquid M.p. −55 °C B.p. 70.5 °C/760 mm Decomp. above 155 °C
$Mo(PF_3)_6$ Colorless crystals M.p. 196 °C Subl. 20 °C/10^{-3} mm Decomp. above 250 °C		$Ru(PF_3)_5$ Colorless crystals M.p. 30 °C Subl. 25 °C/10^{-3} mm Decomp. above 155 °C	$[Rh(PF_3)_4]_2$ Orange-red crystals M.p. 92.5 °C Subl. 20 °C/10^{-3} mm Decomp. above 100 °C	$Pd(PF_3)_4$ Colorless liquid M.p. −41 °C Decomp. above −20 °C
$W(PF_3)_6$ Colorless crystals M.p. 214 °C Subl. 40 °C/10^{-3} mm Decomp. above 320 °C	$[Re(PF_3)_5]_2$ Colorless crystals M.p. 182 °C Subl. 70 °C/10^{-3} mm Decomp. above 228 °C	$Os(PF_3)_5$ [39] Colorless crystals		$Pt(PF_3)_4$ Colorless liquid M.p. −15 °C B.p. 86 °C/730 mm Decomp. above 90 °C

[a] The decomposition points were determined in sealed tubes.

1. Methods of Preparation

Several methods with very different scopes have been found for the preparation of metal(0) trifluorophosphines:

1. The only metal trifluorophosphine known prior to 1963 was tetrakis(trifluorophosphine)nickel, prepared by *Wilkinson* [4] by halogen exchange:

$$Ni(PCl_3)_4 \xrightarrow{SbF_3/SbCl_5} Ni(PF_3)_4$$

In 1961, *Seel et al.* [7] perfluorinated tetrakis(trichlorophosphine)nickel [20] with potassium fluorosulfinate (KSO_2F). However, this method can be used only in the case of nickel, since no homogeneous PCl_3 or PBr_3 complexes of the other metals are known.

2. The classic method for the preparation of the metal carbonyls of the iron metals is based on the direct action of carbon monoxide on the metal [21]. Consequently, after the discovery of tetrakis(trifluorophosphine)nickel, a direct synthesis was attempted under various conditions of temperature and pressure, but at first without success [4, 22]. Recently, however, tetrakis-(trifluorophosphine)nickel was obtained quantitatively at a PF_3 pressure of only 70 atm from nickel powder prepared by thermal decomposition of nickel oxalate [23]:

$$Ni + 4\ PF_3 \xrightarrow[100\ C°]{\geqslant 70\ atm} Ni(PF_3)_4$$

This reaction represents the only direct synthesis of a metal trifluorophosphine so far, and is a further example of the rare direct formation of a nickel(0) complex, NiL_4, from metallic nickel and a compound of trivalent phosphorus [24].

3. A more general preparation involves displacement reactions of suitably coordinated complexes [25]. Ligand exchange under a high PF_3 pressure is particularly successful in the preparation of hexakis(trifluorophosphine)-chromium [26] and hexakis(trifluorophosphine)molybdenum [14]:

$$M(C_6H_6)_2 + 6\ PF_3 \xrightarrow[100-200\ °C]{>200\ atm} M(PF_3)_6 + 2\ C_6H_6\ (M = Cr, Mo)$$

Tetrakis(trifluorophosphine)nickel can also be obtained by ligand displacement:

$$NiL_4 + 4\ PF_3 \xrightarrow{80-300\ atm} Ni(PF_3)_4 + 4\ L$$
$$(L = PCl_3\ [4, 23, 23a],\ L = CO\ [23])$$

and, under mild conditions of temperature and pressure, from $(\pi\text{-}C_5H_5)_2Ni$ and trifluorophosphine [23b, 44].

Except in the case of tetracarbonylnickel, the CO cannot be completely displaced from metal carbonyls (M = Co, Fe, Mn, Cr, Mo) by PF_3 under pressure alone. However, UV irradiation of a mixture of PF_3-substitution products of pentacarbonyliron, $Fe(CO)_{5-x}(PF_3)_x$, or of hexacarbonylmolybdenum, $Mo(CO)_{6-x}(PF_3)_x$, in the presence of trifluorophosphine leads to pentakis(trifluorophosphine)iron [27] or hexakis(trifluorophosphine) molybdenum [27a]. Similar photochemical substitution reactions of metal carbonyls had already been achieved with π [28] and n donors [29]. It may be expected that other metal trifluorophosphines $M(PF_3)_n$ will become available from the metal carbonyls by reaction with PF_3 under pressure to form carbonyltrifluorophosphine-metal complexes (cf. Section VII), followed by photochemically induced total substitution by PF_3 under pressure:

$$M(CO)_n \xrightarrow[>1]{PF_3} M(CO)_{n-x}(PF_3)_x \xrightarrow{PF_3,\ h\nu} M(PF_3)_n.$$

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4. The most important method of synthesis, particularly with respect to simplicity of the starting materials, applicability to a wide range of metals, and high yields, is the "reductive fluorophosphination" of metal salts [30]. This method enabled the preparation of the wide range of trifluorophosphine complexes now known (see Table 3)

This high-pressure method is based on the following principle:

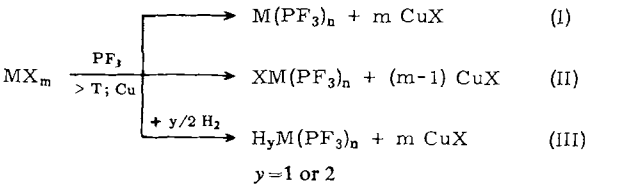


Table 3. Trifluorophosphine complexes prepared by reductive fluorophosphination of metal salts.

Compound	Starting materials and reaction conditions	Yield (%)	Ref.
$Mo(PF_3)_6$	$MoCl_5/Cu,PF_3$ (300 atm) [a],250 °C	15	[31]
$W(PF_3)_6$	WCl_6/Cu, PF_3 (300 atm), 250 °C	12	[32]
$Fe(PF_3)_5$	FeI_2/Cu (Zn),PF_3 (400 atm), 180 °C	70	[33]
$Ru(PF_3)_5$	$RuCl_3/Cu$, PF_3 (400 atm), 270 °C	50	[31]
$Ni(PF_3)_4$	NiI_2/Cu, PF_3 (135 atm), 100 °C	100	[23]
$Pd(PF_3)_4$	$PdCl_2/Cu$, PF_3 (300 atm), 100 °C	*ca.* 80	[34]
$Pt(PF_3)_4$	$PtCl_4/Cu$, PF_3 (40 atm), 100 °C	94	[34]
$[Re(PF_3)_5]_2$	$ReCl_5/Cu,PF_3$(320 atm), > 160 °C	*ca.* 50	[19c,37]
$[Rh(PF_3)_4]_2$	$RhCl_3/Cu,PF_3$ (250 atm), >150 °C	30	[19b]
$HRe(PF_3)_5$	$ReCl_5/Cu$, PF_3 (250 atm), H_2 (100 atm), 300 °C	40	[34a]
$HCo(PF_3)_4$	CoI_2/Cu, PF_3 (50–300 atm), H_2 (100 atm), 170 °C	100	[32]
$HRh(PF_3)_4$	$RhCl_3/Cu$, PF_3 (90 atm), H_2 (100 atm), 70 °C	100	[19a]
$HIr(PF_3)_4$	$IrCl_3/Cu$, PF_3 (160 atm), H_2 (45 atm), 215 °C	100	[35]
$H_2Fe(PF_3)_4$	FeI_2/Zn, PF_3 (300 atm), H_2 (100 atm), 250 °C	traces	[31]
$H_2Ru(PF_3)_4$	$RuCl_3/Cu$, PF_3 (300 atm), H_2 (100 atm), 270 °C	*ca.* 70	[31]
$H_2Os(PF_3)_4$	$OsCl_3/Cu$, PF_3 (400 atm), H_2 (100 atm), 270 °C	*ca.* 80	[31]
$Co(PF_3)_4I$	CoI_2/Cu, PF_3 (70–300 atm), 20 °C	30[b]	[18]
$Re(PF_3)_5Cl$	$ReCl_5/Cu$, PF_3 (250 atm), 160 °C	45	[36,37]
$Fe(NO)_2(PF_3)_2$	$[Fe(NO)_2Br]_2/Cu$, PF_3 (200 atm), 75 °C	90	[38]
$CoNO(PF_3)_3$	$[Co(NO)_2Cl]_2/Cu$, PF_3 (300 atm), 70 °C	46	[38]

[a] Initial pressure at room temperature. [b] Crude yield about 70 %.

An anhydrous metal halide is reduced in an autoclave by a halogen-accepting metal (generally copper or zinc), addition of trifluorophosphine to the metal liberated taking place at the same time under high PF_3 pressure (route I). The temperature and pressure required for this dry reaction depend on the metal. By route II, the process gives a monohalogenated PF_3 complex, particularly with metals having odd atomic numbers; in the presence of other reactants (*e.g.* H_2 or NO), these may even add on to or remain on the metal. The compounds that have been prepared in this way are listed in Table 3.

This process has greatly enriched our knowledge of zerovalent metal complexes, particularly those of ruthenium, osmium [39], palladium, and platinum. Among the homologues of iron, the only known compounds with oxidation state zero were the metal carbonyls $M(CO)_5$ [40] and $M_3(CO)_{12}$ [41], to which were added recently a number of phosphine complexes of ruthenium(0) [42].

The most important outcome of this method was the synthesis of tetrakis(trifluorophosphine)palladium and -platinum [43]; this synthesis can be carried out with $PtCl_4$ [44], $PdCl_2$ [44], $Pd(C_6H_5CN)_2Cl_2$ [23], and $Pd(CO)_2Cl_2$ [45] at relatively low PF_3 pressures and even in the absence of a secondary metal, since trifluorophosphine itself acts as a halogen acceptor in some cases.

These noble metal trifluorophosphines are noteworthy, since only a few other authentic compounds [2] of tetracoordinate Pd(0) and Pt(0) remained when the triphenylphosphine complexes, originally thought to be compounds of Pt(0), were found to be dihydrides of Pt(II) [46]; further, these other tetracoordinate Pd(0) complexes are very unstable. Moreover, no *volatile* complexes of the type M^0L_4 (M = Pd and Pt) have previously been found.

The existence of these tetrakis(trifluorophosphine) complexes also refutes the view [47] that ligands which rely on strong π back-donation are less suitable for the stabilization of the oxidation state zero of palladium and platinum than complex anions such as $[CN]^{\ominus}$ [48] and $[C\equiv C-C_6H_5]^{\ominus}$ [49].

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2. Structure and Properties

Though no detailed X-ray or electron diffraction investigations have been reported, it is fairly certain that the monomeric metal trifluorophosphines are sterically similar to the analogous metal carbonyls. The regular tetrahedral arrangement of the PF_3 groups in tetrakis(trifluorophosphine)nickel was deduced from the Raman spectrum [50]. This is supported by the fact that the IR spectrum, like that of trifluorophosphine itself and those of $Pd(PF_3)_4$ and $Pt(PF_3)_4$ (cf. Table 8), contains only two P–F stretching vibrations. Thus the metal in the tetrakis(trifluorophosphine) complexes is in the sp^3-hybridized state. The infrared spectra of the hexakis(trifluorophosphine) complexes of the chromium group also contain only two P–F stretching bands, demonstrating the regular octahedral coordination of the d^2sp^3-hybridized central atom. The pentakis(trifluorophosphine) complexes of iron and its homologues must be assumed to have a trigonal-bipyramidal structure, simply on the grounds of the strong mutual repulsion of the PF_3 groups. Further evidence of this structure is provided by the absence of a dipole moment and by the ^{19}F-resonance spectrum of the iron compound [31].

The principal physical properties of the mononuclear metal trifluorophosphines are given in Table 2. The strong similarity to the corresponding metal carbonyls is obvious [51]. Features common to all the compounds are their nonpolar behavior and their remarkable stability towards oxidizing agents and moisture. Where their thermal stability is sufficiently high, the trifluorophosphines listed in Table 2 can be steam-distilled without appreciable losses. These heavy metal compounds are distinguished in particular by their volatility which probably results from a mutual repulsion of the molecules due to the high electron density on the ligands. The vapors have musty, stifling odors and cause difficulty in breathing; consequently, care must be exercised in working with volatile trifluorophosphine complexes.

The thermal stability of the metal trifluorophosphines, which is always greater than that of the comparable metal carbonyls should also be emphasized. This stability reaches a maximum with hexakis(trifluorophosphine)tungsten, and decreases from left to right in the periodic table. A striking feature is the stability minimum with the 4d metals. The only metal trifluorophosphine that is unstable at room temperature is $Pd(PF_3)_4$. The thermal decomposition of most of the metal trifluorophosphines leads to deposition of the metal; pentakis(trifluorophosphine)ruthenium appears to give a polynuclear red metal trifluorophosphine above 155 °C.

The compounds are soluble to varying extents in polar and nonpolar organic solvents, but not in water. Only $Fe(PF_3)_5$ exhibits almost unlimited solubility in liquid trifluorophosphine at −105 °C. Dilute or concentrated acids attack the metal trifluorophosphines only when hot, and then only slowly; bases, on the other hand, rapidly hydrolyse the P–F bonds. Ammonolysis of tetrakis(trifluorophosphine)nickel [7] in liquid ammonia leads initially to a colorless solution of the triaminophosphine complex of nickel(0); when this solution is

$$Ni(PF_3)_4 + 24\ NH_3 \rightarrow Ni(P(NH_2)_3)_4 + 12\ NH_4F$$

concentrated, the complex undergoes polycondensation with liberation of NH_3 to form a viscous mass which is evidently the highly polymeric nitride $[Ni(PN)_4]_x$. Similar condensations have been observed with primary amines such as isopropylamine [7].

The most interesting of the complex-chemical properties is the possibility of replacement of the PF_3 groups by donor ligands. Preliminary experiments with the tetrakis(trifluorophosphine) complexes and pentakis(trifluorophosphine)iron showed that the PF_3 groups can be replaced by isonitriles, phosphines, phosphites, tertiary N bases, and even carbon monoxide. The degree of substitution depends on the donor and acceptor properties of the entering ligand, increasing with the acceptor strength.

For example, triphenylphosphine gives the crystalline products $M(PF_3)_{4-x}(PPh_3)_x$ (Ph = phenyl; M = Ni: x = 1 and 2 [23]; M = Pd: x = 2 [52]; M = Pt: x = 1 and 2 [52]) and $Fe(PF_3)_3(PPh_3)_2$ [31]. The weaker donor triphenylphosphite replaces up to three PF_3 groups in tetrakis(trifluorophosphine)nickel, and up to four in tetrakis(trifluorophosphine)platinum. These phosphine and phosphite derivatives (cf. Table 7) are colorless or weakly colored diamagnetic nonelectrolytes, and are therefore true substitution products, in which the characteristic volatility of the metal trifluorophosphines has been lost.

Carbon monoxide, on the other hand, can replace all the PF_3 ligands in tetrakis(trifluorophosphine)nickel [23], (cf. also Section VII).

$$Ni(CO)_4 + 4\ PF_3 \underset{CO(350\ atm)}{\overset{PF_3(350\ atm)}{\rightleftharpoons}} Ni(PF_3)_4 + 4\ CO$$

Even in the final stages of the reactions with triphenylphosphine, the remaining trifluorophosphine can still be displaced by carbon monoxide under pressure.

The ease of substitution of metal trifluorophosphines again increases from left to right in the periodic table. Ease of substitution therefore varies inversely with the stability of the M–PF_3 bonds and the screening of the metal. Thus tetrakis(trifluorophosphine)nickel reacts smoothly with triphenylphosphine, even in boiling benzene, to form the disubstitution product; pentakis(trifluorophosphine)iron gives $Fe(PF_3)_3(PPh_3)_2$ on simultaneous irradiation of the mixture with UV light; and hexakis(trifluorophosphine)chromium is stable towards this donor ligand even under vigorous conditions (150 °C, UV irradiation) [31].

Finally, the reaction of $Pt(PF_3)_4$ with CO under pressure is particularly interesting, since it yields a colorless liquid which

[50] *L. A. Woodward* and *J. R. Hall*, Nature (London) *181*, 831 (1958); Spectrochim. Acta *16*, 654 (1960).

[51] *W. Hieber*, Angew. Chem. *55*, 1 (1942). *J. Chatt, P. L. Pauson*, and *L. M. Venanzi* in *H. H. Zeiss*: Organometallic Chemistry, Amer. chem. Soc. Monograph No. 147. Reinhold, New York 1960, p. 468.

[52] Unpublished work by *Th. Kruck* and *K. Baur*.

is unstable at room temperature (decomposes above about −20 °C), and probably is $Pt(CO)_4$ [36,52]. In view of the stability relationships among the tetrakis(trifluorophosphine) complexes of Ni, Pd, and Pt on the one hand and tetracarbonylnickel and -platinum on the other, it is unlikely that tetracarbonylpalladium can exist under normal conditions, and it is probably obtainable only at low temperatures and high CO pressures.

IV. Trifluorophosphinemetal Hydrides [52a] [*]

The PF_3 complexes of cobalt, rhodium, and iridium are characterized by a strong tendency to form hydrides $HM(PF_3)_4$, which are unusually stable thermally and chemically (see Table 4). The M–H group (M = Co, Rh, or Ir) may be regarded as a "pseudometal atom" (Ni, Pd, or Pt respectively), and the complex hydrides $HM(PF_3)_4$ correspond in many of their physical properties to tetrakis(trifluorophosphine)nickel, -palladium, and -platinum. Tetrakis(trifluorophosphine)ruthenium dihydride and -osmium dihydride, which have only recently been prepared, fit in well, particularly with regard to ease of formation and high thermal stability, with the above compounds $HM(PF_3)_4$, which are the most thoroughly studied so far. Pentakis(trifluorophosphine)rhenium hydride has also been prepared and characterized. The homologous manganese hydride [34a] and even tetrakis(trifluorophosphine)iron dihydride [31] have recently been identified by IR spectroscopy (see Table 4).

Table 4. Trifluorophosphinemetal hydrides and trifluorophosphinemetallates (potassium salts).

$HMn(PF_3)_5$	$H_2Fe(PF_3)_4$	$HCo(PF_3)_4$
	Colorless liquid	Yellowish liquid
Almost colorless liquid	M.p. *ca.* −80 °C	M.p. −51 °C
	$K_2[Fe(PF_3)_4]$	Decomp. above 250 °C
	Colorless crystals	$K[Co(PF_3)_4]$
	Decomp. 205 °C	Colorless crystals
		Decomp. 207 °C
	$H_2Ru(PF_3)_4$	$HRh(PF_3)_4$
	Colorless liquid	Colorless liquid
	M.p. −76 °C	M.p. −40 °C
	Decomp. above	B.p. 89 °C/725 mm
	290 °C	Decomp. slowly above
		20 °C
	$K_2[Ru(PF_3)_4]$	$K[Rh(PF_3)_4]$
	Colorless liquid	Colorless crystals
		Decomp. 145 °C
$HRe(PF_3)_5$	$H_2Os(PF_3)_4$	$HIr(PF_3)_4$
Colorless crystals	Colorless liquid	Colorless liquid
M.p. 42.5 °C	M.p. −72 °C	M.p. −39 °C
Subl. 20 °C/10 mm	Decomp. above	B.p. 95 °C/732 mm
Decomp. above 160 °C	340 °C	Decomp. 246 °C
$K[Re(PF_3)_5]$	$K_2[Os(PF_3)_4]$	$K[Ir(PF_3)_4]$
Colorless crystals	Colorless crystals	Colorless crystals
Decomp. 210 °C		Decomp. 225 °C

[52a] These results were reported to the EUCHEM Conference "Chemistry of Metal Hydrides" in Bristol (England) on April 2nd, 1966, and to the Westdeutsche Chemiedozententagung 1966 in Würzburg (Germany).

[*] *Editors' note*: Binary compounds of hydrogen are known collectively as hydrides regardless of the bonding involved. The term "trifluorophosphinemetal hydrides" for the complexes discussed in this Section is intended as an extension of this definition, without any implication about the metal-hydrogen bonding.

These diamagnetic metal hydrides are monomeric and in most cases readily obtainable by the following principal methods:

1. Reductive fluorophosphination of metal halides in the presence of hydrogen (cf. Table 3), *e.g.*

$$CoI_2 + 2\,Cu + 4\,PF_3 + \tfrac{1}{2}\,H_2 \rightarrow HCo(PF_3)_4 + 2\,CuI.$$

The hydrides of cobalt and its homologues are so readily formed that traces of moisture or any substances containing hydrogen can act as hydrogen donors.

2. Acidification of alkali trifluorophosphinemetallates. This method has also proved suitable for the preparation of the analogous deuterium compounds.

$$K[M(PF_3)_4] + D^{\oplus} \xrightarrow{D_2SO_4} DM(PF_3)_4 + K^{\oplus}.$$

However, the deuterides are also rapidly formed when the hydrogen compounds are shaken with heavy water. The great ease of formation of complex cobalt hydrides containing PF_3 is shown particularly clearly in the synthesis of carbonyltris(trifluorophosphine)cobalt hydride [53] from octacarbonyldicobalt in the presence of hydrogen fluoride or hydrogen on a platinum catalyst:

$$3/2\,[Co(CO)_4]_2 + 6\,PF_3 + 2\,HF \xrightarrow[25\,^\circ C]{500\ atm} 2\,HCo(PF_3)_3CO + CoF_2 + 10\,CO$$

$$[Co(CO)_4]_2 + H_2 + 6\,PF_3 \xrightarrow[Pt,\ 70\,^\circ C]{200\ atm} 2\,HCo(PF_3)_3CO + 6\,CO.$$

Apart from the crystalline rhenium hydride, these substances [including $HCo(PF_3)_3Co$] have low melting points and are mobile liquids under normal conditions. Owing to their high volatility, they can be distilled or sublimed at normal pressure (though losses occur in the case of the rhodium compound). They dissolve readily and without dissociation in nonpolar organic solvents; the solubility in liquid trifluorophosphine decreases in the order Ir, Rh, Co. Their colorless vapors have stifling odors.

Unlike most complex hydrides of transition metals [54], particularly the comparable carbonylmetal hydrides, the trifluorophosphinemetal hydrides and their deuterium analogues are rather inert and have a surprisingly high thermal stability, those of Co, Ir, Ru, and Os being among the most thermostable hydride complexes of the transition metals. For example, Table 5 shows the increase in stability with increasing PF_3 content for cobalt.

Only the rhodium complex slowly loses its hydrogen and part of the trifluorophosphine, even at room temperature, with formation of a deep red, volatile, and apparently polynuclear trifluorophosphinerhodium complex. The relative instability of the metal(0) trifluorophosphines of the second transition series in relation to the lower

[53] *Th. Kruck* and *W. Lang*, Chem. Ber. *98*, 3060 (1965).

[54] Cf. the review article: *M. L. H. Green*, Angew. Chem. *72*, 719 (1960).

Table 5. Decomposition points of trifluorophosphine- and carbonylmetal hydrides.

Compound	Dec. point (°C)	Compound	Dec. point (°C)
$HCo(PF_3)_4$	250 [a]	$HCo(CO)_4$ [55]	−18 [b]
$HCo(PF_3)_3CO$	160 [a]		
$HCo(PF_3)_3(P(C_6H_5)_3)$	193 [a]	$HCo(CO)_3(P(C_6H_5)_3)$ [56]	20
$HRh(PF_3)_4$	140 [a] (slowly > 20) [b]	$HRh(CO)_4$ [57]	−10 [b]
$HIr(PF_3)_4$	246 [a]	$HIr(CO)_4$ [58]	–
$HRe(PF_3)_5$	160 [a]	$HRe(CO)_5$ [58a]	100
$H_2Ru(PF_3)_4$	290 [a]	$H_2Ru(CO)_4$	unknown
$H_2Os(PF_3)_4$	340 [a]	$H_2Os(CO)_4$ [58]	–

[a] Total decomposition. [b] Dehydrogenation.

and higher homologues is thus again found in the hydrogen compounds.

The stability of the trifluorophosphinemetal hydrides towards oxidizing agents is surprising. They generally remain unchanged for several days in dry air; the cobalt compound can even be refluxed for several hours with manganese dioxide without appreciable reaction.

The reactions known at present can be divided into two categories:

1. Formation of Trifluorophosphinemetallates

Except in the case of $HRh(PF_3)_4$, the thermal liberation of hydrogen occurs only at high temperatures and with complete decomposition of the molecule; however, the proton can be removed from all trifluorophosphinemetal hydrides even by weak bases, B, such as tertiary amines, water, tetrahydrofuran, and acetone, with formation of the trifluorophosphinemetallates [19a, 32, 35, 53]. In these bases, the compounds exhibit good electric conductivity, which is due to partial (tetrahydrofuran) or complete dissociation, *e.g.*

$$HM(PF_3)_4 + B \rightarrow [BH]^{\oplus} + [M(PF_3)_4]^{\ominus}.$$

In aqueous systems, the complex hydrides $HM(PF_3)_4$ (M = Co, Rh, Ir) are found to be equally strong acids, comparable in strength to tetracarbonylcobalt hydride. The trifluorophosphinemetal hydrides of the iron group and $HRe(PF_3)_5$ are much less acidic. The anions formed in accordance with the above equation can be precipitated from their solutions by the addition of bulky cations such as $[Cr(C_6H_6)_2]^{\oplus}$ or $[Fe(o\text{-phenanthroline})_3]^{2\oplus}$. The quaternary ammonium trifluorophosphinemetallates, $[NR_3H]$ $[M(PF_3)_4]$, are precipitated when solutions of the complex hydride and of the tertiary amine in petroleum ether are mixed. The colorless pyridinium salt $[C_5H_5NH]$ $[Co(PF_3)_3CO]$ can be sublimed at 40 °C/10^{-3} mm, evidently as a result of thermal dissociation into C_5H_5N and $HCo(PF_3)_3CO$ [59] and recombination on the cooling surfaces [60].

In petroleum ether, the trifluorophosphinemetal hydrides of the cobalt group react even with the very weak Lewis base triphenylphosphine to give the crystalline phosphonium salts $[HP(C_6H_5)_3]$ $[M(PF_3)_4]$, which are also colorless [69].

Thus the acidic nature of the trifluorophosphinemetal hydrides also confirms that PF_3 is similar in its complex chemistry to CO and not to the numerous other phosphine ligands PR_3 (R = organic group), the complex metal hydrides of which possess neither acidic nor basic properties [60a].

In particular, however, the hydrogen of all the trifluorophosphinemetal hydrides can be replaced by alkali metals. The colorless alkali trifluorophosphinemetallates $M_y^I[M(PF_3)_n]$ (y = 1 or 2) are obtained, without cleavage of the P–F bonds, when a solution of a complex hydride in ether is shaken with an alkali metal amalgam; the potassium salts, which crystallize well, are formed readily and mostly quantitatively, *e.g.*:

$$HM(PF_3)_4 + KHg \xrightarrow[20\,^{\circ}C]{(C_2H_5)_2O} K[M(PF_3)_4] + {}^1/_2\,H_2.$$

The carbonyltrifluorophosphinemetal hydrides can be converted similarly into carbonyltrifluorophosphinemetallates, *e.g.* $[Co(PF_3)_3CO]^{\ominus}$ [53].

Trifluorophosphinemetallates can also be obtained by reduction of halogenometaltrifluorophosphines [18, 34a, 37] and of metal(0) trifluorophosphines [19b] with potassium amalgam, *e.g.*

$$ClRe(PF_3)_5 \xrightarrow{KHg} K[Re(PF_3)_5] + KCl$$

$$[Rh(PF_3)_4]_2 \xrightarrow{KHg} 2\,K[Rh(PF_3)_4].$$

The ionic structure of the potassium trifluorophosphinemetallates has been shown by conductivity measurements in acetone, by magnetochemical studies, and by precipitation reactions. The alkali metal salts are diamagnetic; complex salts with the paramagnetic cation $[Cr(C_6H_6)_2]^{\oplus}$ have a magnetic moment of 1.7 B.M. Thus the trifluorophosphinemetallate anions $[M(PF_3)_4]^{y-}$

[55] *W. Hieber* and *H. Schulten*, Z. anorg. allg. Chem. *232*, 29 (1937).

[56] *W. Hieber* and *E. Lindner*, Chem. Ber. *94*, 1417 (1961).

[57] *W. Hieber* and *H. Lagally*, Z. anorg. allg. Chem. *251*, 96 (1943).

[58] *W. Hieber* and *H. Lagally*, Z. anorg. allg. Chem. *245*, 231 (1940); *W. Hieber* and *H. Stallmann*, Z. Elektrochem. angew. physik. Chem. *49*, 288 (1943). Both formulae are assumed since the compound can only be determined qualitatively.

[58a] *W. Beck*, *W. Hieber*, and *G. Braun*, Z. anorg. allg. Chem. *308*, 23 (1961).

[59] This phenomenon is comparable with the dissociation of NH_4Cl during sublimation.

[60] *Th. Kruck*, *W. Lang*, and *A. Prasch*, Lecture at the Westdeutsche Chemiedozententagung, 27–30 April, 1964 in Freiburg (Germany).

[60a] See the summary by *A. P. Ginsberg* in *R. L. Carlin*: Transition Metal Chemistry, Vol. 1. Marcel Dekker, New York 1965, p. 112.

($y = 1$ or 2) are isoelectronic and presumably also isosteric with the tetrakis(trifluorophosphine) complexes of nickel and its homologues

Surprisingly, the potassium salts dissolve in ether, but without dissociation. They are very soluble in water, and give neutral solutions (pH $\approx$ 7). The P–F bonds of these anions readily undergo hydrolytic cleavage, particularly in the case of the rhodium and iridium complexes.

Mention should be made of the stability of the trifluorophosphinemetallates towards oxidizing agents. Even the alkali metal salts can be kept for several days in dry air. This behavior is interesting, since all previously known complexes in which the central metal carries a negative charge, including the carbonylmetallates [61], are extremely sensitive to oxygen, and are often even pyrophoric. The reducing action of the trifluorophosphinemetallates is much weaker than that of the carbonylmetallates. It is not surprising, therefore, that complex salts such as $[M^{+I}(CO)_6][Co^{-I}(PF_3)_4]$ (M = Mn and Re) are stable, whereas the analogous complexes $[M(CO)_6]$ $[Co(CO)_4]$ containing only CO ligands lose CO to form the mixed metal carbonyls $(CO)_5MCo(CO)_4$ even at 20 °C (M = Mn) or 60 °C (M = Re) [62].

The inertness of this complex hydride towards the donor $P(C_6H_5)_3$ is thus in striking contrast to the ease of substitution of the iodine complex $Co(PF_3)_4I$ having the same structure type (cf. Section VI). It is also noticeable that the replacement of the PF_3 group is accompanied by a decrease in thermal stability, whereas the introduction of the ligand $P(C_6H_5)_3$ into $HCo(CO)_4$ increases the stability [56] (cf. Table 5).

The colorless $HCo(PF_3)_3P(C_6H_5)_3$, which is stable in air, reacts quantitatively with potassium amalgam to give potassium tris(trifluorophosphine)triphenylphosphinecobaltate(–I), $K[Co(PF_3)_3P(C_6H_5)_3]$ [18]. The crystalline salt is stable in air, and is hydrolysed by water to the hydrophobic hydride, which is therefore a much weaker acid than $HCo(PF_3)_4$.

3. Structural Relationships

All the trifluorophosphinemetal hydrides exhibit a proton magnetic resonance absorption, characterized by a strong chemical shift to higher field strengths in relation to tetramethylsilane as the internal standard (cf. Table 6). Thus the ^{1}H–NMR signals occur in a range that is generally characteristic of complex transition metal hydrides. These findings indicate that the protons are situated in the immediate neighborhood of the central metal atom, and therefore experience strong diamagnetic shielding. Finally, the splitting of the ^{1}H signal of the rhodium compound as a result of the nuclear spin of the ^{103}Rh nucleus confirms that the hydrogen-metal bonding is covalent.

The covalent nature of the M–H bond in all trifluorophosphinemetal hydrides is confirmed by the M–H stretching vibrations in the 5 μ region of the infrared spectra. The assignment of these weak to medium bands is corroborated by the IR spectra of the deuterium compounds (cf. Table 6).

Table 6. IR and ^{1}H–NMR data for the metal-hydrogen bond in trifluorophosphinemetal hydrides [31, 34a, 35].

Compound	^{1}H-Resonance signal (against $Si(CH_3)_4$)		IR stretching vibrations		$\tilde{\nu}_{M-H}/\tilde{\nu}_{M-D}$	Force constant
	δ (ppm)	J_{M-H} (Hz)	$\tilde{\nu}_{M-H}$ cm^{-1}	$\tilde{\nu}_{M-D}$ cm^{-1}		k_{M-H} (mdyne/Å)
$HCo(PF_3)_4$	12.5		1973	1425	1.384	2.25
$HRh(PF_3)_4$	9.9	$J_{P-H} = 57.4$ $J_{F-H} = 16.6$ $J_{Rh-H} = 5.8$	1992	1431	1.392	2.32
$HIr(PF_3)_4$	11.9	$J_{P-H} = 31.0$ $J_{F-H} = 14.9$	2079	1493	1.393	2.53
$HCo(PF_3)_3CO$	12.7		1978	1428	1.384	2.27
$HCo(PF_3)_3(P(C_6H_5)_3)$	14.8		1944	1400	1.388	2.19
$HFe(NO)(PF_3)_3$	5.87	$J_{P-H} = 23.3$ $J_{F-H} = 10.4$	1900	1370	1.387	2.09
$HRe(PF_3)_5$	8.2		1882	1346	1.397	2.04
$H_2Fe(PF_3)_4$			1935	1396	1.386	2.16
$H_2Ru(PF_3)_4$	8.55	$J_{P_{trans}-H} = 124$ $J_{F_{trans}-H} = 5.5$ $J_{P_{cis}-H} = 16$ $J_{F_{cis}-H} = 4$	1915	1379	1.389	2.14
$H_2Os(PF_3)_4$	10.4	$J_{P_{trans}-H} = 66$ $J_{F_{trans}-H} = 6.5$ $J_{P_{cis}-H} = 19.5$ $J_{F_{cis}-H} = 5$	1996	1436	1.392	2.33

2. Substitution Reactions

Replacement of a PF_3 group in tetrakis(trifluorophosphine)cobalt hydride with triphenylphosphine could be effected by heating for several hours, and was possible only because of the thermal stability of the hydrido complex:

$$HCo(PF_3)_4 + P(C_6H_5)_3 \xrightarrow[\text{Xylene}]{135\,^\circ C} HCo(PF_3)_3P(C_6H_5)_3 + PF_3.$$

[61] For a review, see: *W. Hieber, W. Beck,* and *G. Braun,* Angew. Chem. *72*, 795 (1960).

[62] *Th. Kruck* and *M. Höfler,* Chem. Ber. *97*, 2289 (1964); *Th. Kruck, M. Höfler,* and *M. Noack, ibid. 99*, 1153 (1966); Angew. Chem. *76*, 787 (1964); Angew. Chem. internat. Edit. *3*, 701 (1964).

Evidence of the overall structure of hydrides having an ML_4 molecular skeleton was provided by a comparison of the IR spectra of the isoelectronic complexes $HCo(PF_3)_3L'$ and $Ni(PF_3)_3L'$ [L' = $P(C_6H_5)_3$] [18]. These are identical in the number and intensity of the P–F bands. Since the nickel compound has C_{3v} symmetry, it can be deduced that the complex cobalt hydride has a trigonal-bipyramidal arrangement of the five ligands about the dsp^3-hybridized cobalt atom, the H atom and the triphenylphosphine being situated at opposite ends of the trigonal axis.

The compounds $HM(PF_3)_4$, whose IR spectra are identical in the region of the P–F stretching vibrations (cf. Table 8), indicating a similarity of structure, probably have a similar molecular geometry (C_{3v} symmetry). Finally, the results of the IR and ^1H–NMR studies of the trifluorophosphinemetal hydrides $H_2M(PF_3)_4$ suggest that the d^2sp^3-hybridized central metal atom in these compounds has an "octahedral" environment, with *cis* arrangement of the two hydrogen atoms (C_{2v} symmetry).

In all hydrido complexes of transition metals whose structures have been established by X-ray diffraction (cf. in particular [60a]), the complex ligands adjacent to the hydrogen are displaced towards them. It therefore seems reasonable to assume that the PF_3 ligands in the trifluorophosphinemetal hydrides are also displaced towards the H atoms; the $M(PF_3)_4$ skeletons of the complex hydrides $HM(PF_3)_4$ and $H_2M(PF_3)_4$ thus have a distorted tetrahedral configuration as shown in Fig. 1. In any case, even the rather qualitative results obtained so far in structural investigations show that the H atoms of the trifluorophosphinemetal hydrides do not disappear among the electrons surrounding the central metal, but occupy a normal coordination site on the metal.

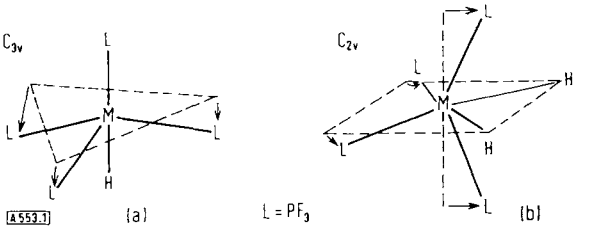
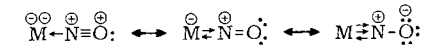


Fig. 1. Structural models for the trifluorophosphinemetal hydrides $HM(PF_3)_4$ (M = Co, Rh, Ir) (a) and $H_2M(PF_3)_4$ (M = Fe, Ru, Os) (b).

V. Nitrosyltrifluorophosphinemetal Complexes

In the metal(0) trifluorophosphines, trifluorophosphine can be partially replaced by the three-electron donor nitric oxide to give mononuclear inner-orbital complexes, in which the inert gas configuration of the metal is preserved. The diamagnetism of the complexes and the position of the N–O stretching vibrations (1788 to 1844 cm^{-1}), which is characteristic of coordinately bonded "$NO^{\oplus}$", indicate that the bonding of the nitric oxide to the metal involves both the σ electron pair on the nitrogen and the unpaired electron. Back-donation M → NO involving π* orbitals of the ligand also make a considerable contribution to the bonding state of the M–N–O linkage, as follows:



Two NO groups correspond electronically to three PF_3 ligands. The uptake of one or two unpaired NO electrons by cobalt or iron respectively gives a pseudonickel atom. (Corresponding remarks apply to metals of the 2nd transition series.)

This leads to the following isoelectronic and apparently isosteric (tetrahedral) series of compounds, the members of which have the general formula $M(NO)_x(PF_3)_{4-x}$ (x = 0, 1, 2, or 3 [63]):

$Fe(NO)_2(PF_3)_2$	$Co(NO)(PF_3)_3$	$Ni(PF_3)_4$
	$Rh(NO)(PF_3)_3$	$Pd(PF_3)_4$

Thus the "nitrosyl displacement law" formulated by *Seel* [64] is evidently also valid for these metal trifluorophosphine derivatives.

The hydrophobic nitrosyltrifluorophosphinemetal complexes, like the "classical" complexes $Co(NO)(CO)_3$ [65] and $Fe(NO)_2(CO)_2$ [66], are red, mobile, and very volatile liquids, which solidify only at low temperatures, and which can be distilled at normal pressure without decomposition. Some of their physical properties are listed in Table 7. Their thermal and chemical stabilities decrease with increasing NO content, but are always greater than those of the analogous nitrosylcarbonylmetal complexes [67]. Their intensely yellow vapors are almost odorless. They all dissolve readily in the common organic solvents, and to a moderate extent in liquid trifluorophosphine. Only the iron compound is rapidly decomposed by water.

The nitrosyltrifluorophosphinemetal complexes can be prepared by a wet or by a dry method. The latter is based on a modified method of reductive fluorophosphination. Thus if the halogenonitrosyl complexes of iron and cobalt are used as the starting materials (cf. Table 3), one or both NO groups remain attached to the metal even under very high PF_3 pressures, and the nitrosyltrifluorophosphine complexes are obtained in good yields, *e.g.*

$$[Fe(NO)_2Br]_2 + 2\ Cu + 4\ PF_3 \rightarrow 2\ Fe(NO)_2(PF_3)_2 + 2\ CuBr$$

A particularly useful preparation may be carried out at atmosheric pressure with the trifluorophosphinemetallates as starting materials [68]. When carbon dioxide is

[63] The existence of a nitrosyltrifluorophosphine complex $M(NO)_3PF_3$ of a metal of Group 7 B is still uncertain.

[64] *F. Seel*, Z. anorg. allg. Chem. *249*, 308, 320 (1942).

[65] *L. Mond* and *A. E. Wallis*, J. chem. Soc. (London) *121*, 32 (1922).

[66] *W. Hieber* and *J. S. Anderson*, Z. anorg. allg. Chem. *208*, 238 (1932).

[67] Nitrosylcarbonylrhodium had not been prepared previously.

[68] A similar method was decribed by *F. Seel*, Z. anorg. allg. Chem. *269*, 40 (1952) and by *F. Seel* and *H. Koss*, Z. Naturforsch. *17b*, 129 (1962) for the nitrosylcarbonyl complexes of iron and cobalt.

Table 7. Typical derivatives of the metal trifluorophosphines.

$Cr(PF_3)_3(CO)_3$ Colorless crystals Subl. 25 °C/10 mm	$Fe(NO)_2(PF_3)_2$ Red liquid M.p. −72 °C B.p. 97 °C/727 mm Decomp. above 118 °C $Fe(PF_3)_4X_2$ (X = Cl, Br, I) Crystalline Volatile	$Co(NO)(PF_3)_3$ Red liquid M.p. −92 °C B.p. 81 °C/732 mm Decomp. above 163 °C $Co(PF_3)_4I$ Brown crystals Highly volatile Decomp. above 7 °C $Co(PF_3)_2(\pi\text{-}C_5H_5)$ Red liquid M.p. −8 °C B.p. 51 °C/13 mm Decomp. above 195 °C	$Ni(PF_3)_{4-x}(CO)_x$ (x = 1—3) Colorless liquids Highly volatile $Ni(PF_3)_{4-x}[P(C_6H_5)_3]_x$ Colorless crystals x = 1: M.p. 123—125 °C x = 2: M.p. 213 °C $Ni(PF_3)[P(OC_6H_5)_3]_3$ Colorless crystals M.p. 89 °C
$Mo(PF_3)_3(CO)_3$ Colorless crystals M.p. 89 °C Subl. 20 °C/10 mm $Mo(PF_3)_3(C_9H_{12})$ Colorless crystals M.p. 160 °C (decomp.) Subl. 100 °C/10^{-3} mm		$Rh(NO)(PF_3)_3$ Red liquid M.p. −87 °C Highly volatile	$Pd(PF_3)_2[P(C_6H_5)_3]_2$ Bright yellow Decomp. above 110 °C
	$Re(PF_3)_5Cl$ Colorless crystals M.p. 153 °C (decomp.) Subl. 20 °C/10^{-2} mm	$Ir(PF_3)_4I$ Yellow crystals Subl. 15 °C/1 mm Decomp. above 25 °C	$Pt(PF_3)_2Cl_2$ Colorless crystals M.p. 102 °C B.p. *ca.* 240 °C (decomp.) $[Pt(PF_3)Cl_2]_2$ Orange red crystals M.p. 155—156 °C B.p. *ca.* 290 °C (decomp.) $Pt(PF_3)_{4-x}[P(C_6H_5)_3]_x$ Colorless crystals x = 1: M.p. 117 °C (decomp.) x = 2: M.p. 202 °C (decomp.)

passed into aqueous solutions of the potassium tetrakis-(trifluorophosphine)metallates containing nitrite, the nitrosyltris(trifluorophosphine) complexes of cobalt and of rhodium are obtained in yields of 50—60%, but not the iridium complex:

$$[M(PF_3)_4]^{\ominus} + NO_2^{\ominus} + CO_2 \rightarrow M(NO)(PF_3)_3 + PF_3 + CO_3^{2\ominus}$$

The complex is removed from the reaction mixture by the current of CO_2, dried with $CaCl_2/P_2O_5$ while still gaseous, and condensed. It is interesting that only one PF_3 group is eliminated in the reaction of $K[Co(PF_3)_3CO]$; the physical properties of nitrosylcarbonylbis(trifluorophosphine)cobalt $Co(NO)(CO)(PF_3)_2$ [69] are as expected from those of the parent compound $Co(NO)(PF_3)_3$.

The reduction of $Fe(NO)_2(PF_3)_2$ with potassium amalgam in cooled ether yields the yellow potassium nitrosyltris(trifluorophosphine)ferrate(−I), $K[Fe(NO)(PF_3)_3]$ which is unstable in air [69a]. The anion is isoelectronic and isosteric with $Co(NO)(PF_3)_3$. Acidification of the crystalline potassium salt with 50% sulfuric acid leads almost quantitatively to nitrosyltris(trifluorophosphine) iron hydride, $HFe(NO)(PF_3)_3$ [69a], an orange, mobile liquid (m.p. −86 °C, b.p. *ca.* 80 °C/720 mm, decomp. 175 °C). The IR and ^1H-NMR spectra (cf. Table 6) of this surprisingly stable nitrosylmetal hydride indicate a structure as shown in Figure 1a, with the H atom and the NO group *trans* to each other on the threefold molecular axis.

[69] *Th. Kruck* and *W. Lang*, unpublished work.

[69a] *Th. Kruck* and *W. Lang*, Chem. Ber. *99*, (1966), in press.

VI. Halogenotrifluorophosphinemetal Complexes

Trifluorophosphine complexes in which the central metal atom is positively charged are particularly interesting from the point of view of bond theory, since the stability limits of metal-PF_3 bonds for higher oxidation states of the central metal atom can be found with the aid of these complexes. In addition to the true cationic complexes of the type $[M(PF_3)_6]^{\oplus}$ [M = Mn(I) and Re(I)], the synthesis of which is being investigated at present, they include the halogenotrifluorophosphinemetal complexes $X_mM(PF_3)_n$ (X = Cl, Br, or I; m = 1 or 2), in which the electron-attracting PF_3 groups have a strongly electronegative competitor. Such complexes of platinum, cobalt, iridium, iron, and rhenium have now been prepared and characterized [70].

1. Syntheses at Atmospheric Pressure

As early as 1891, *Moissan* [71] prepared the first trifluorophosphine complex of a transition metal (though he did not recognize it as such) by the reaction of phosphorus pentafluoride with platinum black. The compound he regarded as "$PtPF_5$" has the formula $[(PF_3)PtF_2]_2$ [22], corresponding to the dimeric complex $[(PCl_3)PtCl_2]_2$ [72]. Thus this is one of the very rare compounds in which fluorine functions as a bridge.

[70] Evidence has also been found for the formation of very unstable PF_3 adducts with CuCl and AuCl [22].

[71] *H. Moissan*, Bull. Soc. chim. France *1891*, 454.

[72] *M. Schützenberger*, Bull. Soc. chim. France *1872*, 482; *K. A. Jensen*, Z. anorg. allg. Chem. *231*, 365 (1937).

In 1951, shortly before the discovery of tetrakis(trifluorophosphine)nickel, *Chatt* [22] synthesized two other halogenotrifluorophosphineplatinum complexes. When PF_3 is passed over platinum(II) chloride at 200–220 °C, the colorless *cis*-dichlorobis(trifluorophosphine)platinum, $Cl_2Pt(PF_3)_2$, and the orange-yellow *trans*-dichlorotrifluorophosphineplatinum, $[(PF_3)PtCl_2]_2$, which is bridged by two chlorine atoms, immediately sublime. Both of these compounds have physical properties very similar to those of the halogenocarbonyl complexes $Pt(CO)_2Cl_2$ and $[(CO)PtCl_2]_2$, but are more volatile and more stable. At the boiling point of the monomer (240 °C) vigorous liberation of PF_3 and formation of the binuclear complex occurs.

The dihalogenotetrakis(trifluorophosphine)iron complexes can be obtained by direct reaction of pentakis(trifluorophosphine)iron with halogens. The deep red iodine compound is formed at 0 °C in pentane; the orange bromine compound and the amber chlorine compound are readily obtained in the gas phase:

$$Fe(PF_3)_5 + X_2 \rightarrow Fe(PF_3)_4X_2 + PF_3.$$

In contrast to the easy, quantitative synthesis [73] of $Fe(CO)_4I_2$ from FeI_2 and CO (6 atm) at 18 °C, attempts to make PF_3 (>200 atm) react with anhydrous iron(II) halides were unsuccessful even with reaction times of several weeks. It appears that in the stepwise addition to the doubly positive iron, the acceptor PF_3 does not encounter sufficient back-donation.

The yellow iodotetrakis(trifluorophosphine)iridium and the red-brown iodotetrakis(trifluorophosphine)cobalt are obtained by the action of iodine on potassium tetrakis(trifluorophosphine)iridate(−I) [37] and by iodination of tetrakis(trifluorophosphine)cobalt hydride with iodoform respectively [18]:

$$K[Ir(PF_3)_4] + I_2 \xrightarrow[-80\,^\circ C]{(C_2H_5)_2O} Ir(PF_3)_4I + KI$$

$$HCo(PF_3)_4 + I_3CH \xrightarrow[0\,^\circ C]{C_5H_{12}} Co(PF_3)_4I + I_2CH_2$$

2. Syntheses Under Pressure

Whereas the reductive fluorophosphination of tungsten hexachloride leads to hexakis(trifluorophosphine)tungsten, the reduction of the pentachloride of its right-hand neighbor in the periodic system, rhenium, under the usual conditions for the high-pressure synthesis of trifluorophosphinemetals (cf. Table 3) essentially stops after four chlorine atoms have been replaced [37]:

$$ReCl_5 + 4\,Cu + 5\,PF_3 \rightarrow Re(PF_3)_5Cl + 4\,CuCl$$

In addition to $Re(PF_3)_5Cl$, another colorless, but less volatile substance was recently isolated from the reaction products and identified as dimeric pentakis(trifluorophosphine)rhenium, $[Re(PF_3)_5]_2$.

It is interesting that cobalt gives a halogeno complex containing the maximum number of PF_3 groups, $Co(PF_3)_4X$, whereas with carbon monoxide only the addition compound $CoI_2 \cdot CO$ is known [74], which is stable under CO pressure only. At room temperature and under a relatively low pressure of PF_3 (about 50 atm), a mixture of anhydrous cobalt(II) iodide and copper powder avidly absorbs trifluorophosphine until a final pressure of about 10 atm is reached [18] (cf. Table 3); the resulting $Co(PF_3)_4I$ can be removed from the autoclave under vacuum.

3. Properties

All the halogen derivatives of this series must be regarded as purely covalent; they show the typical metal(0) trifluorophosphine character. They have definite melting points and dissolve readily in the common organic solvents.

Their volatility is striking, being greatest in iodotetrakis(trifluorophosphine)cobalt and -iridium, and decreasing slightly in the halogenotrifluorophosphineiron complexes in the order Cl, Br, I.

On the whole the halogenotrifluorophosphinemetal complexes are much less stable, chemically and thermally, than the trifluorophosphine complexes of the metals having valence 0 or −1. They tend to decompose rapidly in solution (particularly in polar solvents) and in air. Their thermal stabilities lie between wide limits, the most stable being the compounds of rhenium and platinum. However, the monomeric halogenotrifluorophosphine complexes of the 5d metals exhibit a strong tendency to polymerize. The thermal stabilities of the halogenotrifluorophosphineiron complexes are distinctly lower, but comparable among themselves, and one of the principal properties of $Co(PF_3)_4I$ is the loss of all the PF_3 groups above 7 °C. If the PF_3 liberated is continously removed, a brown substance having the composition "CoI" is finally produced. This substance, which is amorphous to X-rays and still sensitive to heat and air, is probably the hitherto unknown cobalt(I) iodide. The only trifluorophosphine complexes known at present whose metal-PF_3 bonds are unstable under normal conditions are $Co(PF_3)_4I$ and $Pd(PF_3)_4$.

The halogenotrifluorophosphinemetal complexes are very reactive towards donor ligands, since the entry of such ligands into the molecule makes the metal more negative and so strengthens the metal-PF_3 bond. The monohalogeno complexes $Re(PF_3)_5Cl$ and $Co(PF_3)_4I$ [18] exchange one and two PF_3 groups, respectively, for triphenylphosphine; this leads to a considerable increase in thermal and chemical stability, particularly for the disubstitution product of cobalt. At room temperature, the dihalogeno complexes of iron lose all their trifluorophosphine to form $Fe(PPh_3)_2X_2$. Similarly one can explain the fast reduction of the air-sensitive complexes iodotetrakis(trifluorophosphine)cobalt and -iridium to form the much more stable potassium tetrakis(trifluorophosphine)metallates(−I) [18,37]:

$$M(PF_3)_4I + 2\,K\,(Amalgam) \xrightarrow{10\,^\circ C} K[M(PF_3)_4] + KI$$

(M = Co, Ir)

[73] *W. Hieber* and *H. Lagally*, Z. anorg. allg. Chem. *245*, 305 (1940).

[74] *W. Hieber et al.*, Z. anorg. allg. Chem. *243*, 145 (1939).

VII. Carbonyltrifluorophosphinemetal Complexes

This interesting class of substances can be obtained by two routes:

1. The action of trifluorophosphine or carbon monoxide (generally under pressure, with simultaneous UV irradiation) on metal carbonyls or on metal trifluorophosphines, respectively, leads to mixtures of carbonyltrifluorophosphinemetal(0) complexes,

$$M(CO)_n + x\ PF_3 \rightarrow M(CO)_{n-x}(PF_3)_x + x\ CO$$
$$M(PF_3)_n + x\ CO \rightarrow M(PF_3)_{n-x}(CO)_x + x\ PF_3,$$

which, owing to their almost identical volatilities and solubilities, can be separated only by gas chromatography.

The ability of trifluorophosphine to displace carbon monoxide was first observed in tetracarbonylnickel [22]. The ease of this exchange on nickel was later confirmed by *Bigorgne* [75], who found by IR spectroscopy that all the substitution products $Ni(CO)_{4-x}(PF_3)_x$ are formed when trifluorophosphine is simply passed into tetracarbonylnickel. All three carbonyltrifluorophosphinenickel complexes ($x = 1$ to 3) were recently isolated by gas chromatography and identified as colorless liquids with low freezing points [76]. It was also found that ligand exchange takes place in the system $Ni(CO)_4$/$Ni(PF_3)_4$ even on gentle heating, and that when one pure carbonyltrifluorophosphinenickel complex is heated, all five species $Ni(PF_3)_{4-x}(CO)_x$ ($x = 0$ to 4) are eventually formed [76]. Evidence of such commutations and dismutations had been found earlier [14, 26] with the carbonyltrifluorophosphine complexes $M(PF_3)_{6-x}(CO)_x$ of chromium and molybdenum.

The degree of substitution in these equilibria is to a first approximation a function of the quantities of trifluorophosphine and carbon monoxide present. For example, if the reaction of nickel carbonyl with trifluorophosphine is carried out under pressure (350 atm), tetrakis(trifluorophosphine)-nickel is formed in a yield of about 80 %, together with all the intermediate substitution products (see also Section III.2). When the carbon monoxide liberated has been removed, a further reaction of the mixture with PF_3 under pressure leads almost quantitatively to the homogeneous trifluorophosphine complex. The same behavior is found in the reaction of $Ni(PF_3)_4$ with CO under pressure. Comparison of the infrared spectra [75] of the carbonyltrifluorophosphinenickel complexes with those of the colorless liquid products of reactions of tetrakis(trifluorophosphine)platinum with CO under pressure [44] shows that all the intermediate substitution products $Pt(PF_3)_{4-x}(CO)_x$ are formed also in the latter system. Their stability decreases with increasing CO content; the pure products have not yet been prepared.

The CO ligands of pentacarbonyliron can also be progressively replaced by trifluorophosphine to give all the possible substitution products [27]. All the compounds of the series $Fe(CO)_{5-x}(PF_3)_x$ ($x = 1$ to 4) have been isolated; they are light yellow liquids, whose stability towards air and light increases with the PF_3 content.

In reactions of hexacarbonylchromium and -molybdenum with PF_3 under pressure [14,26], it was again found that carbon monoxide can be readily replaced by trifluorophosphine, but in this case the colorless, waxy products were found to be mixtures. The substitutions tend to stop at the stage of the tris(trifluorophosphine) derivatives. Recently, however, all nine complexes $Mo(CO)_{6-x}(PF_3)_x$ ($x = 1$ to 6, including three pairs of *cis-trans* isomers) have been prepared from $Mo(CO)_6$ [77].

2. In the synthesis of specific carbonyltrifluorophosphinemetal complexes, substitution products of metal carbonyls with other relatively loosely bound ligands are subjected to the action of PF_3 under pressure at moderate temperatures (to avoid dismutation) [14,26]:

$$Cr(CO)_3(NH_3)_3 + 3\ PF_3 \xrightarrow[20\,^\circ C]{350\ atm} Cr(CO)_3(PF_3)_3 + 3\ NH_3$$

$$Mo(CO)_3(C_9H_{12}) + 3\ PF_3 \xrightarrow[80\,^\circ C]{350\ atm} Mo(CO)_3(PF_3)_3 + C_9H_{12}$$

(C_9H_{12} = Mesitylene)

The molybdenum compound can also be obtained from $Mo(CO)_3(PCl_3)_3$ by halogen exchange with potassium fluorosulfinate (KSO_2F) [78]. The colorless, crystalline, and very volatile tricarbonyltris(trifluorophosphine) complexes of chromium(0) and molybdenum(0) have octahedral structures with an all-*cis* arrangement of the three PF_3 ligands. Since it is more strongly bonded to the metal, the mesitylene in tricarbonylmesitylene-chromium(0) is eliminated only above 100 °C [26], again giving mixtures of $Cr(CO)_{6-x}(PF_3)_x$.

The carbonyltrifluorophosphinemetal complexes are almost identical with the corresponding metal trifluorophosphines and metal carbonyls in their physical properties such as color, volatility, solubility, *etc.* (cf. Table 7).

Thus trifluorophosphine and carbon monoxide can replace each other unrestrictedly and reversibly in the metal(0) compounds, the resulting mixed complexes being similar in character to the homogeneous metal trifluorophosphines and metal carbonyls. This property of the two monodentate ligands is unique.

In general [79], in reactions of metal carbonyls with Lewis bases B, substitutions are preferred to base reactions (in the sense of a valence disproportionation of the metal carbonyl, *e.g.* $3M^0 \rightarrow 2M^{-I} + M^{+II}$) with increasing tendency of B to enter into M–B back-donation. Thus the strong back-donating tendency of trifluorophosphine can be seen from the fact that only replacement is observed in its reactions with metal carbonyls.

VIII. π-Aromatictrifluorophosphinemetal Complexes

The first member of this group to be studied in any detail was bis(trifluorophosphine)cyclopentadienylcobalt [80], which can be obtained from dicyclopentadienylcobalt in 20 to 30 % yield by a displacement reaction:

$$Co(\pi\text{-}C_5H_5)_2 + 2\ PF_3 \xrightarrow[170\,^\circ C]{350\ atm} Co(PF_3)_2(\pi\text{-}C_5H_5) + [C_5H_5].$$

[75] *M. Bigorgne*, Bull. Soc. chim. France *1960*, 1986.

[76] *R. J. Clark* and *E. O. Brimm*, J. inorg. Chem. *4*, 651 (1965).

[77] *R. J. Clark*, Chem. Engng. News *42*, No. 26, p. 52 (1964).

[78] *R. Schmutzler*: Advances in Chemistry Series No. 37. Amer. chem. Soc., Washington D.C. 1963, p. 150.

[79] *W. Hieber*, *W. Beck*, and *G. Zeitler*, Angew. Chem. *73*, 364 (1961).

[80] *Th. Kruck*, *W. Hieber*, and *W. Lang*, Angew. Chem. *78*, 208 (1966); Angew. Chem. internat. Edit. *5*, 247 (1966).

The red, oily liquid may be regarded as a compound of Co(I); like $Co(PF_3)_4I$, therefore, it is extremely sensitive to oxidation. Its diamagnetism and the ^1H-NMR and IR spectra are in agreement with a π-bonded symmetrical ring.

Tris(trifluorophosphine)mesitylenemolybdenum(0) [80a], $Mo(PF_3)_3(C_9H_{12})$, was obtained when a suspension of $Mo(PF_3)_6$ in mesitylene was irradiated with UV light for several hours, *i.e.* by the direct action of an aromatic compound on a metal(0) trifluorophosphine complex. The volatile product (cf. Table 7) is stable even towards concentrated alkali solutions and dilute acids.

The existence of a tris(trifluorophosphine)benzenechromium(0) has also been reported [77]. This substance, which has not yet been characterized fully, is obtained in an interesting manner: thus, while the aromatic ligand of tricarbonylbenzenechromium(0) is replaced by three PF_3 ligands under high PF_3 pressures, irradiation in hexane solution with UV light in the presence of trifluorophosphine leads to the stepwise replacement of CO by PF_3. However, the only product that could be isolated was the stable $Cr(PF_3)_3(C_6H_6)$.

This photochemically induced reaction throws light on the bonding in the derivatives $Cr(CO)_2L(arene)$ (L = compounds of trivalent phosphorus, amines, *etc.*) and emphasizes the special position occupied by trifluorophosphine as a result of its back-donating power. The photochemical primary reaction [81] of metal carbonyls and their π-arene derivatives leads to a species, A, that contains less CO and is therefore strongly electrophilic, and can then add on a wide range of ligands in the secondary step.

$$Cr(CO)_3(C_6H_6) \xrightarrow[-CO]{h\nu} \underset{A}{\{Cr(CO)_2(C_6H_6)\}} \xrightarrow{+L} \underset{S}{Cr(CO)_2L(C_6H_6)}.$$

When L = $P(C_6H_5)_3$, pyridine, *etc.*, the substitution stops at this first stage, since these donors increase the bond order of the M–C bonds of the remaining CO groups, *i.e.* they increase the contribution of the limiting structure $M{=}C{=}\ddot{O}$; disubstitutions are rare, and trisubstitution has not been observed. On the other hand, if the coordination vacancy in A is filled by the acceptor PF_3, the M–CO bond in the monosubstitution product S is weakened (increased contribution of the structure $M{-}C{\equiv}O^{\oplus}$:), since the $M \rightarrow PF_3$ π bond takes up more of the charge transferred from the aromatic ligand onto the metal. This effect ultimately leads to complete substitution of the carbon monoxide.

Though only three metal trifluorophosphine complexes containing aromatic rings are known at present, their stability and ease of preparation leads one to expect as large a diversity of compounds as in the class of aromatic-ring metal carbonyl complexes.

IX. Bonding

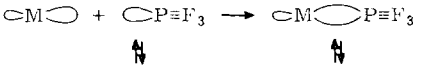
The available chemical, spectroscopic, and magnetochemical data permit only qualitative consideration of the bonding in trifluorophosphine complexes.

The nature of the metal-PF_3 bond is fundamentally the same as that of the metal-CO bond, since the bonding possibilities of the two ligands are similar. However, there are slight differences, which ultimately lead to the marked differences in behavior described above. Some understanding of the complex-chemical behavior of trifluorophosphine can be gained simply from a comparison of its electronic structure (schematic notation) with that of other complex ligands that also form stable bonds with d metals in low oxidation states.

$$:P{\equiv}F_3 \qquad :C{\equiv}O: \qquad :N{\equiv}O: \qquad :C{\equiv}N: \qquad :C{\equiv}N{-}R$$

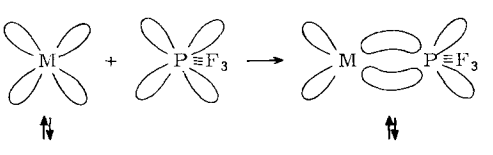
A common feature of these molecules is the presence of a lone pair of electrons and unoccupied π orbitals on the more electropositive donor atom.

In the coordinate bonding of trifluorophosphine to a transition metal atom, the doubly occupied sp^3 orbital of the phosphorus and, above all, its $3d_\pi$ orbitals are of decisive importance. Overlap of the doubly occupied sp^3 orbital of the phosphorus with suitably directed free hybrid orbitals of the metal leads initially to a weak donor σ bond.



Proof of the donor function of trifluorophosphine is provided by the adduct $F_3P \rightarrow BH_3$ with the strong Lewis acid monoborane, even though this adduct is unstable [82]. In boron trifluoride [83], on the other hand, the electrophilic action of the p_z orbital of boron, which already participates in the B–F double bonds, is no longer sufficient for coordinate bonding of the very weak Lewis base PF_3, but can effect bonding with the stronger donor PCl_3 [84], though even the adduct $Cl_3P \rightarrow BF_3$ can exist only up to −6 °C.

The low electric dipole moment [85] of the Pt–PF_3 bond in $Pt(PF_3)_2Cl_2$ is enough to show that this cannot be a simple [86] donor σ bond. The surprising stability of the trifluorophosphine complexes is therefore undoubtedly due to a strong d_π–d_π bond formed by donation from occupied orbitals of the central metal atom to the 3d orbitals of phosphorus; this effect is strengthened by the high electronegativity of the fluorine atoms, since these lower the energy of the 3d orbitals of the phosphorus:



The overall result, however, is probably a synergic type of bonding, since this π bonding increases the electron density on the phosphorus, and hence also its basicity (but cf. [87]).

A deeper insight into metal-trifluorophosphine bonding is provided by the P–F stretching bands in the 10 to 12μ

[80a] *Th. Kruck, A. Prasch,* and *B. Griesel,* unpublished work.

[81] For a summary, see: *W. Strohmeier,* Angew. Chem. *76,* 873 (1964); Angew. Chem. internat. Edit. *3,* 730 (1964).

[82] *R. W. Parry* and *T. C. Bissot,* J. Amer. chem. Soc. *78,* 1524 (1956).

[83] *J. N. Dempsey* and *N. C. Baenzinger,* J. Amer. chem. Soc. *77,* 4984 (1955); *H. S. Booth* and *J. H. Walkup, ibid. 65,* 2334 (1943); *J. Chatt,* Nature (London) *165,* 637 (1950).

[84] *P. Baumgarten* and *W. Bruns,* Chem. Ber. *80,* 517 (1947).

[85] *J. Chatt* and *R. G. Wilkins,* J. chem. Soc. (London) *1951,* 3061.

[86] *M. J. S. Dewar,* Bull. Soc. chim. France *18,* C 79 (1951).

[87] *M. Bigorgne,* J. inorg. nuclear Chem. *26,* 107 (1964).

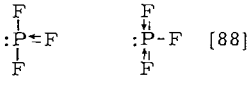
region. Tne IR vibrations of free PF_3 reappear as group frequencies in the IR spectra of its metal complexes, and since they are characteristically altered, they may be used as an important criterion for distinguishing between different types of compounds. The P–F stretching vibrations in the metal(0) trifluorophosphines, trifluorophosphinemetal hydrides, and halogenotrifluorophosphinemetal complexes always occur at higher wave numbers than in free trifluorophosphine, while they are displaced to much lower wave numbers in the trifluorophosphinemetallates and in the substitution products with donor ligands. The P–F stretching vibrations in isosteric compounds are directly comparable (cf. Table 8, columns d and f).

Table 8. Comparison of the P–F stretching vibrations of some trifluorophosphinemetal complexes.

		Compound	$\tilde{\nu}_{P-F}$ (cm^{-1}) [a]
Shift towards shorter wavelengths ↓	a)	$HCo(PF_3)_4$	961 w, 917 vs, 907 (sh), 867 vs
		$HRh(PF_3)_4$	949 w, 912 vs (sh), 904 vs, 863 vs
		$HIr(PF_3)_4$	965 w–m, 925 vs, 910 (sh), 877 vs
	b)	$Cr(PF_3)_6$	916 vs, 851 s
		$Mo(PF_3)_6$	911 vs, 853 s
		$W(PF_3)_6$	914 vs, 852 s
	c)	$Fe(PF_3)_5$	915 vs, 901 vs, 873 w, 864 w, 851 vs
		$Ru(PF_3)_5$	926 vs, 906 vs, 876 s, 856 vs
	d)	$Ni(PF_3)_4$	904 s, 864 vs
		$Pd(PF_3)_4$	910 vs, 860 s
		$Pt(PF_3)_4$	906 vs, 867 vs
		PF_3	892 vs, 848 vs
Shift towards longer wavelengths ↓	e)	$Ni(PF_3)_3(P(C_6H_5)_3)$	856 vs, 824 vs
		$Ni(PF_3)_2(P(C_6H_5)_3)_2$	815 vs (b), 800 vs
	f)	$[Co(PF_3)_4]^{\ominus}$	820 vs, 804 m (sh)
		$[Rh(PF_3)_4]^{\ominus}$	814 vs, 794 m (sh)
		$[Ir(PF_3)_4]^{\ominus}$	830 vs, 811 s (sh)
	g)	$[Co(PF_3)_3P(C_6H_5)_3]^{\ominus}$	873 s (b), 821 w (sh), 788 vs, 775 s (sh), 749 m (sh)

[a] vs = very strong, s = strong, m = medium, w = weak, b = broad, sh = shoulder.

These observations can be readily explained if the P–F bond in trifluorophosphine is assumed to possess double-bond character, which is influenced by the metal-phosphorus bond. The superposition of a π bond on the P–F σ bond results from the overlap of occupied 2p orbitals of fluorine with the 3d orbitals of the phosphorus, so hat limiting structures such as



[88]

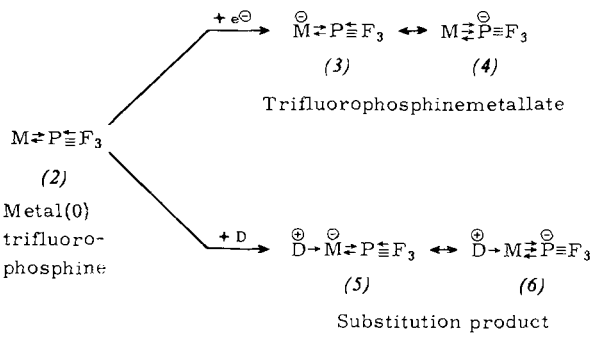
make a considerable contribution to the bonding in trifluorophosphine. This bonding is represented in the following discussion by the formulation $:P \overleftarrow{\equiv} F_3$.

For a given internuclear distance, the value of the overlap integral for p_π–d_π bonds of this type is greatest when the d_π orbital is more diffuse than the p_π orbital [89], *i.e.* has a higher principal quantum number. Since this is the case with the combination phosphorus-fluorine, π bonding plays a considerable part in the overall bonding in trifluorophosphine, though not in any other phosphorus trihalides. This view [53] is supported by the ^{31}P nuclear magnetic resonance of PF_3 [90], since despite the high electronegativity of fluorine, which should lead to an *ionic* bonding component, the diamagnetic shielding of phosphorus is stronger in PF_3 than in any other phosphorus trihalide. Finally, chemical evidence of the existence of F→P π bonding is provided by the considerable stability of trifluorophosphine towards hydrolysis, in comparison with that of the other phosphorus trihalides.

When trifluorophosphine *(1)* is linked to a metal in the zero oxidation state (see Scheme 1), the donor σ bond leads to a decrease in the electron density on the phosphorus, and this necessarily leads to an increase in the π-bond order of the P–F bonds. However, this effect can be only weak, since it is distributed over three P–F bonds, and since it is opposed by the simultaneous metal→phosphorus back-donation *(24)*. Nevertheless, the P–F force constant in $Ni(PF_3)_4$ is 7.73 mdyne/Å, compared with 5.38 mdyne/Å in free PF_3 [50]. However, if the metal is given a (formal) negative charge (*e.g.* by reduction to the trifluorophosphinemetallate or by the introduction of donors D), this is absorbed by the M–P π bond with an increase in the electron density on the phosphorus, with the result that the π-bond component of the P–F bonds decreases [*(4)* or *(6)*]. Thus a displacement of the P–F absorption bands towards lower wave numbers is an indication of an increase in the bond order of the M–PF_3 bond. This is strongest in the hetero-anion $[Co(PF_3)_3P(C_6H_5)_3]^{\ominus}$ (Table 8), since in this case there are two factors that tend to make the metal more negative.

The shift of the M–P stretching frequencies towards higher wave numbers for the trifluorophosphinemetallates and the substitution products of the metal(0) trifluorophosphines as expected from *(4)* and *(6)* has also been experimentally confirmed [91].

It should be stressed that *e.g.* the double arrow of the M–PF_3 bond *(2)* is only a symbol for the bonding, and



Scheme 1. Bonding in trifluorophosphinemetal(0) complexes, in their substitution products, and in trifluorophosphinemetallates.

does not denote a true double bond (*e.g.* as in olefins). The strength of the M–PF_3 linkage resulting from the combined action of the donor σ bond and the acceptor

[88] Cf. *E. Fluck*, Z. Naturforsch. *19b*, 869 (1964).

[89] *L. E. Sutton*: Chemische Bindung und Molekülstruktur. Springer-Verlag, Berlin 1961.

[90] *H. S. Gutowsky* and *D. W. McCall*, J. chem. Physics *22*, 162 (1954).

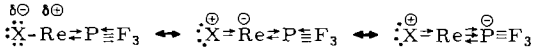
[91] These spectroscopic studies will be fully reported in the near future.

π bond corresponds only to that of a single bond, as is shown by the Ni–P force constant ($k_{Ni-P} = 2.71$ mdyne/Å [50]) in $Ni(PF_3)_4$, [compare $k_{Ni-C} = 2.52$ mdyne/Å in $Ni(CO)_4$].

By influencing the occupation of the d_π orbitals of the phosphorus, the available charge density on the metal atom affects not only the strength of the P–F bonds and hence their stretching frequencies, but also the physical properties and chemical behavior of the trifluorophosphine complexes.

This $M-PF_3$ bonding type explains the fact that the P–F bond order in the hydridotrifluorophosphine complexes of cobalt and its homologues is higher than that in the isoelectronic tetrakis(trifluorophosphine) complexes of nickel, palladium, and platinum. The central atoms of the complex hydrides, partly because of their lower nuclear charge and partly because one electron of the metal is fixed in the covalent M–H bond, have effectively fewer electrons available for back-donation to the PF_3 than nickel and its homologues in the pure metal trifluorophosphines.

The electron-attracting action of trifluorophosphine extends over the metal to other ligands present in the complex and so affects their bonding. The halogenotrifluorophosphinemetal complexes for example, are only formally analogous to the corresponding halogenocarbonylmetal complexes. Their nonpolar character and high volatility suggest covalent M–X bonding. In addition, the wave number of the Re–Cl stretching in $Re(PF_3)_5Cl$ is 37 cm^{-1} higher than that for the corresponding carbonyl complex [37]. This higher M–X bond order is evidently due to an X→M π bond, which is induced by the PF_3 groups, and which is superimposed on the polarized M–X σ bond:



(7) *(8)* *(9)*

A considerable contribution is therefore made by the structures *(8)* and *(9)*.

The extent of the charge transfer from other ligands to the metal, and hence the increase in the $M-PF_3$ bond order in the substituted trifluorophosphine complexes (see Table 9, *(5)* and *(6)*) is naturally also determined by the donor and acceptor properties of the substituents [23]. This explains the fact that the reaction of tetrakis(trifluorophosphine)nickel with triphenylphosphine stops at the stage of $Ni(PF_3)_2(PPh_3)_2$, whereas the weaker donors $P(OR)_3$ readily give trisubstitution, and carbon monoxide, whose acceptor power approaches that of trifluorophosphine, can replace all the PF_3 groups.

The bonding of the trifluorophosphine to the metal is also stronger in the anionic trifluorophosphine complexes than in the metal(0) trifluorophosphines [see Scheme 1, *(4)*]. The surprising chemical stability of the trifluorophosphinemetallates, which contrasts with the ease of oxidation of the carbonylmetallates, is due mainly to the outstanding acceptor strength of this ligand, which leads to extensive withdrawal of the negative charge from the metal.

Thus the π-acceptor power of trifluorophosphine is clearly greater than that of any of the usual ligands, with the exception of the $NO^{\oplus}$ ion. This is impressively shown by its complex-chemical behavior, and has also been repeatedly confirmed by IR spectroscopic studies [14,53,92]. Thus we find a (naturally abridged [93]) sequence of monodentate neutral ligands with decreasing tendency to form acceptor π bonds:

$$PF_3 > CO > PCl_3 > P(OR)_3 > CNR > PR_3 \gg NR_3.$$

The ligands on the right are pure or predominant donors, and have little or no available π-orbital accommodation for the acceptance of M→L back-donation [94]; they therefore preferentially form stable bonds with positively charged metal ions. On the left, however, we find the strongest π acceptors, which mainly stabilize the oxidation state zero or even low (formal) negative valences of transition metals.

I am indebted to K. Baur, A. Engelmann, Dr. W. Lang, and Dr. A. Prasch for their collaboration, and to N. Derner, B. Griesel, M. Negele, and M. Stadler. I am grateful to Prof. W. Hieber and to Prof. E. O. Fischer for their interest in this work and for their generous support. Acknowledgement is also due to the BASF, the Deutsche Forschungsgemeinschaft, and the Fonds der Chemischen Industrie for financial support.

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German version: Angew. Chem. *79*, 27 (1967)

Translated by Express Translation Service, London

[92] *F. A. Cotton*, J. inorg. Chem. *3*, 702 (1964).

[93] Cf. especially: *T. A. Manuel*, Advances organomet. Chem. *3*, 191 (1965); *W. D. Horrocks* and *R. C. Taylor*, J. inorg. Chem. *2*, 723 (1963).

[94] Therefore NF_3 cannot be a ligand comparable to PF_3, even apart from its strong fluorinating properties.

Chemistry of the Incandescent Lamp[**]

BY A. RABENAU[*]

Halogen lamps have been on the market for some time; they are replacing the conventional lamp in many fields except general service (domestic) applications. Their relatively small bulbs contain small amounts of halogen in addition to an inert gas. The mode of action of the iodine lamp, which depends on the presence of traces of oxygen, has been elucidated. Tungsten evaporating from the filament is returned to it by a cyclic process involving a tungsten oxide and WO_2I_2. No tungsten is ever deposited on the bulb wall of such a lamp. A regenerative cycle in which the vaporized tungsten is deposited on the hottest (and hence most vulnerable) parts of the filament can, in principle, be realized by the use of fluorine compounds.

1. Basic Principles

The incandescent lamp is a thermal radiator. The filament, which is normally protected from the atmosphere, is heated to high temperatures by the direct passage of a current. The luminous efficiency[***] is determined by the Stefan-Boltzmann law, according to which the energy of the emitted radiation increases with the fourth power of the absolute temperature, and by Wien's displacement law, according to which the maximum of the energy curve is displaced into the visible region with rising temperature (Fig. 1). The

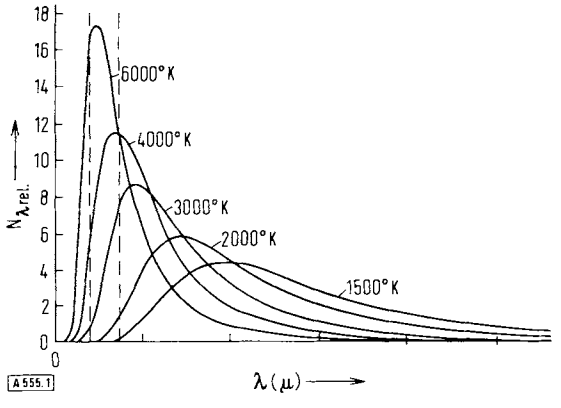


Fig. 1. Spectral energy distribution of a black body. The radiation emitted $N_{\lambda rel}$ is given in arbitrary units. The broken lines indicate the limits of the visible region.

luminous efficiency is highest at about 6000 °K, which corresponds roughly to the surface temperature of the sun. For a black body it is 95 lm/W; by way of comparison, a monochromatic radiator of wavelength λ_m = 555 mμ, the sensitivity optimum of the human eye, has a luminous efficiency of 682 lm/W. The considerable temperature-dependence of the luminous efficiency, brightness, and hence the life of a tungsten filament can be seen from Table 1.

Table 1. Characteristic data for an uncoiled incandescent tungsten filament (diameter 0.01 mm) in vacuum (< 10^{-5} mm).

Temp. (°K)	Brightness (cd/cm²)	Luminous efficiency (lm/W)	Life (hr)
2400	157	9.37	1.17×10^3
2600	347	14.28	3.86×10^1
2800	694	20.43	1.9
3000	1257	27.10	0.15
3200	2110	34.6	—
3400	3370	42.6	—

2. Filament Materials

Filament materials must have a high melting point, a low vapor pressure, and a low rate of evaporation. Moreover, it must be possible to produce filaments having adequate mechanical strength from the materials. This last point in particular has been a deciding factor in the development of the incandescent lamp[1].

Table 2. Compounds and elements with melting points close to or above 3000 °C.

Phase	M.p. (°C)	Phase	M.p. (°C)	Phase	M.p. (°C)
TaC	3880	HfB_2	3250	NbB_2	3000
C	3870	TiN	3205	ThO_2	3050
HfC	3870	Re	3180	BN	3000
ZrC	3530	TaB_2	3120	Ta	3000
NbC	3500	TaN	3090	HfN	2980
W	3410	ZrB_2	3040	ZrN	2980
Ta_2C	3400	Os	3000		

The substances with the highest melting points are listed in Table 2. The first commercial incandescent lamp[*] had a carbon filament[2]. The high vapor

[*] Priv.-Doz. Dr. A. Rabenau
Philips Zentrallaboratorium GmbH.
Weißhausstraße
51 Aachen (Germany)

[**] Based on lectures delivered to the Dechema Colloquium on October 9th, 1964, in Frankfurt/Main and to the Euchem Conference "High-temperature chemistry with special reference to gaseous and solid subcompounds" on April 28th, 1965 at Schloß Elmau (Germany).

[***] The luminous efficiency is the ratio of the luminous flux emitted by the lamp in lumens to the electric power supplied to the lamp in watts (lm/W).

[1] a) *J. W. Howell* and *H. G. Schroeder*: History of the Incandescent Lamp. Maqua. Schenectady, New York 1927; b) *A. A. Bright*: The Electric Lamp Industry. MacMillan, New York 1949; c) *J. A. Moore*, G. E. C. Journal *25*, 174 (1958).

[*] For precursors of this lamp see [1a] and [1b].

[2] *T. A. Edison*, US.-Pat. 223898 (Jan. 27th, 1880).

pressure of carbon limits the maximum useful working temperature to about 2100 °K, since at higher temperatures blackening of the envelope leads to excessive light losses. A search was therefore made for other materials. The Nernst lamp, in which the filament material was a mixed oxide (85 % ZrO_2 + 15 % Y_2O_3), did not become widely used. Owing to the complicated method of ignition, which involves preheating, it was ousted by the metal-filament lamps that appeared on the market in rapid succession. Though tungsten was considered as a filament material at a very early stage [1a], it was many years later that the metallurgy of this metal was mastered. The first filaments were produced from tungsten powder, which was mixed with an organic binder and forced through fine diamond orifices. The binder was then evaporated off in an inert gas, and the metal powder sintered at about 2500 °C. One great disadvantage of lamps containing filaments of this type was their low shock resistance, so that despite their advantages they could not fully replace the carbon-filament lamp.

A turning point was reached with the introduction of the drawn tungsten filament by *Coolidge* in 1908. Rods of compressed tungsten powder are heated by direct passage of a current to temperatures near the melting point and forged into thick wires, from which filaments can be drawn. Following this development, tungsten became generally accepted as a filament material. The dominant position of tungsten is understandable: its vapor pressure at 3000 °C is more than 1000 times lower than that of carbon.

Owing to its outstanding shock resistance, the carbon-filament lamp is still used to a limited extent, *e.g.* in ships and underground railways. Other filament materials such as carbides (Table 2) have been discussed, but have not so far been used.

3. Life of an Incandescent Lamp

The life of an incandescent lamp is determined essentially by two factors: blackening of the bulb and "burning out" of the filament. Both processes are related to the vapor pressure (rate of vaporization), which therefore determines the maximum working temperature.

a) Blackening of the Bulb

During operation vaporized filament material is deposited on the bulb wall, leading ultimately to unacceptably high light losses. To minimize light losses, the bulb must be relatively large. The decrease in luminous efficiency with time is the main problem with carbon lamps and vacuum lamps in general.

b) "Burning out" of the Lamp

While the lamp is burning, thinner parts ("hot spots") are formed in the filament, and these points of high resistance ultimately carry practically the entire load. An increase in temperature, and hence increased vaporization, results and after a time the filament fuses at these points. Though this a random process, the life of a lamp is closely related to its working conditions.

c) Influence of Residual Gases

Reactions caused by impurities, particularly by residual gases, can lead to a considerable transfer of material from the filament to the bulb wall, and so shorten the life of the lamp.

Tungsten reacts with water vapor at the filament temperature as follows:

$$W + x\,H_2O \rightleftharpoons WO_{x(g)} + x\,H_2 \qquad (a)$$

At low temperatures the reaction proceeds from right to left. In vacuum lamps [3] tungsten passes in this way to the bulb wall, while in lamps filled with inert gases [4] it is transferred mainly from hotter to cooler parts of the filament (Fig. 2). The water formed is then used to repeat the process.



Fig. 2. Transport of tungsten from hotter (T_2) to cooler (T_1) parts of an incandescent tungsten coil in the presence of a little water vapor (after [4]). (Magnification 100×; filament temperature about 2500 °K).

In carbon-filament lamps traces of oxygen react with the carbon filament to form CO [5]. This decomposes on the wall to carbon and CO_2, which reacts with the filament to form further CO. Both these processes are examples of chemical transport reactions.

The life and luminous efficiency (working temperature) of incandescent lamps can be improved in two ways: 1. by decreasing the rate of evaporation; and 2. by elimination of the damage caused by vaporization (material transport).

4. Rate of Evaporation

Even in the early stages of development of the incandescent lamp, attempts were made to reduce the rate of evaporation by filling the bulb with inert gases. However, it was found that the additional losses due to

[3] *I. Langmuir*, Trans. Amer. Inst. Electr. Engrs. *32*, 1394 (1913).
[4] *C. J. Smithells*, Trans. Faraday Soc. *17*, 485 (1921).
[5] *H. Schäfer*: Chemical Transport Reactions. Academic Press, New York 1964, Weinheim/Bergstr. 1962, p. 41.

thermal conduction and in particular to convection outweigh the advantages of the use of inert gases. Only after a detailed study of the heat losses [6] could gases be used to advantage. *Langmuir* [6] found that an incandescent body is surrounded by a quasi-stationary layer of gas, because of the increase in gas viscosity with increasing temperature. Heat is lost from this layer only by radiation and conduction. The heat loss W, in watts, due to conduction can be expressed approximately by equation (b) [7],

$$W = Cl\,(a/B)^{0.3} \times 4.19 \int_{T_1}^{T_2} k \, dt \qquad (b)$$

where C is a constant, l is the length and a the diameter of the wire, B is the thickness of the Langmuir layer, and k is the coefficient of thermal conductivity of the gas. The ratio a/B is in the range 0.02–0.2. The equation shows that the heat losses depend largely on the length of the filament, but only to a small extent on its diameter. Thus a short thick wire should be particularly suitable. Since the length is fixed by the specified voltage and power, *Langmuir* coiled the wire so that Langmuir layers of adjacent turns overlapped. A filament of this type behaves like a short cylindrical one whose diameter is the same as the outside diameter of the coil. The "coiled-coil" filament was introduced in the 1930's [8]. Another property of the Langmuir layer, and one of particular importance in the most recent developments, is the fact that thermal conduction inside this layer is independent of the gas pressure.

The lower coefficient of thermal conductivity of gases with higher molecular weight led to the use of argon instead of nitrogen in gas-filled lamps. General-service lamps with powers greater than 40 W nowadays contain 93 % argon and 7 % nitrogen, the nitrogen being added to prevent arcing. Krypton and xenon are used only in special lamps, owing to their high cost.

5. Technology of the Filament

One problem that is particularly noticeable with coiled filaments is "sagging" of the wire. The drawn polycrystalline tungsten wire recrystallizes under working conditions, with the result that slip can occur at grain boundaries that are almost perpendicular to the wire surface, so that the wire sags and finally breaks (Fig. 3).

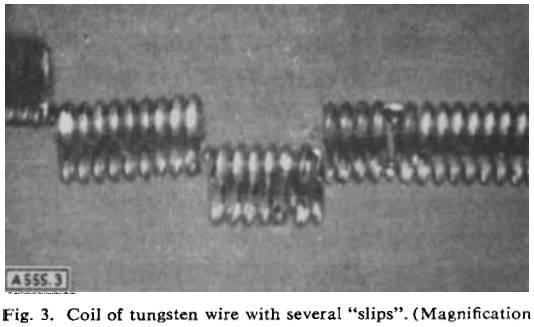


Fig. 3. Coil of tungsten wire with several "slips". (Magnification 65×)

Attempts to avoid this sagging led first to the use of monocrystalline wires (Pintsch wire). However, apart from technological difficulties, the wire sags particularly readily at the points where two monocrystals are joined. Present-day filaments have a staple-fiber structure (Fig. 4), in which the grain boundaries form only a small angle with the surface [9]. This recrystallization structure is obtained by addition of small quantities of sodium or potassium silicate to the tungstic acid before reduction [10].

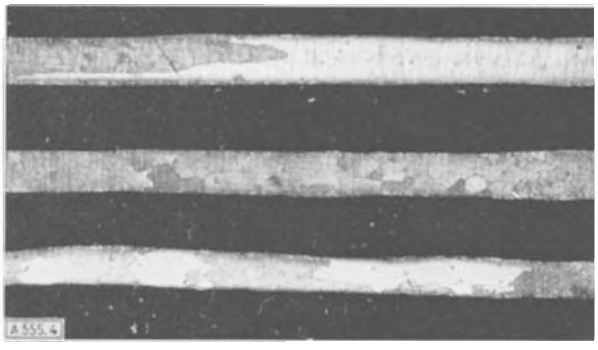


Fig. 4. Crystal structure of recrystallized tungsten wires 180 μ in diameter. The wires were produced from:
top: **doped W powder (staple-fiber structure);**
center: **doped and undoped W powder (1:1);**
bottom: pure W powder.

6. Getters

The examples in Section 3c show that the quality of incandescent lamps depends to a large extent on the care taken in their manufacture. This is particularly true of the quality of the vacuum. *Malignani* used red phosphorus as a getter as early as 1894. Small quantities of red phosphorus are vaporized in the lamp after it has been evacuated and sealed; the phosphorus reacts with residual gases such as water and oxygen to form compounds with low vapor pressures. This discovery was a great advance in lamp technology. Red phosphorus is still used both in vacuum lamps and in gas-filled general-service lamps. It is applied to the coil as a paste, together with other substances, and vaporized.

The first getter specially intended for tungsten lamps was phospham, $(PN_2H)_x$. It was later suggested that this should be replaced by phosphorus nitride, P_3N_5, to avoid the introduction of hydrogen, which causes arcing. The barium (1916) and zirconium getters (1938) also deserve mention in view of their practical importance [11b].

[6] *I. Langmuir*, Physic. Rev. *34*, 501 (1912); Proc. Amer. Inst. Electr. Engrs. *31*, 1011 (1912); Trans. Amer. electrochem. Soc. *23*, 299 (1913).

[7] *J. C. Lokker*, Philips techn. Rev. *25*, 2 (1963/64).

[8] *W. Geiss*, Philips techn. Rev. *1*, 97 (1936).

[9] *G. D. Rieck*, Acta metallurg. *6*, 360 (1958).

[10] *A. Pacz*, US.-Pat. 1410499 (March, 21th, 1922).

7. Wall Reactions

Conversion of the light-absorbing carbon or tungsten deposits into transparent compounds such as halides or oxides was also attempted long ago. Thus as early as 1882, introduction of small quantities of chlorine into carbon-filament lamps was suggested [11]. The "Novak" lamp (with a carbon filament), which was introduced in 1894, contains small quantities of bromine. However, this does not have the desired effect on the life of the lamp, since the small quantities of halogen are consumed in unavoidable side reactions [12].

Large quantities of chlorine, on the other hand, cause lamp failure, *Skaupy* [12] therefore suggested the use of compounds over which there is a low vapor pressure of the active gas, which would consequently maintain reaction with the deposits over long periods. The compounds suggested include thallium(III) chloride, potassium hexachlorothallate, and platinum(II) chloride.

Later, compounds as stable as sodium chloride and cryolite were successfully used in metal-filament lamps, even though the halogen vapor pressure of these compounds is negligible. Compounds such as K_3TlCl_6 react [13] as expected by *Skaupy*. Sodium chloride and cryolite, on the other hand, are effective only when deposited in a finely divided form on the wall and when tungsten vapor comes into contact with them. This effect has not yet been fully explained, but it is thought that these substances affect the structure of the deposit. Cryolite is nowadays added to the phosphorus getters in vacuum lamps.

8. "Positive" Cyclic Processes

Langmuir [14] took two tungsten wires in a tube to different temperatures under low chlorine pressures. It was found that at suitable temperatures, the hotter wire became thicker and the cooler wire thinner. A deposit of tungsten deliberately produced in a lamp disappeared on reaction with atomic chlorine, produced by the dissociation of Cl_2 on the hot wire. This demonstrated the fundamental possibility of transport of material from cooler to hotter zones ("positive" transport).

These results formed a basis for further thought and experimental studies on ways of making practical use of this process [15]. The only gases that can be considered are halogens, since only tungsten compounds containing halogen are sufficiently volatile at relatively low temperatures [eq. (c)]. (Carbonyls cannot be used for this purpose).

$$W + n\,X \rightleftharpoons WX_n \qquad (c)$$

[11] *E. A. Scribner*, US.-Pat. 254780 (March 7th, 1882).

[12] *F. Skaupy*, Ger. Pat. 246820 (Dec. 7th, 1909).

[13] *L. Hamburger*, Chem. Weekbl. *13*, 535 (1916).

[14] *I. Langmuir*, J. Amer. chem. Soc. *37*, 1139 (1915).

[15] *L. Hamburger, G. Holst, D. Lely*, and *E. Oosterhuis*, Versiag kon. Acad. Wetensch. *27*, 702 (1918); Proc. Roy. Soc. Sci. (Amsterdam) *21*, 1078 (1919).

The "inversion temperature" depends on the stability of the tungsten compounds formed, and decreases from fluorine compounds to iodine compounds. All parts of the lamp that can react under the experimental conditions, such as leads and supports, must be at a temperature above the inversion temperature. Cooler parts corrode, and this ultimately leads to failure of the lamp. However, the use of reactions with low inversion temperatures is limited by the low reaction rates. On the other hand, it was impossible to maintain the required temperature of a few hundred degrees at all parts of the lamp.

One interesting technical result of this work is the production of metals such as zirconium and titanium by the iodide process developed by *van Arkel, deBoer*, and *Fast*.

During the development of the high-pressure mercury arc between 1930 and 1950, the introduction of the technique of sealing tungsten into quartz lamps enabled the required temperatures to be maintained, and it was only then that the technical production of the halogen lamp became possible. It was described in a patent as early as 1949 [16], but details of the first commercial lamp were not published until 1959 [17]. Iodine was used as the filling on the basis of the (incorrect) thermodynamic data available at that time [18]. The inversion temperatures for the other halogens are too high.

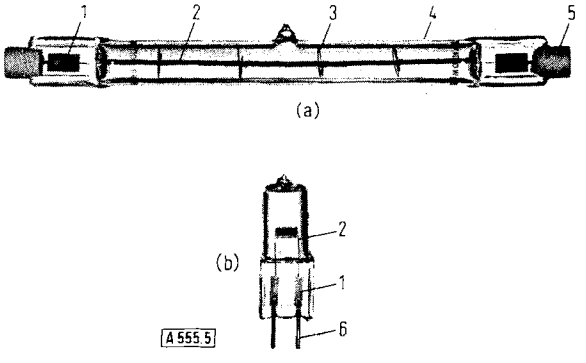


Fig. 5. (a) Halogen photo lamp 220 V, 1000 W; (b) halogen projector lamp, 24 V, 150 W; both lamps half size.

1. Molybdenum foil; 2. tungsten filament; 3. tungsten support; 4. quartz tube; 5. porcelain; 6. nickel pin.

The design of lamps of this type is shown in Figs. 5a and 5b. The cyclic process requires constructions and working conditions different from those of conventional lamps [19]. Thus elongated lamps (Fig. 5a) must be operated within an angle of $\pm$ 4° from the horizontal, since thermal diffusion otherwise causes a depletion of halogen in the upper part of the lamp, leading to premature failure. The envelope, which is made of quartz or a high-melting hard glass, is situated as close as possible to the tungsten coil. The wall temperature is about 600 °C, so that no volatile compounds can condense and be withdrawn from the cycle. The concentration of the iodine vapor is about 0.25 µmole/ml.

[16] *O. Neunhoeffer* and *P. Schulz*, Ger. Pat. 841307 (Oct. 6th, 1949).

[17] *E. G. Zubler* and *F. A. Mosby*, Illuminating Eng. *54*, 734 (1959).

[18] *L. Brewer, L. A. Bromley, P. W. Gilles*, and *L. Lofgren* in *L.L. Quill*: The Chemistry and Metallurgy of Miscellaneous Materials: Thermodynamics. National Energy Series, Div. IV, Vol. 19B. McGraw-Hill, New York 1950; *C. E. Wicks* and *F. E. Bloch*, Paper 8, Bulletin 605, Bureau of Mines 1963, p. 125.

[19] *T. M. Lemons* and *E. R. Meyer*, Illuminating Eng. *59*, 723 (1964).

This construction offers a number of advantages. Since the lamp does not blacken during its working life[19a], there is no need for a large bulb, which would also make the high wall temperatures impossible to maintain. The resulting small volume, about 1 % of the volume of a conventional lamp, permits the economical use of the heavier but expensive inert gases. Since the cross section of the cylinder is roughly the same as the thickness of the Langmuir layer, the heat losses are independent of the pressure, as pointed out earlier. These lamps can therefore be operated at high gas pressures. This is made technically feasible by the increase in mechanical strength resulting from the smaller diameter. Both of these measures lead to a decrease in the rate of evaporation. This possibility can be utilized in two ways: the life of the lamp under comparable conditions may be increased, or the filament temperature may be raised, thus giving a higher luminous efficiency and brightness for the same working life (Table 1).

The most recent developments have been directed away from the iodine lamp. Owing to the color of iodine, the iodine concentration must not exceed 0.25 μmole/ml, since light losses otherwise occur owing to absorption. Since it is also difficult to dose small quantities of iodine in the production of these lamps, attempts were made to replace iodine with other halogens. However, the other halogens can hardly be used in the elementary form, since even bromine attacks the cooler leads and supports. Instead of bromine, it is possible to use hydrogen bromide, which is formed by decomposition of easily dosed dibromomethane on the filament[20]. Lamps of this type are already on the market. The small quantity of carbon formed during the decomposition has no effect on the quality of the lamp. In principle, hydrogen chloride may also be used. Absorption is negligible in either case.

Owing to their special properties, the use of halogen lamps is steadily growing[21,22], particularly in photography, as well as in outdoor lighting and in automobile headlights. Many types of lamps (50 to about 10000 W) are in use.

9. Chemical Reactions in Incandescent Lamps

Tungsten diiodide is assumed to be formed in the iodine lamp[17,22–24]:

$$W + I_2 = WI_2 \qquad (d)$$

This assumption is based on the sparse and outdated literature on tungsten iodides[25], and on estimated thermodynamic data on equilibria in tungsten halides[18]. However, more recent calorimetric measurements on tungsten chlorides[26] and bromides[27] have shown considerable deviations from the estimated values (which were not based on any experimental data, with the exception of an incorrect value for WCl_6). Moreover, no experimental evidence has been found for the formation of a binary tungsten iodide under the conditions prevailing in the iodine lamp[28]. An indication of the true state of affairs was provided by the observation that the cyclic process in the iodine lamp requires the presence of small quantities of oxygen.

Various interpretations were offered for this discovery[29], until the stable tungsten dioxide diiodide, WO_2I_2, was prepared[30]. The cyclic process in an iodine lamp containing no oxygen can be started by the introduction of WO_2I_2. On the basis of experiments and observations in the laboratories at Aachen and Eindhoven[*], it is concluded that the reactions shown in Fig. 6 occur in the iodine lamp. This suggestion does not conflict with practical experience[28].

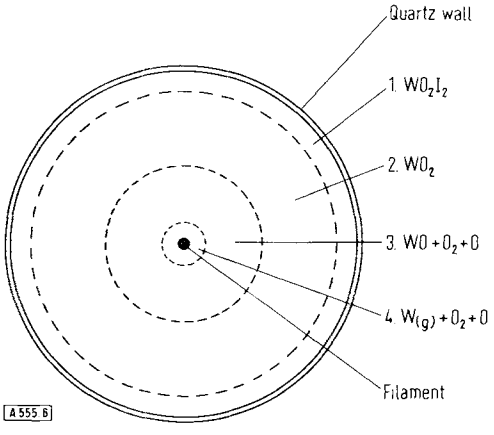


Fig. 6. Transport in an iodine-oxygen lamp. Diagram of the reaction zones with the predominant molecules. The inert gas and iodine, which are present everywhere, are not indicated.

In the neighborhood of the filament (temperature about 3000 °K), tungsten and oxygen react to form a tungsten oxide. Near the wall, the oxide reacts with iodine to form an oxide iodide, which remains gaseous at the high wall temperatures. Owing to the excess of iodine present, WO_2I_2 cannot decompose with deposition of WO_2, which would condense on the wall. It is not yet known whether the oxygen cycle also occurs in the bromine lamp (tungsten bromides are known).

10. The Regenerative Cycle

We have seen that there is no deposition of tungsten in halogen lamps during operation, and hence no blackening of the bulb wall, and that the luminous efficiency

[19a] For a "physical" solution of the problem, see *H. Hörster, H. Lydtin, O. Reifenschweiler*, and *K. G. Fröhner*, Z. angew. Physik, in press.

[20] *G. t'Jampens* and *M. H. A. van der Weijer*, Philips techn. Rev. *27*, 173 (1966).

[21] *J. W. Strange* and *J. Stewart*, Trans. Illum. Eng. Soc. (London) *28*, 91 (1963).

[22] *M. Déribéré*: Lampes à iode; lampes à iodures. Dunod, Paris 1965.

[23] *L. J. Davies*, Trans.Illum. Eng. Soc. (London) *25*, 11 (1960).

[24] *J. A. Moore* and *C. M. Jolly*, G. E. C. Journal *29*, 99 (1962).

[25] Gmelins Handbuch der anorg. Chemie. 8th Edit., System No. 54, Wolfram. Verlag Chemie, Weinheim/Bergstr. 1933, reprinted 1955.

[26] *S. A. Shchukarev, G. I. Novikov, I.V. Vasil'kova, A.V. Suvorov, N.V. Andreeva, B. N. Sharupin*, and *A. K. Baev*, Russ. J. inorg. Chem. (Transl. of Ž. neorg. Chim.) *5*, 802 (1960).

[27] *S. A. Shchukarev, G. I. Novikov*, and *G. A. Kokovin*, Russ. J. inorg. Chem. (Transl. of Ž. neorg. Chim.) *4*, 995 (1959); *S. A. Shchukarev* and *G. A. Kokovin, ibid. 5*, 241 (1960); *9*, 715 (1964).

[28] *J. Tillack*, unpublished.

[29] *E. G. Zubler* and *F. A. Mosby*, US.-Pat. 3160454 (Dec. 8th, 1964).

[30] *J. Tillack, P. Eckerlin*, and *J. H. Dettingmeijer*, Angew. Chem. *78*, 451 (1966); Angew. Chem. internat. Edit. *5*, 421 (1966).

[*] N.V. Philips, Lighting Division, Research Dept., Eindhoven (Netherlands).

remains practically constant throughout the life of the lamp. The question now arises whether the life of the lamp is also prolonged.

The life of the lamp could be increased only if the tungsten were preferentially transported back to the hottest parts, so preventing the development of hot spots. This condition is certainly not satisfied in the iodine and bromine lamps. The compounds responsible for the deposition of tungsten are completely dissociated before they reach the filament, owing to the high temperature of the latter. The tungsten should therefore be preferentially deposited on the cooler parts of the coil; this ultimately corresponds to an axial transfer of material from hotter to cooler parts of the filament. This process has been demonstrated by tracer techniques [31]. A model lamp contained three filaments the center one having been activated in a reactor. After 220 hours of operation, most of the ^{185}W had been deposited near the ends of the unactivated filaments (Fig. 7).

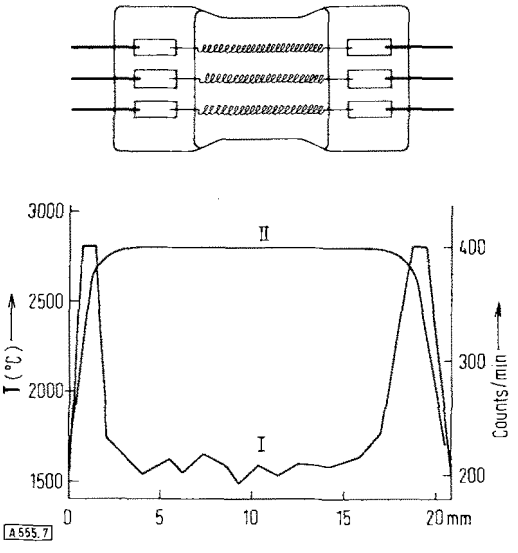


Fig. 7. Transport of tungsten along the filament in a lamp filled with iodine and 0.6 atm of xenon [31]. Top: experimental arrangement, schematic. The center coil contains ^{185}W. Bottom: activity (curve I) of ^{185}W after a burning time of 220 hours, and temperature (curve II) along one of the unactivated coils.

The outstanding improvements achieved with the new lamps are due to the prevention of blackening and the increase in working life resulting from the use of high gas pressures [32, 33] but not to regeneration of the filament. Only the most stable compounds of tungsten can take part in a regenerative cycle. This led *J. Schröder* to study the fluorine cycle in our laboratory [34]. Since fluorine reacts with tungsten even when cold, blackening is prevented even at low temperatures, and any blackening present is reversed.

For example, the blackening on the wall of a tungsten lamp (burning time 10 hours at 3000 °C in argon at 500 mm) could be removed by the introduction of WF_6 (burning time 15 min at 3100 °C, 500 mm of argon + 2 mm of WF_6). Despite considerable experimental difficulties, it could be shown that fluorine has a true regenerative effect. Fluorine is introduced as NF_3, which decomposes on the filament. The glass bulb is protected by a thin layer of MgF_2 and CoF_2. A tungsten loop, the thickness of which has been reduced over half of its length by etching, is heated to high temperatures (Fig. 8a). (The thicker part, which is cooler, is not visible in the photograph). After a burning time of 15 minutes in an atmosphere of WF_6 the loop becomes uniform (Fig. 8b). Microscopic examination shows that its thickness is constant over its entire length. Fig. 9 shows how the temperature along a tungsten coil becomes uniform on treatment with fluorine. In principle, therefore, fluorine satisfies the requirements for a regenerative cycle. Thus while the conditions for a "fluorine lamp" are by no means satisfied, in view of the extreme technological difficulties encountered in the protection of the cooler parts against attack by fluorine, these experiments nevertheless substantiate the above views on the regenerative cycle.

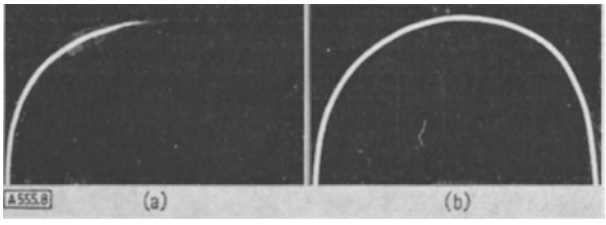


Fig. 8. (a) Tungsten loop immediately after the lamp is switched on. The left-hand side is thinner than the right-hand side. The temperature on the left is 3100 °C, on the right 2800 °C. (b) The same loop after burning for 10 min in 500 mm of Ar + 2 mm of WF_6. The geometry and temperature of the wire have become perfectly uniform (magnification 4×).

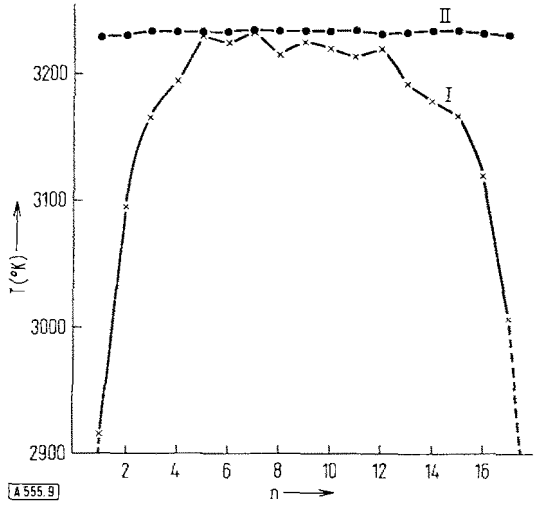


Fig. 9. Temperature along a tungsten filament (n = number of turns). I. No previous treatment. II. Same type of coil, after burning for 5 min in 200 mm of Ar + 4 mm of NF_3.

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Translated by Express Translation Service, London

[31] *P. Bayle, D. Blanc, J. Le Strat, Y. Renaud, L. Scoarnec,* and *P. Waguet,* C. R. hebd. Séances Acad. Sci. *258,* 4710 (1964).

[32] *W. Schilling,* Elektrotechn. Z. *B 13,* 485 (1961).

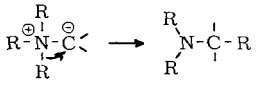
[33] *J. W. van Tijen,* Philips techn. Rev. *23,* 237 (1961/62).

[34] *J. Schröder,* Chem. Engng. News *42,* No. 37, p. 77 (1964); Philips techn. Rev. *26,* 111 (1965).

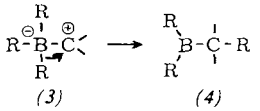
Borate Complexes Derived from Lithium Carbenoids — Mechanism of the "Inverse Stevens Rearrangement" [1]

By *G. Köbrich* and *H. R. Merkle* [*]

Jäger and *Hesse* [2] have contrasted the nitrogen ylides and their ability to undergo the cationotropic Stevens rearrangement, with the boron ylides *(3)* because several anionotropic rearrangements of boron ate-complexes can be ascribed to the fact that the arrangement of their charges is the reverse of that in *(1)*. It has been an open question whether this "inverse Stevens rearrangement" is really to be ascribed to a boron ylide intermediate stage.

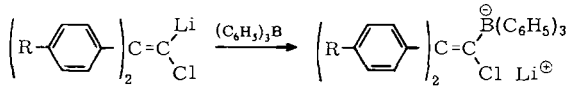


(1) *(2)*



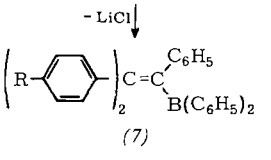
(3) *(4)*

We observed inverse Stevens rearrangements when we treated stable lithium carbenoids *(5)* [3] with triphenylboron. ate-Complexes *(6)* were slowly formed which rearranged to boranes *(7)* with elimination of lithium chloride when the mixture was warmed to room temperature or boiled in tetrahydrofuran.



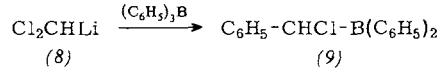
(5) *(6)*

(a), R = H
(b), R = Cl
(c), R = CH_3

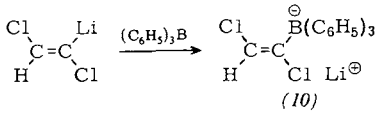


(7)

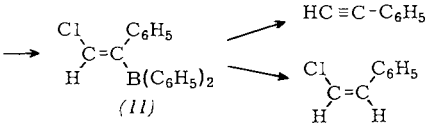
Use of dichloromethyl-lithium *(8)* gives the corresponding (chlorobenzyl)diphenylborane *(9)* The ate-complex *(10)* formed from *trans*-dichlorovinyl-lithium decomposes at −100 °C into pure *cis*-styryl chloride and phenylacetylene (molar ratio about 1:3); presumably the borane *(11)* is first formed.



(8) *(9)*

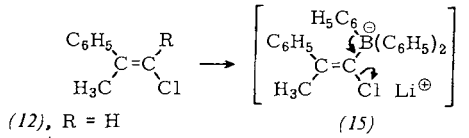


(10)



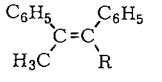
(11)

The ate-complex *(14)* formed from *trans*-methylstyryl chloride *(12)* *via* the *trans*-carbenoid compound *(13)* [4] affords 99% pure *cis*-α-methylstilbene *(17)* [yield 65%, calculated on *(12)*] on rearrangement and acid hydrolysis. The *cis*-isomer of compound *(12)* gives 98 % pure *trans*-α-methylstilbene (yield 71 %). These findings exclude a boron ylide intermediate common to the two isomers. The steps *(12)* → *(13)* → *(14)* and *(16)* → *(17)* are electrophilic reactions at the unsaturated carbon atom with retention of configuration. It then follows that the rearrangement step *(14)* → *(16)* occurs with inversion by rear attack *(15)* of the phenyl group on the carbon atom carrying the chlorine substituent.



(12), R = H
(13), R = Li
(14), R = $^{\ominus}B(C_6H_5)_3$ $Li^{\oplus}$

(15)



(16), R = $B(C_6H_5)_2$
(17), R = H

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[*] Doz. Dr. G. Köbrich and Dipl.-Chem. H. R. Merkle
Organisch-Chemisches Institut der Universität
Tiergartenstraße
69 Heidelberg (Germany)

[1] Part XXII of Stable Carbenoids. — Part XXI: *G. Köbrich, H. Heinemann,* and *W. Zündorf,* Tetrahedron, in press. — We thank the Deutsche Forschungsgemeinschaft, the Wirtschaftsministerium of Baden-Württemberg, and the Fonds der Chemischen Industrie for financial support.

[2] *H. Jäger* and *G. Hesse*, Chem. Ber. *95*, 345 (1962).

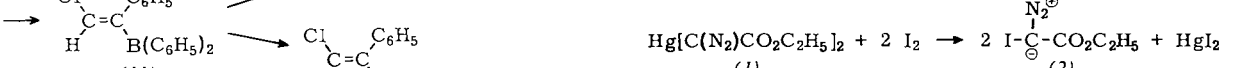
[3] For a review, see *G. Köbrich et al.*, Angew. Chem. *79*, *15* (1967); Angew. Chem. internat. Edit. *6*, 41 (1967). Cf. *G. Köbrich* and *W. Drischel*, Tetrahedron, *22*, 2621 (1966).

[4] *K. Flory*, unpublished experiments (1963); *F. Ansari*, Dissertation, Universität Heidelberg 1966.

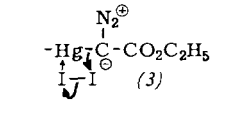
Ethyl Diazoiodoacetate and its Decomposition to Ethoxycarbonyliodocarbene

By *F. Gerhart, U. Schöllkopf,* and *H. Schumacher* [*]

Halogenodiazomethanes are of interest as precursors of halogenocarbenes and as preparative reagents [1]. We obtained ethyl diazoiodoacetate *(2)*, the first characterized halogenodiazoalkane [2], in about 80% yield when we treated diethyl mercuribisdiazoacetate *(1)* [3] in ether with rather less than 2 equivalents of iodine. The filtrate was concentrated (water-pump, room temperature, rotary evaporator) and the residue was digested with petroleum ether (b.p. 40 °C) to remove the last traces of mercuric iodide. Compound *(2)* is a red oil, stable for days at 0–5 °C, giving IR bands at 2080 and 1680 cm^{-1}. Triphenylphosphazine derivative: m.p. 109 to 112 °C (decomp.; precipitated from benzene by petroleum ether).



(1) *(2)*



(3)

We formulate scission of the carbon-mercury bond by iodine as an S_Ei process, depicted in *(3)* [4]. Since this should proceed also with other reagents, it should be possible to prepare further hetero-substituted diazoacetic esters from the compound *(1)* [5].

Photolysis of *(2)* (450 W Hanovia lamp, Pyrex filter) gave ethoxycarbonyliodocarbene *(4)*, from which we obtained ethyl 1-iodo-2,2-dimethylcyclopropanecarboxylate *(5)* (b.p.



(4) *(5)*

45 °C/0.4 mm; yield 40%; NMR signals of the cyclopropane protons as an AB spectrum at $\tau = 8.7$ with $J_{AB} \approx 6$ Hz) on irradiation of *(2)* in isobutene until evolution of nitrogen ceased. Products formed by insertion in the C–H bond were not detected [6]. We conclude that the carbene *(4)* is more selective than ethoxycarbonylcarbene.

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]*] Dipl.-Chem. F. Gerhart, Prof. Dr. U. Schöllkopf, and Dr. H. Schumacher
Organisch-Chemisches Institut der Universität
Windausweg 2
34 Göttingen (Germany)

[1] Cf. *R. Huisgen*, Angew. Chem. *67*, 439 (1955).

[2] Chloro- and bromo-diazomethane were recently prepared *in situ*; they are stable only below –40 °C. Cf. *G. L. Closs* and *J. J. Coyle*, J. Amer. chem. Soc. *87*, 4270 (1965).

[3] *E. Buchner*, Ber. dtsch. chem. Ges. *28*, 215 (1895).

[4] For the mechanism of C–Hg fission by iodine see *S. Winstein* and *T. G. Traylor*, J. Amer. chem. Soc. *78*, 2597 (1956).

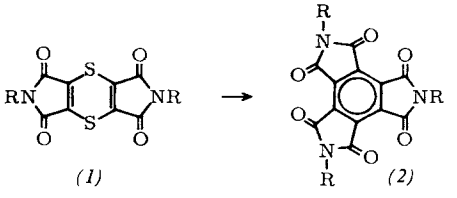
[5] Cf. *U. Schöllkopf* and *P. Markusch*, Tetrahedron Letters *1966*, 6199.

[6] It is possible that they decompose under the conditions of the photolysis.

Evidence for the Intermediate Occurrence of Acetylenedicarboxyimide

By *W. Draber*[*]

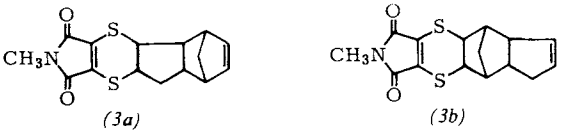
When 1,4-dithiintetracarboxydiimides *(1)* are heated in pyridine at 120 °C, mellittriimides *(2)* are obtained in yields of up to 50% together with sulfur and unidentified brown products. Small quantities of mellittriimide were also occasionally obtained in the preparation of the dithiins *(1)* from dichloromaleimides and H_2S in the presence of a material such as $CaCO_3$ [1] to neutralize the acid formed. Heating the dithiins without pyridine or in indifferent solvents such as xylene or ethanol does not lead to formation of triimides *(2)*.



(1) *(2)*

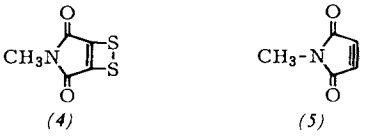
R = H, CH_3, C_6H_5-CH_2

An indication of the course of the reaction was given by the formation of a yellow compound, m.p. 137.5–138 °C, yield 7%, that could be isolated chromatographically together with the mono- and di-adducts of cyclopentadiene to *(1)* and 24% of *(2)*, after the dithiin *(1)* had been heated with an excess of dicyclopentadiene and pyridine under nitrogen for 16 hr at 110 °C. The composition and molecular weight correspond to an adduct of 2 moles of cyclopentadiene to one of maleimide and 2 g-atoms of sulfur. IR spectrum in KBr: 1765, 1715, 1700 cm^{-1} (imide-CO); 1600 (C=C); 1550 (imide-C=C). UV spectrum in ethanol: 240 mμ (log ε = 3.38), 267 (3.85), 424 (3.34). These results indicate a dimercaptomaleimide system. The NMR spectrum at 90 MHz in $CDCl_3$ [τ = 4.34 (2 olefinic protons), 6.97 ($N-CH_3$), 8.42 (1 H), poorly resolved multiplet at τ = 6.4 to 7.9 (9 H)] does not permit unambiguous decision between the structures *(3a)* and *(3b)*.



(3a) *(3b)*

The formation of *(3a)* or *(3b)* is preferred to an asymmetrical decomposition of *(1)* to a compound *(4)* [2] and acetylenedicarboxyimide *(5)*, from which *(2)* is then obtained. The Diels-Alder adduct of cyclopentadiene to *(5)*, not hitherto described, would probably not be stable under the reaction conditions.



(4) *(5)*

Attempts to prepare the Diels-Alder adduct of cyclopentadiene to acetylenedicarboxylic anhydride from the corresponding acid by dehydration with acetic anhydride gave a substance that polymerized rapidly even at room temperature.

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[*] Dr. W. Draber
Shell Grundlagenforschung GmbH.
Schloß Birlinghoven
52 Siegburg (Germany)
Present address: Farbenfabriken Bayer
Wissenschaftliches Hauptlaboratorium
509 Leverkusen-Bayerwerk (Germany)

[1] *W. Draber*, unpublished work.

[2] Compounds of 1,2-dithiete structure are known to add readily to reactive double bonds, yielding 1,4-dithiins: *H. E. Simmons*, *D. C. Blomstrom*, and *R. D. Vest*, J. Amer. chem. Soc. *84*, 4782 (1962).

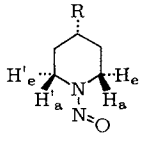
Anisotropic Effects in Heterocyclic Nitrosamines

By *Y. L. Chow*[*]

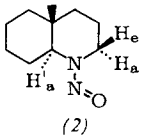
The restricted rotation about the partial N–N double bond of a nitrosamino group derived from a symmetrical amine gives rise to different NMR chemical shifts for the *cis*- and *trans*-α-methylene protons [**]. A conformationally "frozen" heterocyclic nitrosamine should allow direct observation of the long-range shielding of the nitrosamino group, provided that inversion at the amine center is slow.

The 4-substituted *N*-nitrosopiperidines *(1b)* and *(1c)* give four well-separated signals, corresponding to the four α-protons in different environments (see Table 1). The signals were assigned on the basis of their splitting pattern and coupling constant [1] and by decoupling experiments at 100 MHz. The equatorial protons H_e and H'_e, being coplanar, or nearly so, with the $C_\alpha-N-N-O$ plane, absorb at approximately the same (lower) field [2], whereas the axial protons H_a and H'_a absorb at higher fields. Since H_a is situated inside the semi-circular shielding zone of the nitrosamino group, its signal appears at a far higher field. This anisotropy is even better manifested by an unusually large

chemical shift difference ($\Delta\delta$ = 2.4–2.9 ppm) between the axial (H_a) and equatorial (H_e) protons of the *cis*-methylene group. In contrast, the corresponding chemical shift difference of the *trans*-methylene group is much smaller ($\Delta\delta'$ = 1–1.4 ppm).



(1a), R = H
(1b), R = CH_3
(1c), R = CH_2-C_6H_5



(2)

The conformationally rigid and unsymmetrical *trans*-decahydroquinoline gives the *anti*-nitrosamine *(2)* as the sole nitrosation product. The Dreiding model shows that the rigidly held equatorial proton of the β-methylene group in the cyclohexane ring is close to the oxygen in the *syn*-configuration and thus destabilizes this configuration. The chemical shifts of the *cis*-α-methylene protons and particularly the large difference (2.73 ppm) between the shifts of the axial and equatorial protons lead unambiguously to the *anti*-configuration assignment for the nitrosamine *(2)*.

The NMR spectrum of conformationally mobile *N*-nitrosopiperidine *(1a)* is considerably simplified due to rapid interconversion of the conformers, whereby the axial and equatorial protons give an average signal. Since the two conformers are energetically equivalent, the signal of the *cis*-α-methylene protons should occur half-way between the H_a and H_e signals. The observed signal at τ = 6.35 is therefore assigned to *cis*-α-methylene protons and that at τ = 5.87 to *trans*-α-methylene protons. In acyclic nitrosamines *cis*-α-methylene protons also absorb at a higher field than *trans*-α-methylene protons[3].

Table 1. NMR data of nitrosamines at 60 MHZ (τ values, Varian A 56/60 spectrometer, $(CH_3)_4Si$ as internal standard).

Compound	Solvent	H_a	H_e	$\Delta\delta$ [a] (ppm)	H'_a	H'_e	$\Delta\delta'$ (ppm)
(1b) [b]	CCl_4	7.50	5.15	2.35	6.35	5.38	0.87
	C_6H_6	7.83	5.18	2.65	6.80	5.57	1.23
(1c) [b]	CCl_4	7.62	5.17	2.45	6.47	5.38	1,09
	C_6H_6	8.05	5.18	2.87	7.02	5.62	1.40
(2)	CCl_4	7.63 [c]	4.90 [d]	2.73	6.68	—	—
	C_6H_6	7.67	4.83	2.84	7.11	—	—
(1a)	CCl_4		6.35			5.87	
	C_6H_6		6.57			6.23	

[a] $\Delta\delta = \tau(H_a) - \tau(H_e)$.

[b] The axial protons show a triplet, each split into doublets, $J_{gem} \approx J_{aa} \approx$ 12–13 Hz, J_{ae} = 3–4 Hz. The equatorial protons show a doublet that is further split into multiplets. J_{gem} = 13 Hz; $W^1/_2$ = 6–7 Hz.

[c] Determined by decoupling experiments.

[d] Each doublet is further split into multiplets, J_{gem} = 14 Hz and $W^1/_2$ = 7 Hz.

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[*] Dr. Y. L. Chow
Department of Chemistry
Simon Fraser University
Burnaby, B. C. (Canada)

[**] The same convention of *cis-trans* α-protons and *syn-anti* configuration as in [3] is adopted.

[1] *R. U. Lemieux, R. K. Kulling*, and *R. Y. Moir*, J. Amer. chem. Soc. *80*, 2237 (1958); *R. U. Lemieux, R. K. Kulling, H. J. Bernstein*, and *W. G. Schneider, ibid. 80*, 6098 (1958); *F. A. L. Anet, R. A. B. Bannard*, and *L. D. Hall*, Canad. J. Chem. *41*, 2331 (1963).

[2] H_e is slightly less shielded than H'_e by *ca.* 0.25 ppm since H_e is conformationally in juxtaposition with the high electron density of nitrosamino oxygen. *S. Winstein, P. Carter, F. A. L. Anet*, and *A. H. R. Bourn*, J. Amer. chem. Soc. *87*, 5247 (1965); *A. D. Buckingham*, Canad. J. Chem. *38*, 300 (1960).

[3] *G. J. Karabatsos* and *R. A. Taller*, J. Amer. chem. Soc. *86*, 4373 (1964).

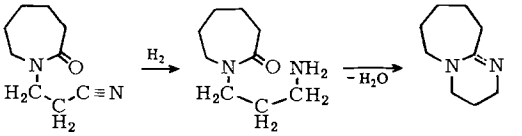
1,5-Diazabicyclo[5.4.0]undec-5-ene, a New Hydrogen Halide Acceptor

By *H. Oediger* and *Fr. Möller*[*]

1,5-Diazabicyclo-4.3.0]non-5-ene *(1)* can be used to introduce double bonds by removal of hydrogen halide[1,2]. We have now found that 1,5-diazabicyclo[5.4.0]undec-5-ene *(2)*, obtained, analogously to *(1)*[1,3] from caprolactam and acrylonitrile by way of compounds *(3)* and *(4)*, is considerably superior to the base *(1)* for this purpose.



(1)



(3) *(4)* *(2)*

As shown in the table, the yields of alkene are considerably improved by use of the base *(2)*.

Bromoalkane	Alkene	Yield (%) on use of *(1)*	Yield (%) on use of *(2)*
4-Bromoheptane	3-Heptene	60	91
2-Bromoheptane	1- and 2-Heptene (*ca.* 1:4) [a]	36	78
2-Bromooctane	1- and 2-Octene (*ca.* 1:4) [a]	40	84

[a] Molar proportions.

Method: A mixture of equimolar amounts of bromoalkane and base is warmed to 80–90 °C and the alkene formed is distilled off. A solvent such as dimethyl sulfoxide may be added.

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[*] Dr. H. Oediger and Dr. Fr. Möller
Wissenschaftliches Hauptlaboratorium
Farbenfabriken Bayer AG.
509 Leverkusen (Germany)

[1] *H. Oediger, H. J. Kabbe, Fr. Möller*, and *K. Eiter*, Chem. Ber. *99*, 2012 (1966).

[2] *H. Oediger, K. Eiter, Fr. Möller*, and *H. J. Kabbe*, German Pat. 1186063 (15th May, 1962).

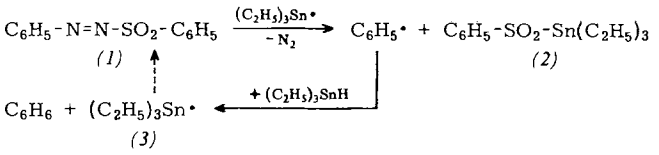
[3] *Fr. Möller*, German Pat. Appln. F 47138 IV d/12 p.

Free-Radical Decomposition of Azo Compounds Induced by Organotin Hydrides

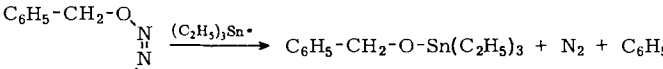
By *W. P. Neumann* and *H. Lind*[*]

We have observed a radical-induced decomposition of the azo compounds R–N=N–X–R′ and R–X–N=N–X–R′, where X is a covalently bound polar group.

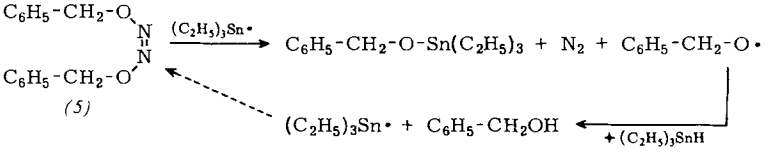
Homolysis of phenyl phenylazo sulfone *(1)*[1] in dilute toluene solution is accelerated ten-fold, even at 80 °C, if an organotin hydride is present ($t_{1/2}$ = 8 min). Benzene, N_2, and a stannyl phenylsulfinate *(2)*, m.p. 67 °C, are formed in equimolar amounts. Occurrence of free phenylsulfonyl radicals can be excluded; they would afford the sulfinic acid and, with further hydride, H_2. Stannyl radicals *(3)* induce the acceleration and their covalent attachment to the sulfonyl group is synchronous with the detachment of the azo group (S_R2 mechanism).



A side reaction is the free-radical hydrostannation of *(1)* at the azo group to the hitherto unknown *N'*-phenyl-*N*-phenylsulfonyl-*N*-stannylhydrazines, *e.g. (4)*, m.p. 116 °C, the yield of which depends on the relative amounts of the reagents and on the temperature.



Homolysis of dibenzyloxydiimide *(5)* [2] cannot be induced in solution, either by increasing the concentration of the diimide, or by the radical scavengers galvinoxyl [**], iodine, chloranil, methanol, or *p*-t-butylthiophenol. It is first order in benzene, chloroform, and chlorobenzene, giving 1.0 mole of N_2, 0.50 mole of benzyl alcohol and, contrary to previous assumption [2], only 0.25 mole of benzaldehyde, together with a resin of average composition $(C_6H_5{-}CHO)_4$ and some benzyl benzoate. Evidently the benzaldehyde captures benzyloxy radicals.



However, in dilute benzene solution at 30 °C the homolysis of the diimide *(5)* is accelerated eight-fold if an organotin hydride is added ($t_{1/2}$ = 22 min). This effect is largely eliminated by the powerful radical-trapping agent galvinoxyl. An S_R2 mechanism operates here also, attachment of a benzyloxy group to the attacking stannyl radical being synchronous with its detachment from the azo group. The other benzyloxy group is liberated as a radical and then is trapped by the hydride. N_2 is also formed.

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[*] Prof. Dr. W. P. Neumann and Dipl.-Chem. H. Lind
Institut für organische Chemie der Universität
Ludwigstr. 21
63 Giessen (Germany)

[1] *A. J. Rosenthal* and *C. G. Overberger*, J. Amer. chem. Soc. *82*, 108 (1960).

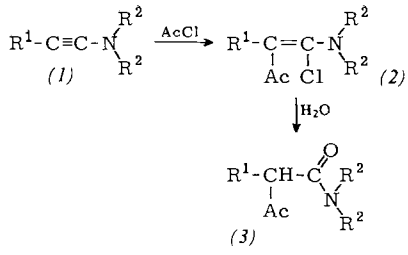
[2] *A. Hantzsch* and *L. Kaufmann*, Liebigs Ann. Chem. *292*, 317 (1896): *J. Harris, J. Marshall*, and *K. B. Jarrett*, Nature (London) *159*, 843 (1947); *S. Nair* and *J. B. de Sousa*, J. chem. Soc. (London) *1962*, 4464.

[**] 2,6-Di-t-butyl-4-(3,5-di-t-butyl-4-oxocyclohexylidenemethyl)phenoxyl.

Acylation, Alkylation, and Protonation of Alkynylamines [1]

By *H. G. Viehe, R. Buijle, R. Fuks, R. Merényi*, and *J. M. F. Oth* [*] [2]

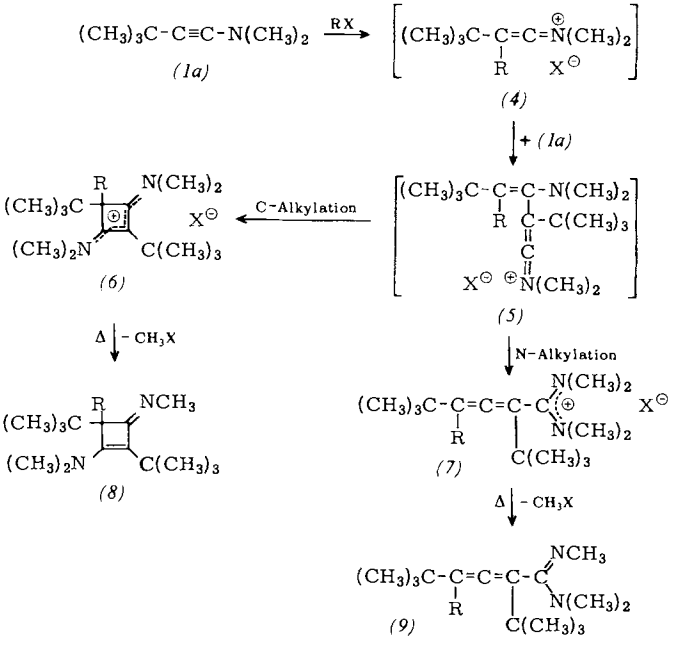
On acylation with acyl chlorides (such as C_6H_5COCl. CH_3COCl, $COCl_2$) in toluene at room temperature alkynylamines (ynamines) *(1)* afford 2-acyl-1-chloroalkenylamines *(2)*, which are hydrolysed to 2-acylcarboxamides *(3)* by water even at room temperature.



R^1	R^2	Ac	R^3	*(2)*	*(3)*
$(CH_3)_3C$	CH_3	COCl	CO_2H	B.p. 76–78 °C/0.5 mm, yield, 85 %	M.p. 127 °C, yield 94 %
C_6H_5	C_2H_5	COC_6H_5	COC_6H_5	Not isolated	M.p. 112 °C, yield 88 %
CH_3	$R^2_2 = (CH_2)_5$	$COCH_3$	$COCH_3$	Not isolated	B.p. 93 °C/0.2 mm, yield 91 %

Alkylation of (3,3-dimethyl-1-butynyl)dimethylamine *(1a)* with methyl bromide and reaction with a second molecule of alkynylamine gives the salts *(6)* and *(7)*. The ketene iminium salt of type *(4)* is probably first formed and reacts with further alkynylamine to afford the iminium salt *(5)* and this is then stabilized by intramolecular *N*- or *C*-alkylation. When 5.3 g (42 mmoles) of compound *(1a)* is heated with 3.4 g (36 mmoles) of methyl bromide without a solvent in a sealed tube for 30 hr at 90 °C, a solid salt mixture (yield 73 %) is formed that contains 35 % of the "cyclobutanecyanine" *(6)*, R = CH_3, and 65 % of the amidinium salt *(7)*. These products can be separated by recrystallization from acetone. Both salts lose methyl bromide on distillation, *(6)* giving an 80 % yield of the iminocyclobutenylamine *(8)* at 250 °C/0.2 mm, and *(7)* giving a 94 % yield of the allenecarboxamidine *(9)* at 225 °C/0.2 mm.

On protonation of the alkynylamine *(1a)* with HCl or HBF_4, only the cyclobutanecyanine *(6)*, R = H, is formed. A solution of 3 mmoles of HCl in 20 ml of dichloromethane is added slowly to 6 mmoles of compound *(1a)* in 5 ml of dichloromethane at −5 °C. The salt *(6)*, R = H, X = Cl, remains on evaporation of the solution and is recrystallized from alcohol/



	R	$X^{\ominus}$	B.p. (°C/mm) or m.p. (°C)	NMR [b]					IR	UV [d]	
				−CH	$-C-CH_3$	$-C(CH_3)_3$ [c]	$-N(CH_3)_2$	$=N-CH_3$	λ_{max} (μ)	λ_{max} (mμ)	ε
(6)	CH_3	$Br^{\ominus}$	251–252		8.42	8.63 8.87	6.63		C=C 5.91 C=C 6.35	220 293	5800 23700
	H	$Cl^{\ominus}$	258	5.70		8.64 8.87	6.63		C=C 5.91 C=N 6.35	227 290	5600 22300
	H	$BF_4^{\ominus}$	219–220	6.04		8.65 8.90	6.74		C=C 5.90 C=N 6.32	221 290	7000 24300
(8)	CH_3		140/12 [a]		8.55	8.73 8.98	7.13	6.82	C=C 5.97 C=N 6.35	277	13000
	H		130/12 [a]	6.64		8.72 8.99	7.13	6.94	C=C 5.97 C=N 6.35	275	11800
(7)	CH_3	$Br^{\ominus}$	237–238		8.18	8.79 8.88	6.55		C=C=C 5.11 C=N 6.18	242	10200
(9)	CH_3		67–70/0.2		8.33	8.88 8.98	7.20	6.75	C=C=C 5.20 C=N 6.25	222 (sh)	6600

[a] The temperatures recorded are bath-temperatures. [b] τ-Values using tetramethylsilane as internal standard. [c] Of the two values the upper is in each case for the group $(CH_3)_3C-C<$ or $(CH_3)_3-C<^{\oplus}$, and the lower for the group $(CH_3)_3C-C(R)<$ or $(CH_3)_3C-C<_{R}$. [d] Measured in methanol. sh = shoulder.

ether. Yield of pure material 44%. At 275 °C/0.2 mm compound *(6)* loses CH_3Cl and gives a 90% yield of compound *(8)*, R = H. Use of HBF_4 in place of HCl with *(1a)* leads to the salt *(6)*, R = H, X = BF_4, in 59% yield (recrystallized from ethanol).

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[*] Priv.-Doz. Dr. H. G. Viehe, Dr. R. Buijle,
Dr. R. Fuks, Dipl.-Ing. R. Merényi, and
Dr. J. M. F. Oth
Union Carbide European Research Associates
95, rue Gatti de Gamond
Bruxelles 18 (Belgium)

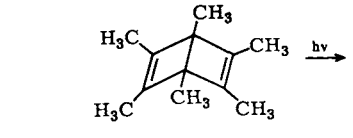
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[2] We thank Messrs. *M. Reinstein* and *W. Rennerts* for experimental assistance.

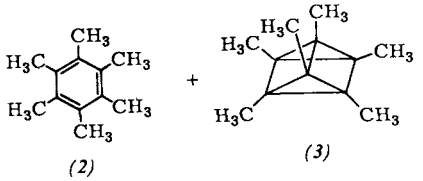
Synthesis of Hexamethylprismane

By *W. Schäfer, R. Criegee, R. Askani,* and *H. Grüner* [*]

If a solution of 80 g of hexamethyl(Dewar benzene) *(1)* [1] in 450 ml of anhydrous ether is irradiated for 170 hr at *ca.* 3 °C by UV light of wavelength 254 mμ (33W low-pressure immersion lamp; Hanau, type PL 368-NK 6/20), a mixture of hexamethylbenzene *(2)* (yield, 11 g = 14%) and hexamethylprismane *(3)* (yield, 4 g = 5%) is obtained and 80% of the starting material is recovered.



(1)



(2) *(3)*

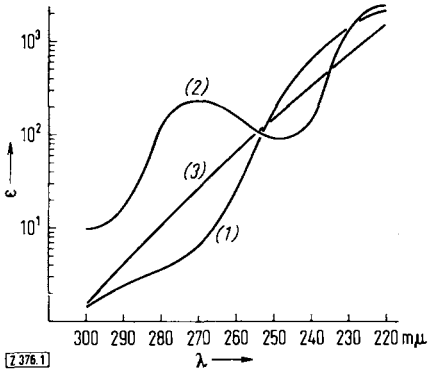
The ether is distilled off at atmospheric pressure, the main part (8–9 g) of the product *(2)* is filtered off, and the filtrate is distilled in a water-pump vacuum, yielding a mixture, b.p. 58–60 °C/18 mm, of *(1)* and the prismane derivative *(3)* which is readily volatile because of its spherical shape [distillation residue *ca.* 1.5 g of *(2)*]. The mixture, which has solidified after 12 hr in a refrigerator, melts on warming slowly to room temperature on a Buchner funnel under nitrogen. Hexamethylprismane *(3)* forms the filter cake and is recrystallized from, *e.g.*, ethanol.

Irradiation of a 1% ethereal solution of *(1)* at 0 °C for 3 hr with a 100W low-pressure mercury lamp (Gräntzel, Karlsruhe) gives a mixture of *(3)* 7%, *(1)* 47%, and *(2)* 45%. After distilling off the ether the residue is treated with ethanol (25 ml for 5 g of mixture). Hexamethylprismane distils in a rotary evaporator with the alcohol at 25 °C/30 mm and crystallizes out when the receiver is cooled to −30 °C.

Hexamethylprismane forms colorless prisms of m.p. 91 °C. It is sensitive to shock and deflagrates when rubbed in a mortar or placed in a flame. It explodes when placed in a melting-point capillary on a block heated at 250 °C or when concentrated sulfuric acid or iodine is added to it in a test tube.

As expected, the NMR spectrum shows only one singlet τ = 9.03.

The IR spectrum, which contains few lines, is characterized by bands (measured for a molten film) at 2850–2950 (s), 2722 (w), 1440 (s), 1375 (m), 1085 (w), 1045 (s), and 803 (s) cm^{-1} [2].



UV spectrum of hexamethylbenzene *(2)*, hexamethyl(Dewar benzene) *(1)*, and hexamethylprismane *(3)* in isooctane.

The UV absorption of *(3)* is unexpectedly intense, as is that of *(1)*, in the region where aromatic and conjugated systems absorb.

Pyrolysis of *(3)* in *o*-dichlorobenzene can be followed by means of the NMR spectrum. At 110 °C half of it has reacted after 2 hr to give a mixture containing 62% of *(2)* and 38% of *(1)*. Since the half-reaction time for the con-

version *(1)* → *(2)* is 2 hr only at 150 °C, the pyrolysis *(3)* → *(1)* + *(2)* must proceed to some extent by way of an intermediate of high energy.

Hexamethylprismane is the third prismane derivative to become known[3,4].

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[*] Dr. W. Schäfer
Forschungslaboratorien, Chemische Werke Hüls AG.
437 Marl (Germany)
Prof. Dr. R. Criegee, Dr. R. Askani, and Dr. H. Grüner
Institut für Organische Chemie der Technischen Hochschule
75 Karlsruhe (Germany)

[1] *W. Schäfer*, Angew. Chem. *78*, 716 (1966); Angew. Chem. internat. Edit. *5*, 669 (1966).

[2] s = strong, m = medium, w = weak.

[3] *K. E. Wilzbach* and *L. Kaplan*, J. Amer. chem. Soc. *87*, 4004 (1965).

[4] *R. Criegee* and *R. Askani*, Angew. Chem. *78*, 494 (1966); Angew. Chem. internat. Edit. *5*, 519 (1966).

Preparation of Derivatives of Bicyclo[4.2.2]deca-2,4,7,9-tetraene from Tricarbonylcyclooctatetraeneiron

By *U. Krüerke*[*]

We have prepared derivatives of bicyclo[4.2.2.]deca-2,4,7,9-tetraene *(1)* by addition of alkynes to the monocyclic form of cyclooctatetraene. Our starting material was tricarbonylcyclooctatetraeneiron *(2)* in which the metal atom is π-bonded to two of the double bonds[1].

When an equivalent amount of tolan is slowly (1 hr) added to the complex *(2)* in boiling mesitylene under nitrogen a hydrocarbon $C_{22}H_{18}$, m.p. 147–148 °, whose NMR spectrum is in accordance with the structure *(4a)* is formed, besides hexaphenylbenzene and $Fe_2(CO)_6(C_{28}H_{20})$ *(3)*[2]. Repeated chromatography on Al_2O_3 (eluent hexane/benzene-5 %) was necessary to separate the products *(3)* and *(4)*. Passage of carbon monoxide during the reaction increased the yield of *(4a)* to 35 %. The carbon monoxide stabilises the tricarbonyliron group in its complex *(2)* and almost wholly prevents the carbonylmetal-catalysed trimerisation[3] of tolan. No further increase in yield results when the carbon monoxide is under slight pressure (2–4 atm). Free cyclooctatetraene does not react with tolan over a period of 2 hr at 160 °C.

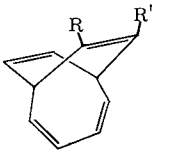
The compounds *(4b)* (m.p. 53 °C; yield 15 %) and *(4c)* (m.p. 74 °C; yield *ca.* 10 %) are formed from the complex *(2)* and methyl phenylpropiolate or trimethyl(phenylethynyl)silane, respectively. Attempted synthesis by reaction of *(2)* with $CH_3C{\equiv}CCH_3$, $C_6H_5C{\equiv}CH$, $C_6H_5C{\equiv}CCN$, and $CH_3OOCC{\equiv}CCOOCH_3$ was unsuccessful since trimerisation of the alkyne, formation of organoiron carbonyls, and decomposition predominated. Some 2,3-dimethylnaphthalene was obtained in the reaction with $CH_3C{\equiv}CCH_3$. $C_6H_5C{\equiv}CH$ yielded, besides a little 2-phenylnaphthalene, as main product a carbonyliron complex *(5)*, m.p. 180–181 °C (with slow decomp.), whose NMR spectrum indicated the presence of 9,10-dihydro-2-phenylnaphthalene as ligand.

Occurrence of the naphthalene derivatives demonstrates the primary formation but thermal instability of derivatives of bicyclo[4.2.2]decatetraene also in these reactions. In fact, the compound *(4a)* decomposes at 170–180 °C in a sealed and evacuated (*ca.* 10^{-3} mm) tube, mainly to 2,3-diphenylnaphthalene and diphenylbicyclo[3.3.2]deca-2,6,9-triene *(6)*, m.p. 110 to 116 °C. It was not possible to isolate the further products that were shown by thin-layer chromatography. The NMR spectrum of a non-crystalline hydrocarbon mixture gave no evidence for the presence of diphenylbullvalenes.

The compound *(6)* gives a very complicated NMR spectrum, so that the positions of the phenyl groups could not be determined unambiguously; but positions 2,6, 3,7, and 9,10 can be excluded on symmetry grounds. Since the melting point of the compound is unsharp a mixture of isomers may be present alongside a main component.

After irradiation of compound *(4a)* in cyclohexane with UV light for 5 hr at 20 °C, column chromatography on Al_2O_3 (eluent hexane/benzene -50 %) led to isolation of unchanged *(4a)* (40 %) and a viscous oil of composition $C_{22}H_{18}$ whose NMR spectrum was temperature-dependent and which thus probably contained diphenylbullvalene. It has not yet been possible to separate the components disclosed by the NMR spectrum; all the components of the oil decompose rapidly on thin-layer chromatography on SiO_2.

We have been unable to confirm the formation of bullvalene from the complex $(C_{10}H_{10})Fe_2(CO)_6$[4] which contains the ligand *(1)*.

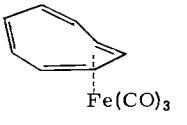


(1), R = R' = H

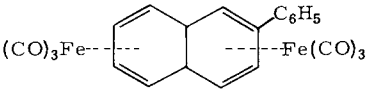
(4a), R = R' = C_6H_5

(4b), R = C_6H_5, R' = $COOCH_3$

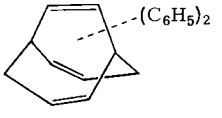
(4c), R = C_6H_5, R' = $Si(CH_3)_3$



(2)



(5)



(6)

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[*] Dr. U. Krüerke
Union Carbide European Research Associates
95, rue Gatti de Gamond
Bruxelles 18 (Belgium)

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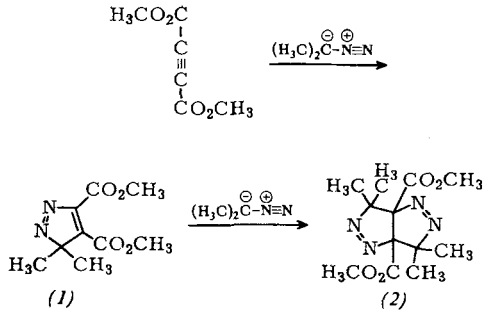
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Double 1,3-Dipolar Addition to a Triple Bond to give the Bicyclo[1.1.0]butane System

By *M. Franck-Neumann*[*]

Acetylenes and secondary diazoalkanes give 3*H*-pyrazoles[1], pyrolysis of which leads to cyclopropenes[2]. We have found that dimethyl acetylenedicarboxylate and the very reactive 2-diazopropane[3] afford dimethyl 3,3a,6,6a-tetrahydro-3,3,6,6-tetramethylpyrazolo-[4,3-*c*]pyrazole-3a,6a-dicarboxylate *(2)* together with dimethyl 3,3-dimethyl-3*H*-pyrazole-4,5-dicarboxylate *(1)*:



(1) *(2)*

The compound *(2)*, m.p. 59 °C, is obtained in 85 % yield by using an excess of 2-diazopropane under the following conditions: Dimethyl acetylenedicarboxylate is added dropwise to a well stirred, red solution of 2-diazopropane in ether/xylene at −20 °C until discoloration occurs. A further amount of diazopropane (50% of the amount previously employed) is added to the mixture which is then allowed to stand at room temperature until it becomes colorless. It is then filtered and the solvents are removed from the filtrate by evaporation *in vacuo*, whereupon the compound *(2)* crystallizes on standing.

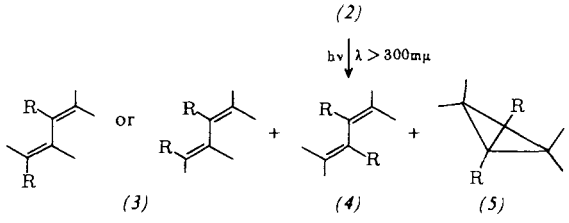
The product *(1)* has a strong IR absorption band at 1735 cm^{-1} (α,β-unsaturated ester) and a further strong band at 1635 cm^{-1} characteristic of 3*H*-pyrazoles [4], but *(2)* absorbs only at 1745 cm^{-1} (ester) and 1560 cm^{-1} (azo group). UV spectra (in C_2H_5OH) confirm the structures assigned [*(1)*: λ_{max} = 358 mμ (ε = 168), 244 mμ (ε = 4450); *(2)*: λ_{max} = 328 mμ (ε = 237)].

NMR spectra of compounds *(1)* to *(5)* (tetramethylsilane as internal standard; δ values in ppm; unspecified signals are singlets; q = quartet)

Compound	CH_3 on sat. C atom	CH_3 on double bond	$R-CO_2-$	Intensity ratio
(1) in $CDCl_3$	1.59		3.97 4.06	2:1:1
(2) in $CDCl_3$	1.58 1.83		3.85	1:1:1
(3) in $CDCl_3$		1.75 1.76 (q [*]) 2.09 (q [*]) 2.16	3.74 3.80	1:1:1:1:1:1
(3) in C_6H_6		1.47 1.87 (q [*]) 2.08 2.30 (q [*])	3.40 3.46	1:1:1:1:1:1
(4) in $CDCl_3$		1.75 2.20	3,72	1:1:1
(5) in $CDCl_3$	1.44 1.48		3.78	1:1:1
(5) in C_6H_6	1.26 1.65		3.43	1:1:1

[*] With J = 1.5 Hz.

On irradiation of the pyrazolopyrazole in benzene with a high-pressure Hg lamp, N_2 was evolved and three isomers *(3)*, *(4)*, and *(5)* (ratio 1:2:2; total yield 50 %) of composition $C_{12}H_{18}O_4$ were formed, as well as other products which were not obtained pure. The three isomers were separated by column and gas chromatography (silicone column, 150 °C). UV spectra: *(3)*, λ_{max} = 216 mμ (ε ≈ 21000); *(4)*, λ_{max} = 219.5 mμ (ε ≈ 18000); *(5)*, λ_{max} = 213.5 mμ (ε ≈ 8000). The IR spectra of *(3)* and *(4)* indicate an α,β-unsaturated ester group (C=O and C=C bands), but *(5)* gives only one band, at 1725 cm^{-1} (ester), in the 1500 to 2000 cm^{-1} region. From these data and the NMR values given in the table the structures illustrated are assigned to compounds *(3)*, *(4)* and *(5)*.



(3) *(4)* *(5)*

As expected [5], compound *(5)* is thermally unstable; when it is heated at 150 °C, it affords, besides other compounds, the substance *(4)* which is the sole gaseous pyrolysis product at 270 °C. The half-reaction time for ring opening of *(5)* at 150 °C is about 3 hr (NMR analysis in perchlorobutadiene).

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[*] Dr. M. Franck-Neumann
Institut de Chimie
Laboratoire Associé au CNRS
Strasbourg (France)

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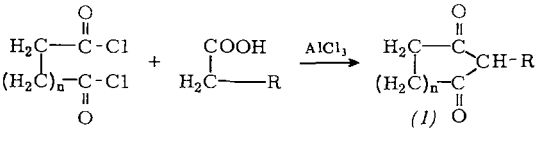
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Synthesis of 2-Alkyl-1,3-cycloalkanediones by Friedel-Crafts Acylation

By *H. Schick, G. Lehmann*, and *G. Hilgetag* [*]

2-Alkyl-1,3-cyclopentanediones are important intermediates in the total synthesis of steroids [1–3]. They have hitherto been prepared by multistage processes [4–6].

We have found that 2-alkyl-1,3-cyclopentanediones *(1)*, n = 1, are obtained in a single step by condensation of succinyl chloride with carboxylic acids under Friedel-Crafts conditions.



(1)

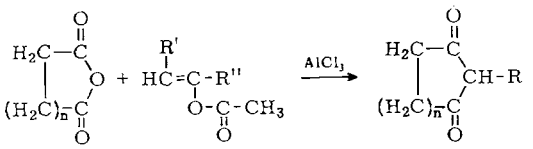
(1), R	*n*	Yield (%)	M.p. (°C)
CH_3	1	35 [a] 45 [b] 25 [c]	214–216
C_2H_5	1	30 [b]	175–177
CH_3	2	40 [b]	204–206

[a] In 500 ml of 1,2-dichloroethane. [b] In 300 ml of nitromethane. [c] In 300 ml of nitrobenzene.

When glutaryl chloride is used in place of succinyl chloride, 2-alkyl-1,3-cyclohexanediones *(1)*, n = 2, are formed. Nitromethane, nitrobenzene, and 1,2-dichloroethane are suitable solvents.

Succinic anhydride or succinyl chloride react analogously with enol acetates of aldehydes, methyl alkyl ketones, symmetrical dialkyl ketones, or cyclic ketones to give 2-alkyl-1,3-cyclopentanediones *(2)*, n = 1, in a single step. Use of glutaryl chloride instead of succinic acid derivatives yields 2-alkyl-1,3-cyclohexanediones *(2)*, n = 2.

2-Methyl-1,3-cyclopentanedione: 1) 155 g (1 mole) of succinyl chloride and 148 g (2 moles) of propionic acid are added to a suspension of 320 g (2.4 moles) of $AlCl_3$ in 300 ml of nitromethane with cooling and exclusion of moisture. The mixture is heated for 3 hr at 80 °C, then cooled to 10 °C and poured



(2), R	R′	R″	n	Reaction time (hr)	Yield (%)	M.p. (°C)
CH_3	CH_3	H	1	1 [b]	15	
	CH_3	CH_3	1 [a]	3.5 [b]	50	214–16
	CH_3	CH_3	1	3 [c]	25	
	CH_3	C_2H_5	1	3 [b]	45	
CH_3	CH_3	CH_3	2 [a]	3 [d]	45	204–06
C_2H_5	C_2H_5	H	1	1 [d]	15	
	C_2H_5	CH_3	1	2 [d]	32	177–79
	C_2H_5	n-C_3H_7	1	2 [d]	45	
n-C_3H_7	n-C_3H_7	CH_3	1	3 [d]	45	180–82
n-C_4H_9	n-C_4H_9	CH_3	1	2 [d]	25	155–57
$(CH_2)_3COOH$	$(CH_2)_3$		1	2 [d]	12	165–67
$(CH_2)_4COOH$	$(CH_2)_4$		1	2 [d]	12	153–55

[a] Dicarboxylic acid dichloride instead of the anhydride.
[b] In nitromethane. [c] In nitrobenzene.
[d] In 1,2-dichloroethane.

onto 500 g of ice. After cooling to about 0 °C, the crude 2-methyl-1,3-cyclopentanedione that has separated is filtered off, washed with 50 ml of cold water, and recrystallized from water (with charcoal). The aqueous phase of the filtrate is boiled with charcoal, filtered, and continuously extracted with ether. A second fraction crystallizes after concentration of the ether extract. Total yield, 50 g (45 %).

2) Methyl ethyl ketone enol acetate (114 g; 1 mole) is added over 10 min to a solution of 264 g (1 mole) of sublimed $AlCl_3$ and 100 g (1 mole) of succinic anhydride in 500 ml of anhydrous nitromethane with exclusion of moisture and cooling in ice; the temperature rises to 30–40 °C. The mixture is heated for $3^1/_2$ hr at 80 °C, then cooled to about 10 °C and poured onto 400 g of ice. The crude 2-methyl-1,3-cyclopentanedione deposited is filtered off, washed with 50 ml of cold water, and recrystallized from water with charcoal. A further crop can be obtained by boiling the aqueous phase of the filtrate with charcoal, filtering, and extracting with ether. Total yield, 56 g (50 %).

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[*] Dr. H. Schick, Dr. G. Lehmann, and Prof. Dr. G. Hilgetag
Institut für Organische Chemie der Deutschen Akademie der Wissenschaften zu Berlin
1199 Berlin-Adlershof (Germany)

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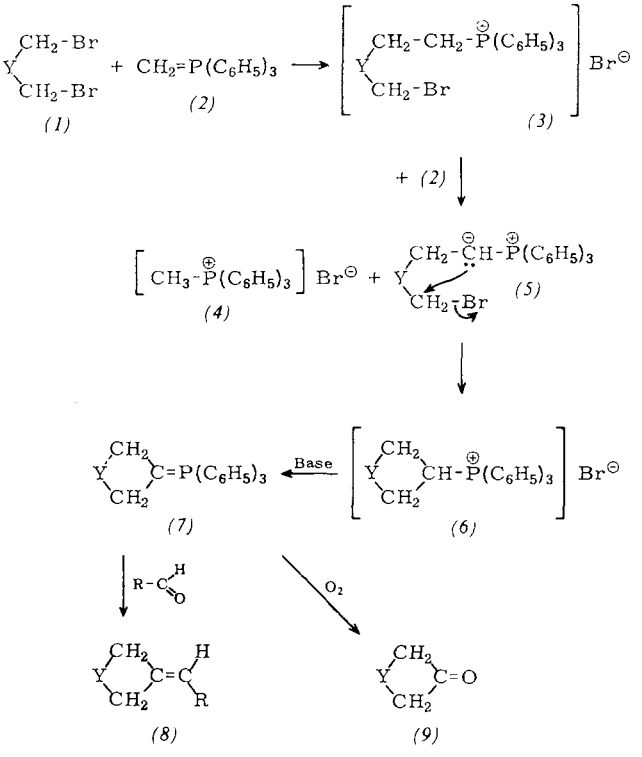
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A New Ring-Closure Reaction

By *H. J. Bestmann* and *E. Kranz* [*]

Dihalogen compounds of type *(1)* react with methylenetriphenylphosphorane *(2)* in boiling benzene to give phosphonium salts *(3)*, which at once react with a second molecule of the phosphorane *(2)*, yielding by "transylidation" [1] the ylides *(5)* and methyltriphenylphosphonium halide *(4)* [2]. The alkylidenephosphoranes *(5)* give the cyclic phosphonium salts *(6)* by intramolecular *C*-alkylation [2,3].



	Y	(8), R = C_6H_5 B.p. (°C/mm) or m.p. (°C)	(8) Yield (%)
1	$-CH_2-$	111/21	60
2	$-CH_2-O-CH_2-$	129–131/14	56
3	$-CH_2-S-CH_2-$	170/19	74
4	Cyclobutylidene	91/0.05	75
5	1,2-Cyclohexylene	105/0.05	31
6	4-Cyclohexen-1,2-ylene	186/17	30
7	3,3-Diphenyl-1.2-cyclopropylene	64	64
8	Oxacyclohex-2,6-ylene	43–45	39

	Y	(9) B.p. (°C/mm) or m.p. (°C)	(9) Yield (%)
9	$-(CH_2)_2-$	145 [a]	64
10	$-(CH_2)_3-$	184 [a]	71
11	$-(CH_2)_4-$	62–64/3	61

[a] M.p. of dinitrophenylhydrazone.

In the examples 5–8 of the table, the bromomethyl group in the corresponding dihalogen compounds *(1)* must be in the *cis* position with respect to the ring. Example 5 then gives the bicyclic compound *(10)*, example 8 leads to the oxygen-bridged compound *(11)*. The synthesis of the compound *(12)* *via* example 4 demonstrates the possibility of preparing spiro compounds by means of the new ring closure method.

The structures of the compounds *(8)* and *(9)* were proved by elemental analyses and UV, IR, and NMR spectra.

The intermediates *(3)* and *(5)* were not isolated. The mixture of salts *(4)* and *(6)* is precipitated from the reaction medium. Since *(4)* readily dissolves in water it can usually be easily separated from the less soluble *(6)*. In many cases, however, this separation is unnecessary before further reaction. The yields of *(6)* or of the mixture of *(4)* and *(6)* amount to 75–95 %.

The salt *(6)* can again be converted by bases into an ylide *(7)*, which can be used in various reactions [2,4]. Thus the Wittig reaction [5] of the ylide *(7)* with aldehydes gives cyclic

compounds with exocyclic double bonds *(8)*, and on autoxidation [6] it gives cyclic ketones *(9)*.

Experimental:

A solution of 1 mole of the dihalogen compounds *(1)* in benzene is added to a salt-free solution of 2 moles of the ylide *(2)* in pure benzene [4] (the addition is carried out dropwise and slowly while the reactants are stirred under reflux). After a short time a mixture of *(4)* and *(6)* begins to precipitate, the reaction being completed as soon as the yellow color of the ylide has disappeared.

A salt-free solution of the ylide *(7)* in absolute tetrahydrofuran is prepared from the salt *(6)* or the mixture *(4)* and *(6)* (if these have proved inseparable). On addition of an aldehyde *(7)* undergoes a Wittig reaction [5] or autoxidation of the solution occurs [6]. After evaporation of the solvent the residue is extracted with a little ether, whereupon a large part of the triphenylphosphine oxide produced remains undissolved. The remaining triphenylphosphine oxide is removed from the ether extracts on an alumina column (activity: Grade II; eluent ether). After evaporation of the eluted solvent, the products *(8)* and *(9)* are obtained by fractional distillation.

All operations in which the ylide is present must be carried out in an atmosphere of dry nitrogen.

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[*] Prof. Dr. H. J. Bestmann and Dipl.-Chem. E. Kranz
Institut für Organische Chemie der Universität
Erlangen-Nürnberg
Henkestr. 42
852 Erlangen (Germany)

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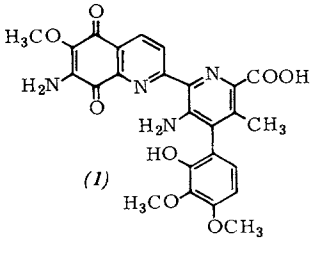
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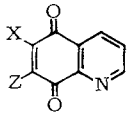
Synthesis of 7-Amino-6-methoxy-5,8-quinolinedione

By *T. K. Liao, W. H. Nyberg*, and *C. C. Cheng* [*]

The antitumor antibiotic streptonigrin *(1)* [1] contains a 5,8-quinolinedione system, the attempted synthesis of which has so far yielded only 7-amino-6-hydroxy-5,8-quinolinedione *(2a)* [2].



(1)



(2), X = OCH_3, Z = NH_2
(2a), X = OH, Z = NH_2
(3), X = OCH_3, Z = Br
(4), X = NH_2, Z = Br
(5), X = OCH_3, Z = N_3

We have now synthesised 7-amino-6-methoxy-5,8-quinolinedione *(2)*. On bromination [3] of 6-methoxy-5,8-quinolinedione [4], 7-Bromo-6-methoxy-5,8-quinolinedione *(3)*, m.p. 185 to 187 °C (decomp.), was formed in quantitative yield. However, ammonolysis of *(3)* in water or ethanol at room temperature did not yield *(2)*, but gave exclusively 6-amino-7-bromo-5,8-quinolinedione *(4)* m.p. 314 °C (decomp.) by the nucleophilic attack [3,5] of NH_3 at the 6-position. When compound *(3)* was treated with an equimolar amount of sodium azide in 50 % aqueous ethanol at room temperature, a near quantitative yield of 7-azido-6-methoxy-5,8-quinolinedione *(5)* [orange-yellow flakes; m.p. 145 °C (decomp.); IR bands at 1270 (aromatic ether), 1652 and 1680 (carbonyl), 2130 cm^{-1}, (azide)] was obtained, possibly by nucleophilic attack [5] and addition of an azide ion at the 6-position whereupon a triazol ring closure, $Br^{\ominus}$ loss, and synchronous ring opening take place at the 7-position.

Hydrogenation [6] of *(5)* in methanol at room temperature with hydrogen and platinum oxide affords 7-amino-6-methoxy-5,8-quinolinedione *(2)* as dark purple flakes [m.p. 202–203 °C (decomp.), from ethylacetate; λ_{max} (at pH = 1 and 11) = 232 mμ (ε = 16300 and 17000), 271 (13700 and 17400), 475 (2550 and 2800); IR bands: 1270 (aromatic ether), 1700 (carbonyl), 3250 (hydroxyl), 3500 cm^{-1} (amino)].

The further synthesis of streptonigrin *(1)* from *(2)* can be outlined as a multistep addition of *(2)* to 4-[2-alkoxy-3,4-dimethoxy]-5-alkylamino-6-lithium-3-methyl-2-pyridinecarboxylate.

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[*] Dr. T. K. Liao, W. H. Nyberg, and Dr. C. C. Cheng
Midwest Research Institute
425 Volker Boulevard
Kansas City, Missouri (U.S.A.)

[1] *K. V. Rao* and *W. P. Cullen*: Antibiotics Annual (1959 to 1960). Interscience, New York 1960, p. 950; *J. J. Oleson, L. A. Calderella, K. J. Mjos, A. R. Reith, R. S. Thie*, and *I. Toplin*, Antibiotics and Chemotherapy *11*, 158 (1961); *W. L. Wilson, C. Labra*, and *E. Barrist, ibid. 11*, 147 (1961); *K. V. Rao, K. Biemann*, and *R. B. Woodward*, J. Amer. chem. Soc. *85*, 2532 (1963); *S. L. Rivers, R. M. Whittington*, and *T. J. Medrek*, Cancer Chemotherapy Reports *46*, 17 (1965); *P. F. Nora, J. C. Kukral, T. Soper*, and *F. W. Preston, ibid. 48*, 41 (1965).

[2] *T. Kametani* and *K. Ogasawara*, J. pharmac. Soc. Japan (Yakugaku Zasshi) *85*, 985 (1965); *86*, 55 (1966).

[3] *W. A. Remers* and *M. J. Weiss*, J. Amer. chem. Soc. *88*, 804 (1966).

[4] *Y.T. Pratt* and *N. L. Drake*, J. Amer. chem. Soc. *77*, 37 (1955).

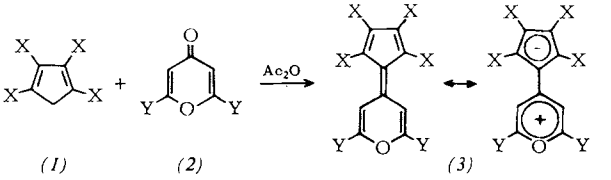
[5] *Y.T. Pratt*, J. org. Chemistry *27*, 3905 (1962).

[6] *L. F. Fieser* and *J. L. Hartwell*, J. Amer. chem. Soc. *57*, 1482 (1935).

Synthesis of Substituted Cyclopentadienylidene-pyrans and Tetramethyl 7,8,9,10-Sesquifulvalene-tetracarboxylate

By *G. Seitz* [*]

Compounds containing active methylene groups condense readily with 4-pyrones in acetic anhydride, yielding pyranylidene derivatives [1]. However, this reaction fails when cyclopentadiene is used as CH-acidic component.



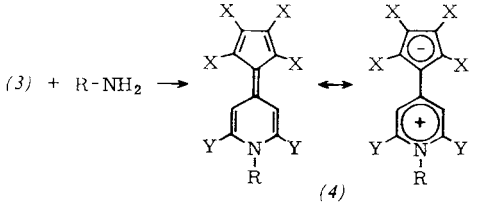
(1) *(2)* *(3)*

	X	Y	M.p. (°C)	λ_{max} (mμ)	(log ε) [a]	Yield (%)
(3a)	Cl	CH_3	>150 (decomp.)	425	(4.59)	45
(3b)	Cl	C_6H_5	212	464	(4.57)	34
(3c)	$COOCH_3$	CH_3	227	456	(4.55)	52
(3d)	$COOCH_3$	C_6H_5	236	505	(4.59)	68
(3e)	$COOCH_3$	Styryl	150 (decomp.)	541	(4.67)	18
				452	(4.46) Sh	

[a] In methylene chloride. Only the longest-wavelength bands are recorded. Sh denotes shoulder

We have found that substituted cyclopentadienes such as tetrachlorocyclopentadiene *(1a)*[2] and tetramethyl 1,2,3,4-cyclopentadienetetracarboxylate *(1b)*[3] react with 4-pyrones *(2a)* to *(2c)* in acetic anhydride even at room temperature, yielding deeply colored cyclopentadienylidenepyrans *(3)*. After 12 hr the precipitated crystals are collected and recrystallized from acetonitrile or dimethylformamide.

The compounds *(3)* exchange oxygen for nitrogen with primary amines, smoothly yielding *N*-substituted 1,4-dihydro-4-cyclopentadienylidenepyridines *(4)*. The mixture of amine and pyran is warmed in dimethylformamide; when it is cooled the product crystallizes and can be recrystallized from dimethylformamide [*(4c)* from methanol].

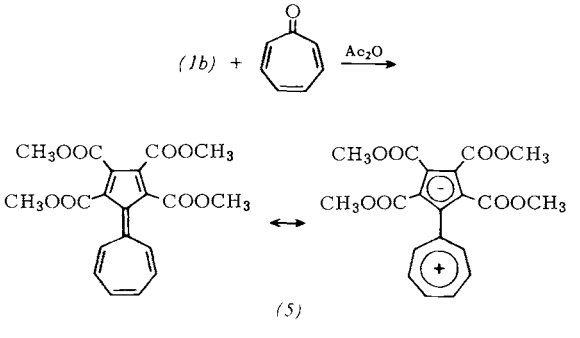


(4)

	X	Y	R	M.p. (°C)	λ_{max} (mμ)	(log ε)	Yield (%)
(4a)	Cl	CH_3	CH_3	>150 (decomp.)	432	(4.58)	48
(4b)	Cl	CH_3	$CH_2C_6H_5$	>170 (decomp.)	436	(4.64)	42
(4c)	$COOCH_3$	CH_3	CH_3	238	424	(4.34)	25

Attempts to replace the oxygen of *(3)* by sulfur with sodium sulfide or sodium hydrogen sulfide were unsuccessful. However, *(1a)* can also be converted in acetic anhydride to the cyclopentadienylidenethiopyrone corresponding to *(3b)* with 2,6-diphenyl-1-thiopyrone (yield 43%, m.p. 264 °C, λ_{max} = 505 mμ, log ε = 4.55 in CH_2Cl_2).

Tetramethyl 7,8,9,10-sesquifulvalenetetracarboxylate *(5)*, which is iso-π-electronic with the cyclopentadienylidene-pyrans and -dihydropyridines, was obtained in 60% yield from *(1b)* and tropone; it crystallizes from the reaction mixture as permanganate-colored needles with a metallic luster, m.p. 209 °C (decomp.), λ_{max} = 540 mμ (log ε = 4.39), 251 (4.48) in CH_2Cl_2. The NMR spectrum of *(5)* (in D_3CSOCD_3, tetramethylsilane as internal standard) shows two sharp singlets (intensity 6) at 3.70 and 3.75 ppm for the



(5)

12 methoxy protons. The signal for the six protons of the tropylium system at 8.46 ppm is a broad singlet; it shows that the hydrogen atoms are almost equivalent. The shift to lower fields indicates a high contribution of the ionic limiting structure to the ground state of the molecule.

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[*] Dr. G. Seitz
Institut für Pharmazeutische Chemie der Universität
Marbacher Weg 6
355 Marburg (Germany)

[1] *L. L. Woods*, J. Amer. chem. Soc. *80*, 1440 (1958); *M. Ohta* and *H. Kato*, Bull. chem. Soc. Japan *32*, 707 (1959); *F. Eiden*, Arch. Pharm. *293*, 404 (1960); *J. Kelemen* and *R. Wizinger*, Helv. chim. Acta *45*, 1908 (1962).

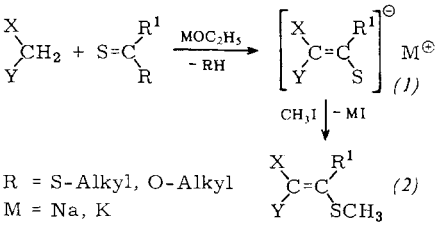
[2] *A. Roedig* and *L. Hörnig*, Chem. Ber. *88*, 2003 (1955); *E. T. McBee*, *R. K. Meyers*, and *C. F. Baranauckas*, J. Amer. chem. Soc. *77*, 86 (1955).

[3] *G. Seitz*, Angew. Chem. *78*, 680 (1966); Angew. Chem. internat. Edit. *5*, 670 (1966).

A New Synthesis of Isothiazoles [**]

By *K. Hartke* and *L. Peshkar* [*]

Active methylene groups can be thioacylated[1,2] with esters of dithiocarboxylic, thionocarboxylic, trithiocarbonic, or xanthic acid in anhydrous ethanol in the presence of an equimolar amount of alkali alkoxide as catalyst within a few hours at room temperature. The hitherto unknown salts *(1)* that are formed (in yields of over 70%) either separate or can be isolated after evaporation of the solvent. In order to characterize these salts, some of which are hygroscopic, they are



(1)

(2)

R = S-Alkyl, O-Alkyl
M = Na, K

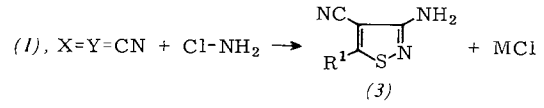
(2)	X	Y	R^1	B.p. (°C/mm) or m.p. (°C)	Yield (%)
(a)	CN	CN	CH_3	36.5	60
(b)	CN	CN	C_6H_5	98	60
(c)	CN	CN	$C_6H_5CH_2$	73.5	95
(d)	CN	CN	SCH_3	80	50
(e)	CN	CN	OC_2H_5	47	60
(f)	CN	$CONH_2$	CH_3	149	60
(g)	CN	$COOC_2H_5$	CH_3	131	88
(h)	$COOC_2H_5$	$COOC_2H_5$	CH_3	94/1	50

methylated to the sulfides *(2)*. The salts are dissolved or suspended in ethanol and left with a small excess of methyl iodide at room temperature for about 1 hr; after evaporation of the ethanol and addition of water the crystalline sulfides *(2)* are filtered off, or the liquid ones are extracted with ether.

Compounds *(1)* and *(2)* are of interest as intermediates for the preparation of heterocyclic compounds. Thus, in reactions analogous to those of the corresponding enol ethers, the sulfides *(2)* give pyrimidines with amidines or guanidines, pyrazoles with hydrazines, isoxazoles with hydroxylamines, and pyrroles with 2-amino carboxylic esters. Owing to the great reactivity of the unsaturated sulfides *(2)* towards nucleophilic reagents these condensations occur within a few hours at room temperature. The resulting heterocycles either separate out or can be isolated after evaporation of the solvent (ethanol). The salts *(1)* are alkylated also by α-chloro ketones, or α-chloro carboxylic esters or nitriles (reaction conditions as for methyl iodide); the resulting sulfides cyclize to thiophenes when warmed for ½ hr on the water-bath after addition of triethylamine.

Salts of type *(1)* containing two nitrile groups[3] yield isothiazoles *(3)* when treated with aqueous chloramine solution: 0.015 mole of aqueous chloramine solution[4] is added to a solution of 0.01 mole of *(1)* in 10 ml of water, and the resulting immediate crystalline precipitate is filtered off after 2 hr and recrystallized from ethanol. The derivatives *(3a)* and *(3c)* are obtained also on using hydroxylamine-*O*-sulfonic acid under the same conditions and in about the same yields, but attempts to prepare *(3b)* and *(3d)* with hydroxylamine-

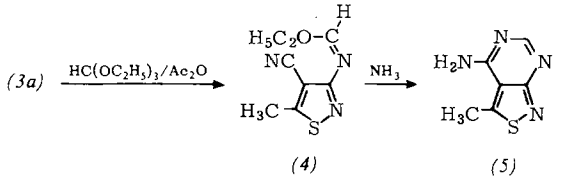
O-sulfonic acid gave products of as yet unclarified structure. The isothiazole structure *(3)* follows from the IR and UV spectra and from elemental analyses.



(1), X=Y=CN + Cl-NH_2 → *(3)* + MCl

(3)	R^1	M.p. (°C)	Yield (%)
(a)	CH_3	176	86
(b)	OC_2H_5	198	77
(c)	SCH_3	176	72
(d)	$C_6H_5CH_2$	144	93

As α,β-amino nitriles the isothiazoles *(3)* can undergo further reactions. For instance, when 0.01 mole of *(3a)* is heated with 40 ml of an equimolar mixture of ethyl orthoformate and acetic anhydride[5] on the water-bath for 3 hr, evaporation affords the derivative *(4)*, m.p. 76 °C, in 90% yield, which with an excess of alcoholic ammonia at room temperature gives compound *(5)*, decomp. *ca.* 230 °C, in 85% yield. This is the first isothioazolo[3,4-*d*]pyrimidine reported.



(3a) $\xrightarrow{HC(OC_2H_5)_3/Ac_2O}$ *(4)* $\xrightarrow{NH_3}$ *(5)*

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[*] Dr. K. Hartke and L. Peshkar B.Sc.
Institut für Pharmazeutische Chemie und Lebensmittelchemie der Universität
Marbacher Weg 6
355 Marburg (Germany)

[**] We thank the Verband der Chemischen Industrie and the Deutsche Forschungsgemeinschaft for financial support.

[1] For thioacylation of cyclopentadiene with trithiocarbonic esters see *K. Hartke*, Tetrahedron Letters *1964*, 2737; *K. Hartke, E. Schmidt, M. Castillo*, and *J. Bartulin*, Chem. Ber. *99*, 3268 (1966).

[2] For condensation of acetophenone with *O*-methyl thiobenzoate see *E. Uhlemann* and *H. Müller*, Angew. Chem. *77*, 172 (1965); Angew. Chem. internat. Edit. *4*, 154 (1965).

[3] The yield of isothiazole from salts containing one nitrile group is small.

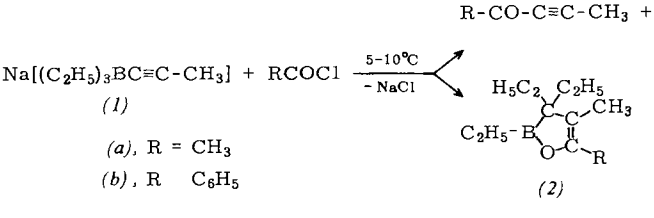
[4] The chloramine solution was prepared at 0 °C from NaOH 20 g, water 100 ml, ice 100 g, chlorine 14 g, and 25% aqueous NH_3 8.5 g; the molar quantity stated refers to the NH_3 content.

[5] *E. C. Taylor* and *K. Hartke*, J. Amer. chem. Soc. *81*, 2456 (1959).

Preparation of Substituted Oxaboroles from Sodium 1-Alkynyltrialkylborates and Acyl Chlorides

By *P. Binger*[*]

Sodium triethyl-1-propynylborate and acetyl chloride give only about 35% of methyl propynyl ketone and triethylborane, since about 50% of the borate is converted into the alkyl derivative *(2a)* of the hitherto unknown 2,3-dihydro-1,2-oxaboroles. Other possible products, such as methyl ethyl ketone and diethylpropynylborane, could not be detected.



$Na[(C_2H_5)_3BC{\equiv}C\text{-}CH_3]$ + RCOCl $\xrightarrow[-NaCl]{5\text{-}10\,°C}$ *(2)* + $R\text{-}CO\text{-}C{\equiv}C\text{-}CH_3$ + $B(C_2H_5)_3$

(1)

(a), R = CH_3

(b), R = C_6H_5

A solution of 32 g (0.2 mole) of *(1)* in 60 ml of dichloromethane is added dropwise and slowly at 5–10 °C, with cooling in ice-water, to 15.6 g (0.2 mole) of acetyl chloride. A yellow color develops and sodium chloride separates. Distillation of the filtrate gives, apart from the solvent, two fractions. Fraction I (8.4 g, b.p. 32–33 °C/12 mm) contains 71% of methyl propynyl ketone (gas-chromatographic analysis); fraction II (17.5 g, b.p. 68–69 °C/12 mm) is almost pure *(2a)*.

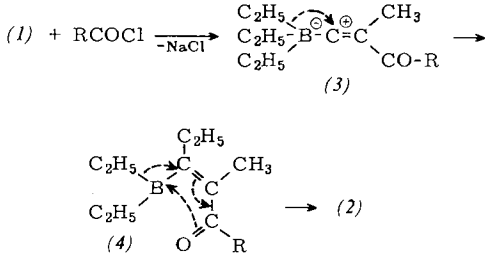
Benzoyl chloride and the salt *(1)* under the same conditions afford 2,3,3,4-tetraalkylated 5-phenyl-2,3-dihydro-1,2-oxaborole *(2b)* (b.p. 68 to 70 °C/10^{-3} mm) in up to 30% yield together with some phenyl propynyl ketone (6%) and ethyl phenyl ketone (7%). The remainder consists almost wholly of dark, tarry products.

The structure of the compound *(2a)* is proved by the mass spectrum (molecular weight 180, one boron atom), the infrared spectrum ($\nu_{C=C}$ = 1690 cm^{-1}), and the ^1H-NMR spectrum [1 C_2H_5 (on B): τ = 8.99 ppm; 2 C_2H_5 (on C-3): τ_{CH_2} = 8.6 ppm (quartet), τ_{CH_3} = 9.44 ppm (triplet); 1 CH_3 (on C-4): τ = 8.59 ppm; and 1 CH_3 (on C-5): τ = 8.07 ppm].

The reaction can be extended to other sodium alkynyltrialkylborates; *e.g.* $Na[(C_3H_7)_3BC{\equiv}C\text{-}CH_3]$ and acetyl chloride yield 4,5-dimethyl-2,3,3-tripropyl-2,3-dihydro-1,2-oxaborole, with methyl propynyl ketone.

The substituted oxaboroles are sensitive to oxygen but are not attacked by substances containing active protons (water, ethanol, ethylene glycol) up to about 100 °C. They do not form stable addition compounds with tertiary amines.

Like 1,2-diborylated alkenes, the compounds *(2)* are formed probably by way of "borenylides" *(3)*[1]. The ketones *(4)* initially formed can be isolated only when trapped with pyridine. The free compounds evidently rearrange readily to *(2)*.



(1) + RCOCl $\xrightarrow[-NaCl]{}$ *(3)* → *(4)* → *(2)*

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[*] Dr. P. Binger
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1
433 Mülheim (Germany)

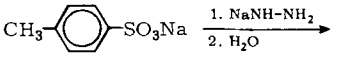
[1] *P. Binger* and *R. Köster*, Tetrahedron Letters *1965*, 1901.

Two New Syntheses of Arylhydrazines

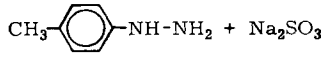
By *W. Burkhardt* and *Th. Kauffmann*[*]

Since a high temperature is required in the synthesis of phenols or arylamines from arenesulfonates and alkali hydroxides or alkali amides, it did not appear promising to attempt an analogous synthesis of arylhydrazines by means

of sodium hydrazide[2] because of the thermolability of the hydrazide. Surprisingly, however, sodium hydrazide reacts rapidly with sodium arenesulfonates in a hydrazine-ether mixture (about 1:10 v/v)[3] even at 35 °C, giving, in most cases, almost quantitative yields of the corresponding hydrazine derivative. Since no di- or tri-arylhydrazine or, as in the reaction of sodium *p*-toluenesulfonate *(1)*, position isomers of the arylhydrazine are formed, the reactions occur by the addition-elimination mechanism of nucleophilic aromatic substitution and not by the aryne mechanism.



(1)



(2)

The reaction of sodium benzenesulfinate shows that the arenesulfinates also give arylhydrazines *(2)*.

Sodium salt	Reaction time (hr)	Hydrazine formed	Yield (%)
Benzenesulfonate	1 [a]	Phenyl	97
Benzenesulfinate	1 [a]	Phenyl	93.5
o- or *p*-toluenesulfonate	1 [a]	*o*- or *p*-Tolyl	92 or 98
2,4-, 2,5-, or 3,4-Dimethylbenzenesulfonate	1	2,4-, 2,5-, or 3,4-Dimethylphenyl	90, 89, or 94
2,4,6-Trimethylbenzenesulfonate	2	2,4,6-Trimethylphenyl (+ 73 % of mesitylene)	15
4-Biphenylsulfonate	3	4-Biphenylyl	75
2-Naphthalenesulfonate	1	2-Naphthyl	98
1,3-Benzenedisulfonate	1.5	*m*-Sulfophenyl	91

[a] Molar ratio, sulfonate (or sulfinate): $NaNH-NH_2$: NH_2-NH_2 = 1:5:5; in other cases, 1:5:25.

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[*] Dipl.-Ing. W. Burkhardt
Institut für Organische Chemie
der Technischen Hochschule
61 Darmstadt (Germany)
Prof. Dr. Th. Kauffmann
Organisch-Chemisches Institut der Universität Münster
Hindenburgplatz 55
44 Münster (Germany)

[1] Cf. *A. Wurtz*, Liebigs Ann. Chem. *144*, 121 (1867); *F. Sachs*, Ber. dtsch. chem. Ges. *39*, 3006 (1906).

[2] Cf. *Th. Kauffmann*, Angew. Chem. *76*, 206 (1964); Angew. Chem. internat. Edit. *3*, 342 (1964).

[3] The reaction probably takes place in the hydrazine phase.

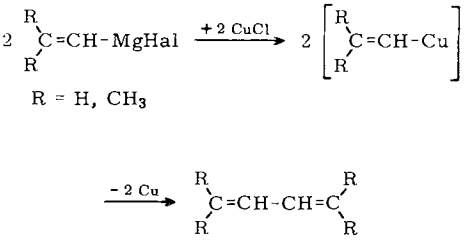
Synthesis of Dienes from Vinyl Halides *via* Organocopper Compounds [1]

By *Th. Kauffmann* and *W. Sahm* [*]

Tetrahydrofuran solutions of vinylmagnesium halides are readily accessible from vinyl halides[2]. On dropping such solutions into a suspension of CuCl in tetrahydrofuran under nitrogen at −60 to −40 °C we obtained intensely green or red mixtures which presumably contain vinylcopper(I) compounds. When such mixtures are warmed to +20 °C, conjugated dienes are formed in good yield, the intense color disappearing and elemental copper separating[3].

Conversions Effected:

Vinylmagnesium chloride → 1,3-butadiene[5] (yield[4] 60.5 %; green intermediate). 2-Methylpropenylmagnesium bromide → 2,5-dimethyl-2,4-hexadiene (yield 97 %; deep green intermediate). *cis*- and *trans*-Propenylmagnesium bromide (4.8:1) → mixture (yield 81 %; red intermediates) of *cis,cis*-, *cis,trans*-, and *trans,trans*-2,4-hexadiene (14.4:7.3:1).



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[*] Prof. Dr. Th. Kauffmann and cand. chem. W. Sahm
Organisch-Chemisches Institut der Universität
Hindenburgplatz 55
44 Münster (Germany)

[1] We thank the *Deutsche Forschungsgemeinschaft* and the *Verband der Chemischen Industrie* for support of this work.

[2] *H. Normant*, Bull. Soc. chim. France *1957*, 728.

[3] Cf. the formation of dicyanogen from CuCN [*J. U. Nef*, Liebigs Ann. Chem. *287*, 323 (1895)], of diacetylenes from copper acetylides [Chem. Reviews *57*, 215 (1957)], and of biphenyl from phenylcopper [*H. Gilman* and *J. M. Straley*, Receuil Trav. chim. Pays-Bas *55*, 821 (1936)].

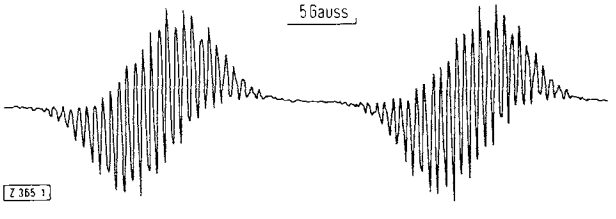
[4] All yields are calculated with respect to the Grignard compound.

[5] According to *Ch. J. Leyes* [German Pat. 569343 (1929); Chem. Abstr. *1930*, 2142], 1,3-butadiene results when vinyl chloride is passed over Cu or Fe turnings at 100 to 400 °C.

A New, Stable Phosphorus Radical

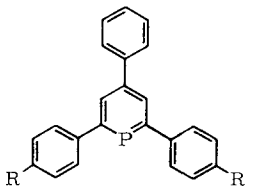
By *K. Dimroth*, *N. Greif*, *H. Perst*, and *F. W. Steuber* [*]
With the cooperation of *W. Sauer* and *L. Duttka*

While oxidation or reduction of phosphamethinecyanines[1] (the first compounds with delocalized C=P−C bonds) gives a number of radicals not yet identified, reaction of 2,4,6-triphenylphosphabenzene *(1a)*[2] with 2,4,6-triphenylphenoxyl *(2a)*[3] in benzene leads to immediate decoloration of the red phenoxyl solution and formation of a stable greenish-yellow, weakly fluorescing solution which, as shown by its ESR spectrum (see Figure), contains a phosphorus radical.

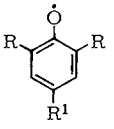


The phosphorus coupling constant a_P amounts to 23.2 gauss. The same spectrum is obtained on treatment of *(1a)* with 2,6-bis(pentadeuterophenyl)-4-phenylphenoxyl *(2b)*, 2,4,6-tris(pentadeuterophenyl)phenoxyl *(2c)*[4], 4-t-butyl-2,6-diphenylphenoxyl, or [^{17}O]-2,4,6-triphenylphenoxyl. This shows that the ESR spectrum of the new radical is independ-

ent of the oxidizing phenoxyl radical and that the oxygen, since it is not coupled with the phosphorus, is probably not chemically bound to it.



(1a) R = H
(1b) R = OCH_3



(2a) R = R^1 = C_6H_5
(2b) R = C_6D_5, R^1 = C_6H_5
(2c) R = R^1 = C_6D_5

The phosphabenzene *(1a)* does not react with 2,4,6-tri-t-butylphenoxyl or 2,6-di-t-butyl-4-phenylphenoxyl. Whether this is because the redox potential of these radicals is too low[5] or because the *ortho*-t-butyl groups hinder the reaction sterically is being studied. If the redox potential of *(1a)* is lowered by introduction of two *p*-OCH_3 groups into the phenyl rings at C-2 and C-6 *(1b)*, then oxidation can be effected even with lead dioxide and an analogous phosphorus radical is obtained. The fine structure of the doublet in its ESR spectrum is poorly resolved, but the coupling constant a_P is almost the same as that for the radical from *(1a)*.

The new phosphorus radical is stable in benzene at 0 °C when air is excluded: no decrease in radical concentration was observed after storage for 14 days.

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[*] Prof. Dr. K. Dimroth, Dipl.-Chem. N. Greif,
Dr. H. Perst, and Dr. F. W. Steuber
Institut für Organische Chemie der Universität
Bahnhofstr. 7
355 Marburg (Germany)

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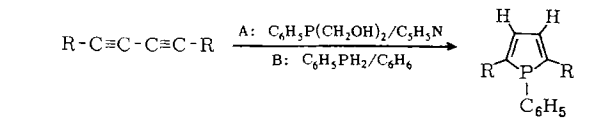
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A Simple Synthesis of Phospholes

By *G. Märkl* and *R. Potthast* [*]

Phospholes *(1)* are analogous to pyrroles and are thus of interest because they may have aromatic bonding character.

Previous syntheses of phospholes[1] are restricted to special cases. We have now found a general phosphole synthesis in the reaction of butadiynes with phenylphosphine, which is analogous to the syntheses of pyrroles[2] and thiophenes[3]. Whereas only traces of phospholes are formed in thermal or free-radical reactions, the cycloaddition can be effected under conditions in which intermediate phenylphosphine anions are formed. Reaction of bis(hydroxymethyl)phenylphosphine (easily accessible from phenylphosphine[4]) with butadiyne in boiling pyridine yields phospholes (method A); phenylphosphine itself adds smoothly to butadiynes in benzene even at room temperature in the presence of catalytic amounts of phenyl-lithium (method B).



(1)

(1), R	B.p. (°C/mm) or m.p. (°C)	Yield (%) A	Yield (%) B	NMR spectrum in $CDCl_3$
Phenyl	184—186	20.5	60	Complex band at τ = 2.45 to 3.0
2-Naphthyl	230—231	17.5	89.5	
p-Tolyl	194—196	29	59	Singlet at τ=7.75(6H) Complex band at τ = 2.49 to 3.16 (15 H)
p-Bromophenyl	200—202	16.5		Complex band at τ = 2.67 to 2.90
CH_3	66—69/0.2	0	51	Doublet at τ = 8.02 (6 H), J_{P-CH_3} = 10 Hz [a] Doublet at τ = 3.61 (2 H), J_{P-H} = 12.5 Hz [a] Complex band at τ = 2.59 to 2.92 (5 H)

[a] The weak coupling H—C=C—CH_3 leads to formation of a shoulder.

2,5-Dimethyl-1-phenylphosphole is the first phosphole without aryl groups attached to the ring C atoms. Comparison of the chemical shift of the NMR signals of the protons on C-3 and C-4 with the shift in 2,5-dimethylfuran ($\tau_{3,4-H}$ = 3.61, τ_{CH_3} = 7.86), 2,5-dimethylthiophene ($\tau_{3,4-H}$ = 3.61, τ_{CH_3} = 7.70), and 1,2,5-trimethylpyrrole ($\tau_{3,4-H}$ = 4.41, $\tau_{2,5-CH_3}$ = 7.99)[5] is not inconsistent with the assumption of aromatic bonding in phospholes *(1)*.

Method A (1-phenyl-2,5-di-p-tolylphosphole): 0.8 g (3.5 mmole) of 1,4-di-*p*-tolyl-1,3-butadiyne is added to a solution of bis-(hydroxymethyl)phenylphosphine [prepared[4] from 0.55 g (5 mmole) of phenylphosphine] in 4 ml of anhydrous pyridine, and the mixture is refluxed for 5 hr. Crystallization of *(1)*, R = *p*-CH_3—C_6H_4, is completed by addition of water; yield 0.35 g.

Method B (2,5-dimethyl-1-phenylphosphole): 2.34 g (30 mmole) of 2,4-hexadiyne is added at room temperature to a solution of 3.3 g (30 mmole) of phenylphosphine and 8 mmole of phenyl-lithium in 15 ml of benzene/tetrahydrofuran (1:1 v/v). The product is distilled off under nitrogen 18 hr after the vigorous reaction has ceased; yield 2.7 g of colorless liquid.

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[*] Priv.-Doz. Dr. G. Märkl and cand. chem. R. Potthast
Institut für Organische Chemie der Universität
Röntgenring 11
87 Würzburg (Germany)

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Tetraphenyldiphospha^{V}-1,3,5-triazines and their Salts[1]

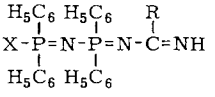
By *A. Schmidpeter* and *J. Ebeling*[*]

Amidinium chlorides *(1)* condense with tetraphenylimidodiphosphinic trichloride chloride *(2)*[2] with elimination of 3 mol. equivalents of HCl when equimolar amounts are heated together in a vacuum. Structures *(3a)* to *(3c)* (X = Cl)

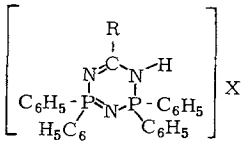
$$[RC(NH_2)_2]Cl + [N((C_6H_5)_2PCl)_2]Cl \longrightarrow 3\ HCl + RC((C_6H_5)_2P)_2N_2HCl$$

(1) *(2)* *(3)*

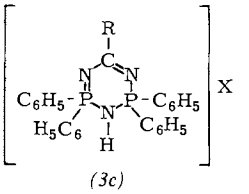
must be considered for the condensation products. Convertibility into a tetraphenylborate [X = $B(C_6H_5)_4$] indicates an ionic and thus a cyclic structure.



(3a)



(3b)



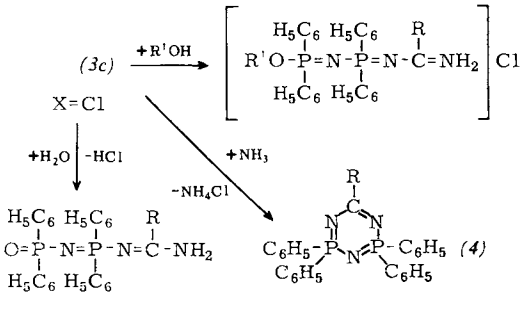
(3c)

Equivalence of the two phosphorus atoms and thus the symmetrical structure *(3c)* follow from the ^{31}P–NMR spectra and from splitting of the proton signal of the *C*-substituent (R=CH_3 or C_6H_5–CH_2) to a triplet[3]. The location of the proton at position 3 is surprising in view of the difference in basicity between amidine-nitrogen (pK ≈ 12[4,5]) and phosphazene-nitrogen (pK ≈ 2[6]) and indicates extensive equalization of electron density throughout the ring skeleton.

(3c) R	X	M.p. (°C)	$\delta^{31}P$ [a] (ppm)	$\delta^{1}H$(NH) (ppm)	$\delta^{1}H$(CH aliphatic) (ppm)	J_{PH} (Hz)
CH_3	Cl	192–195	−19.0	−15.2	−2.63	1.8
CH_3	$B(C_6H_5)_4 \cdot 2\ CH_3CN$	114–116 (decomp.)	−20.4		−1.80	1.6
C_6H_5–CH_2	Cl	182–184	−19.9	−14.2	−4.22	2.6
C_6H_5	Cl	218–225 (decomp.)	−21.9			

[a] The chemical shifts were measured for CH_2Cl_2 solutions [7] and are given as negative for lower fields with reference to 85 % H_3PO_4 or tetramethylsilane. The strongly negative chemical shift of the signal for the proton attached to nitrogen confirms its 3-position. The NH signal of protonated cyclophosphazenes had previously [8] been anticipated at −12.5 ppm, by analogy with that of protonated organic nitrogen heterocycles.

Diphospha^{V} -1,3,5-triazinium chlorides *(3c)* readily undergo hydrolysis and alcoholysis with opening of the ring between positions 1 and 2. However, diphospha^{V}-1,3,5-triazine

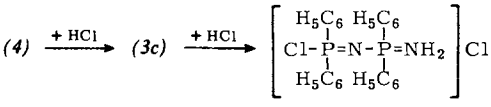


bases *(4)*[9] are liberated by ammonia. When R = C_6H_5 removal of HCl from *(3c)* may be effected by prolonged heating in vacuum.

(4), R	M.p. (°C)	$\delta^{31}P$ [a] (ppm)	$\delta^{1}H$(CH aliphatic) (ppm)	J_{PH} (Hz)
CH_3	175–177	−15.6	−2.17	2.7
C_6H_5–CH_2	113–114	−15.9	−3.67	3.2
C_6H_5	239–241	−17.3		

[a] $\delta^{31}P$ was measured in CH_2Cl_2 or C_6H_5Cl, and $\delta^{1}H$ in CCl_4.

A solution of a diphospha^{V}-1,3,5-triazine *(4)* absorbs HCl at atmospheric pressure, reversing the synthetic route, but the extent of this reaction depends on the nature of the substituents that determine the basicity: one equivalent is absorbed when R = C_6H_5, but two when R = CH_3:



The compounds *(4)* prepared are soluble in polar organic solvents and in aromatic compounds, and sparingly soluble in ether, aliphatic hydrocarbons, or water. Diphospha^{V}-1,3,5-triazines are stable towards water and bases but are decomposed by aqueous acids to *(1)* and tetraphenylimidophosphinic acids $(C_6H_5)_2OP$–NH–$PO(C_6H_5)_2$.

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[*] Dr. A. Schmidpeter and Dipl.-Chem. J. Ebeling
Institut für Anorganische Chemie der Universität
Meiserstr. 1
8 München 2

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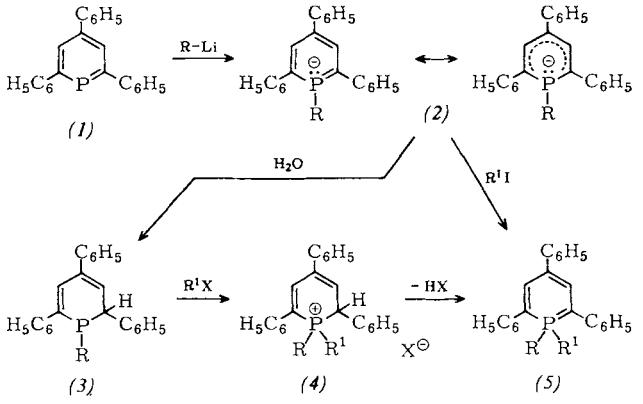
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Electrophilic Reactions of 2,4,6-Triphenylphosphabenzene

By *G. Märkl*, *F. Lieb*, and *A. Merz*[*]

Whereas we were unable to alkylate triphenylphosphabenzene *(1)*[1] with methyl iodide or $[(C_2H_5)_3O]BF_4$, it reacts with nucleophilic reagents such as lithium alkyls and aryls in benzene even at room temperature.

In contrast to the course of comparable nucleophilic substitutions of pyridine[2,3], the base adds directly to the phosphorus, whose valence shell expands to a decet [as in *(2)*]. Hydrolysis of the deep indigo solutions obtained gives 1-alkyl and 1-aryl-1,2-dihydrophosphabenzenes *(3)*, which are isolated by freeze-drying.



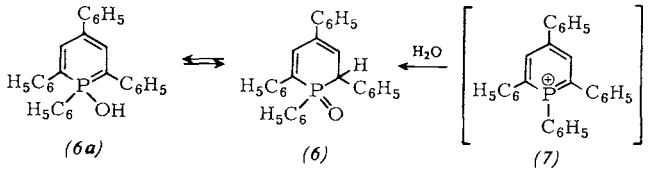
(3), R = C_6H_5 (recrystallization from ethanol under nitrogen), m.p. 144–145 °C, yield 64 %, λ_{max} = 327 mμ, ε = 7300 (in benzene); ^{1}H–NMR: quartet at τ = 5.79 (benzyl-H), J_{P-CH} = 13 Hz, $J_{Ha/Hb}$ = 4 Hz; doublet at τ = 3.6 (1 H), J = 4 Hz; complex band at τ = 2.15 to 3.15 (21 H).

(3), R = n-butyl (chromatography on Al_2O_3 under nitrogen), pale yellow oil, yield 52 %; ^{1}H–NMR: quartet at τ = 5.96 (benzyl-H), J_{P-CH} = 8 Hz, $J_{Ha/Hb}$ = 4 Hz; doublet at τ = 3,78 (1 H); complex band art τ = 2.1 to 3.1 (16 H) and at τ = 8.5 to 9.6 (9 H).

The phosphonium salts *(4)* (R = C_6H_5, R^1 = CH_3, $X^\ominus$ = $I^\ominus$; m.p. 160–162 °C that are readily obtained from *(3)* yield the red, non-crystalline, 1,1-disubstituted PV-phosphabenzenes *(5)*[4] when treated with dilute aqueous NaOH at room temperature. Compounds *(2)* react in benzene solution directly with alkyl iodides, *e.g.* CH_3I, yielding solutions of the ylides *(5)*.

Oxidation of the dihydro-compound*(3)*, R = C_6H_5, with H_2O_2 at 0 °C affords the oxide *(6)* as bundles of fine, colorless needles, m.p. 156–158 °C, λ_{max} = 332 mμ (ε = 6300–6600; in benzene); ^{1}H–NMR: quartet at τ = 5.72 (benzyl-H), J_{P-CH} = 16.5 Hz, $J_{Ha/Hb}$ = 4 Hz; quartet at τ = 3.6 (1 H), J_{P-CH} = 16.5 Hz, complex band at τ = 2.2 to 3.0 (21 H). The oxide *(6)* is also obtained (on chromatography of the reaction mixture) from phenylphosphine and 2,4,6-triphenylpyrylium fluoroborate[5], being formed by reaction of the intermediate 1-phenylphosphabenzene cation *(7)* with water.

The ultraviolet spectrum of the oxide *(6)* in methanol shows an isosbestic point at 372 mμ and two maxima at 340 and 432 mμ, which indicate the equilibrium *(6)* ⇄ *(6a)*. Even with weak bases and in water, *(6a)* gives the brilliant red, resonance-stabilized anion (λ_{max} = 348, 365, and 475 mμ in benzene).



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[*] Priv.-Doz. Dr. G. Märkl, cand. chem. F. Lieb, and cand. chem. A. Merz
Institut für Organische Chemie der Universität
Röntgenring 11
87 Würzburg (Germany)

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Synthesis of Silyl Phosphinites [**]

By *K. Issleib* and *B. Walther* [*]

According to their ^{31}P–NMR and IR spectra, secondary phosphine oxides have the structure $R_2P(O)H$ and not that of a "phosphinous acid" R_2POH; but when heated with alkali metals in aprotic solvents they evolve an equivalent amount of hydrogen to yield compounds of type R_2POM.

If a salt R_2POK (R = n-C_4H_9[1] or C_6H_5[2]), prepared by heating $R_2P(O)H$ with potassium in dioxane, is dropped onto $(CH_3)_3SiCl$ (method A), compounds *(1)* and *(5)* are formed. Organosilanes containing more chlorine give inhomogeneous products in this reaction.

When secondary phosphine oxides are heated directly with various substituted organo-chlorosilanes in benzene in the presence of triethylamine (method B), subsequent filtration and concentration of the solutions, followed by distillation in a vacuum or by recrystallization from n-hexane, give the compounds *(1)* to *(7)* in good yields. The spectra and chemical behavior of these compounds prove the silyl phosphinite structure and exclude the formation of tertiary phosphine oxides $[R_2P(O)]_nSiR'_{4-n}$.

		Method	B.p. (°C/mm) or m.p. (°C)	Yield (%)	Chem. shift [a] (ppm)
(1)	$(C_6H_5)_2P-O-Si(CH_3)_3$	A	103–106/0.5	55	−94.1 ± 1.0
		B		81	
(2)	$[(C_6H_5)_2P-O-]_2Si(CH_3)_2$	B	215–218/0.5	70	−98.1 ± 0.5
(3)	$[(C_6H_5)_2P-O-]_3Si\,CH_3$	B	non-dist. oil	–	−97.7 ± 1.5
(4)	$(C_6H_5)_2P-O-Si(C_6H_5)_3$	B	85–88	82	−98.0 ± 1.0
(5)	$(C_4H_9)_2P-O-Si(CH_3)_3$	A	99–101/12	68	−116.0
		B		70	
(6)	$[(C_4H_9)_2P-O-]_3Si\,CH_3$	B	128–130/0.01	73	−119.0
(7)	$(C_4H_9)_2P-O-Si(C_6H_5)_3$	B	165–167/0.01 41–42	72	−122.8 ± 0.5
(8)	$(C_4H_9)_2P-O-Ge(C_4H_9)_3$	A	136–138/1	72	−116.8 ± 1.0
(9)	$(C_4H_9)_2P-O-Sn(C_4H_9)_3$	A	165–167/1	77	−65.6 ± 0.5

[a] Calc. relative to 85 % aqueous orthophosphoric acid. We thank Dr. *E. Fluck*, Heidelberg, for the ^{31}P–NMR measurements.

Germyl and stannyl phosphinites can be prepared in the same way, as is shown by the formation of *(8)* and *(9)* by method A. Compound *(9)* is also obtained from $R_2P(O)H$ and tributyldiethylaminostannane.

The ^{31}P–NMR spectra of compounds *(1)* to *(9)* all show only one resonance line, whose large negative chemical shift is of the same order of size as those of other P compounds of coordination number 3. IR spectroscopy does not disclose any P=O stretching vibration between 1150 and 1250 cm^{-1}. Unlike alkyl and aryl phosphinites, the compounds *(1)* to *(7)* do not isomerize to tertiary phosphine oxides when heated with iodine as catalyst. Attempts to prepare isomers of *(4)* and *(7)* by treating $R_2P(O)Cl$ (R = n-C_4H_9 or C_6H_5) with $LiSi(C_6H_5)_3$ in tetrahydrofuran led to $(C_6H_5)_6Si_2$ and $R_4P_2(O)_2$ as the result of metal-halogen exchange. Compounds *(1)* to *(7)* react with alkyl iodides in the sense of an Arbusov reaction, yielding tertiary phosphine oxides and organo-iodosilanes (a), and they are hydrolysed by water (b).

$$(R_2P{-}O{-})_nSiR^1_{4-n} + n\,R^2I \rightarrow n\,R_2R^2P(O) + SiI_nR^1_{4-n} \quad (a)$$

$$(R_2P{-}O{-})_nSiR^1_{4-n} + n\,H_2O \rightarrow n\,R_2P(O)H + Si(OH)_nR^1_{4-n} \quad (b)$$

Heating compounds *(1)* to *(7)* and *(9)* with sulfur in benzene gives the corresponding silyl and stannyl thiophosphinites.

Treatment of $(n\text{-}C_4H_9)_2P(O)H$ with $SiCl_4$ in the molar ratio 4:1 by method B does not yield silyl tetrakis(di-n-butyl phosphinite) but instead tetrabutyldiphosphine monoxide *(10)*, R = n-C_4H_9 (75% yield), and silica. This product *(10)*

$$4\,R_2P(O)H + SiCl_4 \xrightarrow{N(C_2H_5)_3} 2\,R_2P{-}P(O)R_2 + 4\,HCl + SiO_2$$

(10)

was prepared for ^{31}P-NMR-spectral comparison from $(n\text{-}C_4H_9)_2P(O)H$ and $(n\text{-}C_4H_9)_2PCl$ in benzene in presence of $N(C_2H_5)_3$ (64% yield). It is a colorless liquid, b.p. 120–125 °C/0.01 mm, and gives a derivative, $(n\text{-}C_4H_9)_2P(O){-}P(O)(n\text{-}C_4H_9)$, b.p. 150–152 °C/0.01 mm. The ^{31}P-NMR spectrum of *(10)*, R = n-C_4H_9, has an AB structure, giving signals at 55.6, 46.7, −45.3, and −54.8 ppm with J_{PP} = 216 Hz.

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[*] Prof. Dr. K. Issleib and Dipl.-Chem. B. Walther
Anorganisch-Chemisches Institut der Universität
Weinbergweg
X 402 Halle (Germany)

[**] Part L of Alkali-metal-Phosphorus Compounds.-Part XLIX: *K. Issleib* and *G. Harzfeld*, Z. anorg. allg. Chem., in press.

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Silicon-Nitrogen Heterocycles containing C=N Double Bonds

By *O. J. Scherer* and *P. Hornig* [*]

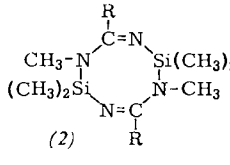
No Si–N ring system incorporating C=N bonds has been reported hitherto and those with C=C bonds can be prepared only in the form of mono- or di-*o*-phenylene derivatives [1].

We have prepared Si–N heterocycles incorporating C=N bonds by treating the addition product *(1)* of benzonitrile and lithium methylamide with dichloro(dimethyl)silane in the presence of triethylamine.

$$R{-}C{\equiv}N + LiNHCH_3 \rightarrow R{-}C(=NLi){-}NHCH_3$$

(1)

$$2\,(1) + 2\,(CH_3)_2SiCl_2 + 2\,(C_2H_5)_3N \rightarrow$$



$$+ 2\,LiCl + 2\,(C_2H_5)_3N \cdot HCl$$

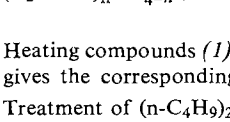
(2)

R = C_6H_5

The product of this reaction, 1,2,2,5,6,6-hexamethyl-4,8-diphenyl-1,3,5,7-tetraaza-2,6-disila-3,7-cyclocatadiene *(2)*, forms colorless crystals which are very sensitive to moisture, readily soluble in ether, benzene, or CCl_4, and moderately soluble in petroleum ether. M.p. 77–79 °C; yield, 43 %.

If lithium methylamide is also present during the reaction, a six-membered heterocycle is formed containing only one C=N bond, namely, 1,2,2,3,4,4-hexamethyl-6-phenyl-1,3,5-triaza-2,4-disila-5-cyclohexene *(3)*, in 45 % yield. This forms colorless crystals, of m.p. 62–64 °C, which are also very sensitive to moisture and dissolve readily in ether, benzene, CCl_4, or petroleum ether.

(1) + 2 $(CH_3)_2SiCl_2$ + 2 $(C_2H_5)_3N$ + $LiNHCH_3$ →



+ 2 LiCl + 2 $(C_2H_5)_3N \cdot HCl$

(3)

R = C_6H_5

Whereas the protons of the product *(3)* give five sharp ^1H-NMR signals [τ = 9.90 and 9.78 (CH_3Si), τ = 7.51 and 7.43 (CH_3N), τ = 2.78 (C_6H_5) (Varian A 60, 60 MHz; 10% solution in CCl_4; tetramethylsilane as internal standard)], the spectrum of product *(2)* at room temperature has sharp signals only at τ = 7.32 (CH_3N) and τ = 2.74 (C_6H_5). At 30 °C the protons of the dimethylsilyl group afford two broad signals [τ = 10.12 and 9.49 (CH_3Si)], at *ca.* 0 °C two sharper signals, and at *ca.* 50 °C one broad signal, behavior indicating the presence of conformational isomers. The relative areas observed for the two compounds agree well with calculated values.

Bands at 1620 cm^{-1} in the IR spectra of *(2)* and *(3)* can be assigned to C=N, and are accompanied in both cases by two weaker bands at 1600 and 1580 cm^{-1}.

Reaction of both products with ethanol is exothermic. With *(2)* it gives *N*-methylbenzamidine (identified as hydrochloride) and diethoxy(dimethyl)silane with quantitative cleavage of the Si–N bonds. Reaction of *(3)* gives, besides

$$(3) + 2\,C_2H_5OH \rightarrow R{-}C(=NH){-}NHCH_3 + \left[C_2H_5O{-}Si(CH_3)_2{-}\right]_2 NCH_3$$

(4)

the amidine derivative, *N*-methyl-bis[ethoxy(dimethyl)silyl]-amine *(4)* in 60% yield [τ = 9.89 (CH_3Si), τ = 8.85(t) and 6.38(q) (C_2H_5), τ = 7.52 (CH_3N)] as a colorless liquid of b.p. 50–53 °C/0.1 mm.

Experimental:

Synthesis of *(2)*: 3.1 g (100 mmoles) of CH_3NH_2 is dissolved in 50 ml of ether and metalated at −70 °C with 6.4 g of butyl-lithium in hexane (100 mmoles in 44 ml of solution) (stirring; exclusion of moisture; N_2-atmosphere). The suspension is treated at 0 °C with 10 g (97 mmoles) of C_6H_5CN in 35 ml of ether and stirred for 2 hr at room temperature. After addition of 10.1 g (100 mmoles) of $(C_2H_5)_3N$, 12.9 g (100 mmoles) of $(CH_3)_2SiCl_2$ in 30 ml of ether is added dropwise, resulting in vigorous boiling. The mixture is stirred for 2 hr, filtered, washed with ether, and fractionally distilled. B.p. 174–176 °C/0.1 mm, m.p. 77–79 °C (recrystallized from pentane). Yield 43 %, calculated on the C_6H_5CN used [forerun, *ca.* 40 %, a mixture of C_6H_5CN and *(3)*].

Synthesis of *(3)*: The compound is prepared under the same conditions as *(2)*, except that only 5 g (48.5 mmoles) instead of 10 g of C_6H_5CN is used. Product *(3)* is isolated on fractionation as a turbid oil, b.p. 103–106 °C/0.1 mm, and is purified by dissolution in ether, filtration, and a second distillation. B.p. 104 °C/0.1 mm; m.p. 62–64 °C. Yield 45 %, calculated on the C_6H_5CN used [forerun, *ca.* 5 % of C_6H_5CN; residue, *ca.* 30 % of *(2)*].

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[*] Dr. O. J. Scherer and Dipl.-Chem. P. Hornig
Institut für Anorganische Chemie der Universität
Röntgenring 11
87 Würzburg (Germany)

[1] *W. Fink*, Angew. Chem. *78*, 803 (1966); Angew. Chem. internat. Edit. *5*, 760 (1966).

Preparation of Phosphoryl Difluoride Isothiocyanate and Phosphoryl Fluoride Diisothiocyanate

By *H. W. Roesky* [*]

Phosphoryl fluoride isocyanates were previously unknown. They can be used as starting materials for the preparation of new phosphorus compounds.

For the synthesis of phosphoryl difluoride isothiocyanate *(2)*, difluorophosphoric anhydride *(1)* [1] was stirred vigorously with potassium thiocyanate (molar ratio 1:1.2) for 12 hr at 25 °C. After filtration, the liquid was fractionated under reduced pressure. The yield of *(2)* (b.p. 35–36 °C/87 mm, mol. wt. 142.5 by Regnault's method, 168 cryoscopically in benzene) was 50 %. By-products of the reaction are POF_3, $(SCN)_2$, and $(SCN)_x$.

$$\underset{(1)}{F_2P(O)-O-P(O)F_2} + KSCN \longrightarrow \underset{(2)}{F_2P(O)NCS} + K[PO_2F_2]$$

If the difluoride *(2)* is heated for an hour under nitrogen at 65 °C and atmospheric pressure, phosphoryl trifluoride *(3)* and phosphoryl fluoride diisothiocyanate *(4)* are obtained,

$$2\ \underset{(2)}{F_2P(O)NCS} \longrightarrow \underset{(3)}{POF_3} + \underset{(4)}{FP(O)(NCS)_2}$$

the latter in 40 % yield (b.p. 64–65 °C/3.5 mm, mol. wt. 203, cryoscopically in benzene). $(SCN)_x$ is formed as a by-product. Compounds *(2)* and *(4)* are colorless liquids. Traces of moisture decompose them, with yellow to brown coloration. Reaction of potassium cyanate with compound *(1)* (molar ratio 1.2:1) at 25 °C gives phosphoryl difluoride isocyanate

$$(1) + KOCN \longrightarrow \underset{(5)}{O{=}P(F)_2{-}NCO} + K[PO_2F_2]$$

(5) [2], which after filtration of the reaction mixture is obtained by distillation (b.p. 69 °C; yield 50 %).

	^{19}F–NMR [a]			^{31}P–NMR [a]		
	J_{F-P} (Hz)	δ_F (ppm)	Intensity	J_{P-F} (Hz)	δ_F (ppm)	Intensity
(1)	1054	+ 81	1:1	1048	+ 39.3	1:2:1
(2)	1012	+ 71.6	1:1	1016	+ 36.4	1:2:1
(4)	957	+ 55 0	1:1	940	+ 47.7	1:1
(5)	998	+ 72.2	1:1	1000	+ 29.5	1:2:1

[a] CCl_3F or 85 % H_3PO_4 was used as external standard.

	ν (CN)	ν (PO)	ν (SC)	ν_{as} (PF)	ν_s (PF)	Deformation vibrations
(2) [a]	1995 vs [c]	1380 vs	1090 w	965 vs	895 vs	657 w
				ν (PF)		528 w
(4) [b]	1930 vs	1320 vs	1074 w	885 vs		505 vs
						650 vs

[a] Determined for the gas phase. [b] Determined for the liquid.
[c] vs = very strong; w = weak.

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[*] Dr. H. W. Roesky
Anorganisch-Chemisches Institut der Universität
Hospitalstr. 8–9
34 Göttingen (Germany)

[1] *E. A. Robinson*, Canad. J. Chem. *40*, 1725 (1962); *U. Wannagat* and *J. Rademachers*, Z. anorg. allg. Chem. *289*, 66 (1957).

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Synthesis of Thiophosphoryl Difluoride Isothiocyanate and Thiophosphoryl Fluoride Diisothiocyanate

By *H. W. Roesky* [*]

Thiophosphoryl fluoride isothiocyanates have not previously been described. As starting material for their synthesis we used thiophosphoryl triisothiocyanate *(1)* [1]. If antimony trifluoride *(2)* is treated dropwise, at 100 °C and a pressure of 1 to 2 mm, with triisothiocyanate *(1)* (molar ratio 1.5:1), thiophosphoryl difluoride isothiocyanate *(3)* and thiophosphoryl fluoride diisothiocyanate *(4)* are formed.

$$\underset{(1)}{2\,SP(NCS)_3} + \underset{(2)}{SbF_3} \rightarrow \underset{(3)}{SPF_2NCS} + \underset{(4)}{SPF(NCS)_2} + Sb(NCS)_3$$

The product *(4)* is distilled off during the reaction (yield 45 %, b.p. 66–67 °C/1.5 mm), whereas *(3)* is collected in a cold trap (–78 °C; acetone-dry ice), which is placed after the first collecting vessel, and is purified by subsequent fractionation (yield 18 %, b.p. 89.5–90 °C/760 mm).

Elemental analysis proves the composition of *(3)* and *(4)*. Molecular weights are 159.1 (Regnault), 160 (cryoscopic in benzene) for *(3)* and 199 (cryoscopic in benzene) for *(4)*.

From the temperature-dependence of the vapor pressure of *(3)* it is possible to obtain the vapor pressure equation

$$\log p = (-1756.3/T) + 7.7150,$$

an extrapolated boiling point of 90.1 ± 0.5 °C, a latent heat of evaporation of L = 8.049 kcal/mole, and a Trouton constant of 22.2 cal/degree.

Both compounds are pale liquids that decompose in the presence of traces of water with yellow to brown coloration.

	^{19}F–NMR[a]			^{31}P–NMR[a]		
	J_{F-P} (Hz)	δ_F (ppm)	Intensity	J_{P-F} (Hz)	δ_P (ppm)	Intensity
$SP(NCS)_3$	–	–	–	–	+ 9.1	1 [2]
$SP(NCS)_2F$	1061	+27.4	1:1	1060	–12.2	1:1
$SP(NCS)F_2$	1123	+36.6	1:1	1132	+28.6	1:2:1

[a] CCl_3F and H_3PO_4 (85 %), respectively, were used as external standard.

	ν(CN)	ν(SC)	ν_{as}(PF)	ν_s(PF)	ν(PS)	Deform.
$SP(NCS)F_2$	1970 vs [b]	1080 s	934 s	910 s	735 s	590 m
						487 s
$SP(NCS)_2F$	1950 vs	1065 s	νPF		745 s	640 vs
			905 s			485 s

[b] All the numerals denote cm^{-1}. m = medium, s = strong, vs = very strong.

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[*] Dr. H. W. Roesky
Anorganisch-Chemisches Institut der Universität
Hospitalstr. 8–9
34 Göttingen (Germany)

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[2] Cf. *E. Fluck*, Z. Naturforsch. *19b*, 869 (1964).

N-Cyaniminosulfur Difluoride

By *W. Sundermeyer* [*]

On treating bis(trimethylsilyl)carbodiimide [1] with sulfur tetrafluoride we obtained *N*-cyaniminosulfur difluoride *(1)* in a smooth reaction [2].

$$R_3Si{-}NCN{-}SiR_3 + SF_4 \rightarrow \underset{(1)}{F_2S{=}N\ CN} + 2\,R_3SiF \quad (R = CH_3)$$

The product is formed quantitatively if the reactants (on a 2-molar scale, slight excess of SF_4) are heated at 50 °C in a closed vessel (200 ml) for 2 hr. The trimethylfluorosilane and the excess of sulfur tetrafluoride can be separated by low-temperature vacuum-distillation, the pure product *(1)* remains behind as a clear colorless liquid (b.p. 58 °C/100 mm, 43 °C/49 mm; vapor pressure = 14 mm at 20 °C). The boiling point (extrapolated to atmospheric pressure) is 111 °C. The compound partly decomposes above 50 °C and becomes yellow. Melting point −34 °C. Molecular weight (Dumas) = 111.

The mass spectrum shows typical fragments FSNCN (*m/e* = 96), SNCN (72), SF_2 (70), and SF (51), as well as the molecule ion (110). The ^{19}F–NMR spectrum includes a singlet at −48.1 ppm ($CFCl_3$ as external standard). The IR spectrum, measured for the NaCl and KBr region, shows absorption bands (with tentative assignments) at 2255 (s, ν_{as}NC–N[3]), 1463 (m), 1337 (vs, νS=N), 844 (vs, ν_sNCN), 764 (vs, ν_{as}SF), 725 (vs, ν_sSF), 615 (m), and 527 (m). The spectroscopic data are in accordance with the structure assigned and with the data for *N*-cyaniminosulfur difluoride prepared by a different method[4].

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[*] Priv.-Doz. Dr. W. Sundermeyer
Anorganisch-Chemisches Institut der Universität
Hospitalstr. 8–10
34 Göttingen (Germany)

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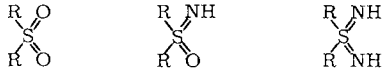
[3] vs = very strong, s = strong, m = medium.

[4] *J. K. Ruff*, Inorg. Chem. *5*, 1787 (1966).

N,N'-Dihalogeno-*S,S*-dimethylsulfur Diimide[1]

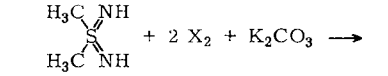
By *R. Appel* and *D. Hänssgen*[*]

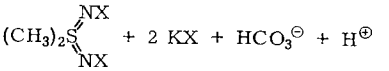
Of the isoelectronic compounds



(1)

the dialkylsulfur diimides *(1)* have been known for only a short time[2]. We have now found that reactive *N,N'*-dihalogeno-*S,S*-dialkylsulfur diimides *(2)* can be prepared, some of them in good yield, by halogenation of *(1)* in aqueous solution buffered by potassium carbonate.





(2)

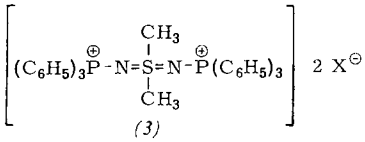
	X	M.p. (°C)	Decomp. pt. (°C)	Yield (%)
(2a)	Cl	58	60	19
(2b)	Br	150	152	76
(2c)	I		134–136	97

Preparation of N,N-dibromo-S,S-dimethylsulfur diimide (2b): 7.6 g of bromine in 100 ml of methanol is added dropwise, with stirring, over 30 min, to a solution of 1.8 g of *S,S*-dimethylsulfur diimide and 10.4 g of potassium carbonate in 400 ml of water. The mixture is stirred for a further 30 min and the dibromo compound is filtered off.

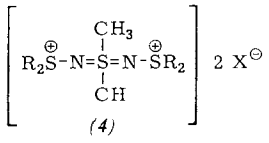
This is washed with a little water and methanol and dried in a vacuum. Yield: 3.8 g.

N,N-Dihalogeno derivatives of the higher dialkylsulfur diimides are accessible by the same method. Methylene chloride, ethyl acetate, and acetonitrile are suitable as solvents for compounds *(2a)* and *(2b)*; *(2a)* also dissolves in alcohols and nitromethane; *(2c)* is only sparingly soluble in the usual solvents.

Compounds *(2a)* to *(2c)* have the usual properties of *N*-halogeno compounds. This is so for halogenations as well as for oxidations. They undergo nucleophilic substitution with phosphines and sulfides, the halogen being lost as anion and the compounds *(3)* and *(4)* formed. The salt-like character of *(3)* and *(4)* was proved by determination of ionogenic halogen and by conductivity measurements. The structures of *(3)* and *(4)* were confirmed by analysis and chemical reactions.



(3)



(4)

Large quantities of *(2a)* should not be prepared since even amounts of less than 1 g often explode spontaneously at 0 °C. Compound *(2b)* detonates when struck but, like *(2c)*, can be kept for months without decomposition.

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[*] Prof. Dr. R. Appel and Dipl.-Chem. D. Hänssgen
Anorganisch-Chemisches Institut der Universität
Meckenheimer Allee 168
53 Bonn (Germany)

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Tricarbonylhexamethylborazolechromium[1]

By *R. Prinz* and *H. Werner*[*]

Borazole complexes analogous to dibenzenechromium[2] and tricarbonylbenzenechromium[3] were previously unknown. The synthesis of tricarbonylhexamethylborazolechromium according to eq. (a)

$$(CH_3CN)_3Cr(CO)_3 + B_3N_3(CH_3)_6 \xrightarrow{\text{dioxane}} [B_3N_3(CH_3)_6]Cr(CO)_3 + 3\,CH_3CN \qquad (a)$$

represents the first preparation of such a complex. The composition of the complex was established by elemental analysis, and osmometric molecular-weight determination in benzene

gave a value of 297. (The preparation of $(CH_3CN)_3Cr(CO)_3$ was as described by *Tate*[4].) Reaction conditions: stirring at 30 °C and 15 mm/Hg for some hours.

Table 1. Comparison of tricarbonylhexamethylborazolechromium with a typical π-complex and a Lewis-base complex.

	$B_3N_3(CH_3)_6Cr(CO)_3$	$C_6(CH_3)_6Cr(CO)_3$	$(C_6H_{11}NH_2)_3Cr(CO)_3$
Appearance	orange-yellow needles	yellow crystals	yellow powder
Behaviour in high vacuum	sublimes at 90 °C without decomp.	sublimes at 90 °C without decomp.	does not sublime
Decomposition temperature (°C)	141	250	183
Stability in air	days	days	some hours
Solubility in benzene	readily soluble	readily soluble	insoluble
ν(CO) (cm^{-1})	1867 in C_6H_{12} 1963 [m]	1888 in C_6H_{12} 1962 [5]	1724 in KBr 1873
UV Maxima in C_6H_{12} ν (cm^{-1}); log ε	25320 3.65 36760 [sh] 3.78 46080 4.37	30960 3.98 45670 4.42 49500 4.44	insoluble in cyclohexane
Dipole moment in benzene (D)	7.24 ± 0.05	6.22 ± 0.02 [6]	insoluble

[m] medium intensity band. [sh] shoulder.

Table 2. NMR Spectra [7].

	$B_3N_3(CH_3)_6Cr(CO)_3$		$B_3N_3(CH_3)_6$	
	N—CH_3	B—CH_3	N—CH_3	B—CH_3
^{1}H—NMR [a]	τ = 7.11	τ = 9.29	τ = 7.11	τ = 9.51
^{14}N—NMR [b]	+299 ppm		+252 ppm	

[a] Varian A 60, 60 MHz, in $CDCl_3$ with $CHCl_3$ as internal standard.
[b] Varian HR 100, 7,22 MHz, 23490 gauß; reference signal: NO_3-group of NH_4NO_3 as external standard. Standardisation by side-band technique. Solvent: dioxane.

The following ions were determined by mass spectrometry[7].

$B_3N_3(CH_3)_6Cr(CO)_3^{\oplus}$, $B_3N_3(CH_3)_6Cr(CO)^{\oplus}$, $B_3N_3(CH_3)_6Cr^{\oplus}$ and $B_3N_3(CH_3)_6^{\oplus}$.

Atlas CH 4 mass spectrometer, 50 eV; the calculated and observed isotope ratios $^{10}B:^{11}B$, $^{14}N:^{15}N$ agree.

The chemical properties and spectroscopic data indicate that hexamethylborazolechromium tricarbonyl is analogous to the aromatic metal tricarbonyl complexes. An X-ray crystallographic study should provide further information on this point.

Work in progress indicates that the analogous molybdenum and tungsten complexes of hexamethylborazole are probably also obtainable.

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[*] Dipl.-Chem. R. Prinz and Dr. H. Werner
Anorganisch-Chemisches Laboratorium
der Technischen Hochschule
Arcisstr. 21
8 München (Germany)

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[7] We thank Dr. *K. Schwarzhans* for the ^{14}N-NMR results and Dr. *J. Müller* for the mass-spectra.

Oxygen Complexes of Zerovalent Nickel, Palladium, and Platinum

By *G. Wilke*, *H. Schott*[1], and *P. Heimbach*[*]

Oxygen reacts at −78 °C with olefinbis(triphenylphosphine)-nickel(0) complexes and also with tetrakis(triphenylphosphine)nickel(0), in ether or toluene, giving a compound of composition $[(C_6H_5)_3P]Ni{\cdot}O_2$ which is stable in solution below −35 °C. It is probably the bis(triphenylphosphine)-nickel(0), which is present at least in traces in all the equilibrium mixtures, that enters into these reactions.

The analogous complexes $[(C_6H_{11})_3P]_2Ni{\cdot}O_2$ and $[(C_5H_{10}N)_3P]_2Ni{\cdot}O_2$, which are stable up to about −5 °C and −30 °C, respectively, were prepared from ethylenebis(tricyclohexylphosphine)nickel(0) and ethylenebis(tripiperidinophosphine)nickel(0), respectively. The increase in stability of

$$Ni^0(TPP)_4 \underset{+2\,TPP}{\overset{-2\,TPP}{\rightleftharpoons}} [Ni^0(TPP)_2] \underset{-Olefin}{\overset{+Olefin}{\rightleftharpoons}} (TPP)_2Ni(Olefin)$$

$$[Ni^0(TPP)_2] \xrightarrow{+O_2} (TPP)_2Ni{\cdot}O_2$$

TPP = $(C_6H_5)_3P$

the complexes in the order triphenylphosphine < tripiperidinophosphine < tricyclohexylphosphine parallels the increase in stability of the analogous ethylene complexes[2].

Analogous complexes were also obtained by the action of oxygen on $Pd^0(TPP)_4$ and $Pt^0(TPP)_4$ in benzene at 20 °C.

$$M^0(TPP)_4 + O_2 \rightarrow (TPP)_2M{\cdot}O_2 + 2\,TPP\ (\text{in part TPPO})$$

TPPO = $(C_6H_5)_3PO$

These complexes (M = Pd or Pt) are more stable than the nickel complex, but they nevertheless decompose when stirred for days, *e.g.* in benzene, at 20 °C. The decomposition of all the complexes takes place according to the scheme:

$$(TPP)_2M{\cdot}O_2 \rightarrow M + 2\,TPPO$$

M = Ni (rapid reaction above −35 °C).
M = Pd or Pt (rapid reaction above +90 °C, slow reaction even at +20 °C in solution).

The metal that is liberated can be trapped as a M(0) complex by addition of an excess of triphenylphosphine.

$$(TPP)_2M{\cdot}O_2 + 4\,TPP \rightarrow 2\,TPPO + M^0(TPP)_4$$

M = Ni (−35 °C, yield 56%).
M = Pd (+50 °C, yield 85%).

The $M^0(TPP)_4$ formed can again react further with oxygen, giving $(TPP)_2M{\cdot}O_2$. If a mixture of $Ni^0(TPP)_4$ and an excess of TPP in toluene is allowed to react with oxygen at such a temperature (above −35 °C for Ni) that the oxygen compounds decomposes again, then the TPP is oxidized catalytically to TPPO by molecular oxygen. With Ni^0 complexes, 50 molecules of TPP can be oxidized per Ni atom present. For Pd the ratio is at least 1:500. The maximal catalytic yield has not been determined.

Hydrolysis of $(TPP)_2Ni{\cdot}O_2$ with water-saturated ether and acetylacetone at −78 °C gives H_2O_2 in 83.5% yield, as well as TPP. Bromine reacts with $(TPP)_2Ni{\cdot}O_2$ at −78 °C or with $(TPP)_2Pd{\cdot}O_2$ at 0 °C in ether, liberating 31 and 83%, respectively, of the oxygen that was bound in the complex.

Infrared spectra could be obtained for the relatively stable complexes $[(C_6H_{11})_3P]_2Ni{\cdot}O_2$, $[(C_6H_5)_3P]_2Pd{\cdot}O_2$, and $[(C_6H_5)_3P]_2Pt{\cdot}O_2$. Besides the bands from triphenylphosphine, the Pd and Pt compounds gave bands at *ca.* 875 and 830 cm^{-1}, respectively, which can be ascribed to the O—O vibration of the complex-bound oxygen molecules. The O—O

band cannot be recognized in the spectrum of the Ni compound because tricyclohexylphosphine absorbs in the same region. In this connection mention should be made of the complex $O_2IrCl(CO)(TPP)_2$ which has been synthesised by *L. Vaska* [3].

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[*] Prof. Dr. G. Wilke, Dr. H. Schott, and Dr. P. Heimbach
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1
433 Mühlheim/Ruhr (Germany)

[1] *H. Schott*, Dissertation, Technische Hochschule Aachen, 1965.

[2] *G. Herrmann*, Dissertation, Technische Hochschule Aachen, 1963.

[3] *L. Vaska*, Science (Washington) *140*, 809 (1963).

Dicyclopentadienyltechnetium Hydride

By *E. O. Fischer* and *M. W. Schmidt* [*]

In contrast to earlier work [1], we have obtained dicyclopentadienyltechnetium hydride $Tc(C_5H_5)_2H$ in 14% yield, and not the dimeric dicyclopentadienyltechnetium $[Tc(C_2H_5)_2]_2$, from the reaction of technetium tetrachloride with cyclopentadienylsodium in tetrahydrofuran (THF) and in the presence of sodium tetrahydridoborate. This hydride is analogous to the known dicyclopentadienylrhenium hydride [2].

Cyclopentadienylsodium NaC_5H_5 (10.5 g) was added to a suspension of $TcCl_4$ (3.9 g) in THF (60 ml) at −50 °C. After warming to 20 °C, $NaBH_4$ (1.0 g) was added to the purple reaction mixture which was then stirred at 50 °C for 10 hours. Evaporation of the solvent and sublimation of the residue at 40–60 °C/10^{-2} mm gave a yellow solid. A further small quantity of the sublimate was obtained after a second treatment of the residue with THF. Resublimation and recrystallization from toluene, gave golden-yellow, pure platelets. Dicyclopentadienyltechnetium hydride is very sensitive to air, but thermally stable. The solid, which melts without decomposition at 150 °C, is readily soluble in benzene and toluene but less so in hexane. The molecular weight [3] was found osmometrically in benzene to be 225 (calc. 230.2).

The infrared spectrum of $Tc(C_5H_5)_2H$ in KBr shows the following bands which are characteristic of π-cyclopentadienyl complexes (in cm^{-1}) [4]: 3045 m, 2910 w (ν_{CH}); 1400 s, 1097 s (ω_{CC}); 995 s (δ_{CH}); 803 m, 773 vs (γ_{CH}). [c.f. $Re(C_5H_5)_2H$ 3062 m, 2910 w, 1408 m, 1392 s, 1095 s, 998 s, 987 s, 816 s, 795 s]. The Tc–H stretching vibration occurs at 1930 m (KBr) and 1923 (CS_2 solution). [cf. ν(Re–H) in $Re(C_5H_5)_2H$ 2032 w, 2000 m (KBr); 2016 (CS_2)]. The force constant k(Tc–H) is calculated to be 2.20 mdyn/Å [cf. k(Re–H): 2,41 mdyn/Å]. The metal-hydrogen bond in $Tc(C_5H_5)_2H$ is thus somewhat weaker than in the rhenium analogue. The same difference is found for $Mo(C_5H_5)_2H_2$ and its tungsten analogue [5].

The NMR spectrum [6] of a saturated benzene solution of $(C_5H_5)_2TcH$ shows a singlet at $\tau = 5.6$ (halfwidth 1.7 Hz) and a broad signal in the hydride region at $\tau = 17.8$ (halfwidth 40 Hz) at 25 °C. The relative intensity of these signals is approximately 10:1. $Re(C_5H_5)_2H$, however, shows a doublet at $\tau = 5{,}75$ (splitting 1.2 Hz) and a sharp signal at $\tau = 23.0$ (halfwidth 6 Hz), at 25 °C. The low field shift of the Tc–H signal compared with that of Re–H indicates a weaker shielding in the former. This may be explained by a decreased negative charge on the hydrogen attached to technetium [7].

The mass spectrum [8] of $(C_5H_5)_2TcH$ shows strong peaks at *m/e* 230 and 229 which may be assigned to the molecule-ion and to the ion $[Tc(C_5H_5)_2]^+$ respectively. The two peaks are of approximately equal intensity. In the mass spectrum of $Re(C_5H_5)_2H$ measured under similar conditions, the ion $[Re(C_5H_5)_2]^+$ has only ~ 65% of the intensity of the molecule-ion. This change in intensity is a further indication of a weakening in the metal-hydrogen bond in the technetium compound. Other mass peaks are weak in comparison to the two mentioned and nothing was observed at *m/e* 458 which would correspond to $[Tc(C_5H_5)_2]_2$.

Dicyclopentadienyltechnetium hydride is a typical base. It may be extracted from benzene into 2 N aqueous HCl. Neutralisation of the aqueous solution of dihydridodicyclopentadienyltechnetium chloride with 2 N NaOH yields the free hydride again.

$$Tc(C_5H_5)_2H \underset{NaOH}{\overset{HCl}{\rightleftharpoons}} [Tc(C_5H_5)_2H_2]Cl$$

The dihydridodicyclopentadienyltechnetium cation may be precipitated as the rather insoluble white hexafluorophosphate $[Tc(C_5H_5)_2H_2]PF_6$, which may be purified by crystallisation from acetone/hexane, from aqueous solutions of the chloride.

The infrared spectrum of this compound in KBr shows the normal vibrations (in cm^{-1}) of the cyclopentadienyl ligands at 3130 s, 2915 vw, 1428 s, 1410 s, 1108 w, 1022 m, 1003 m, 764 vs, broad [cf. $[Re(C_5H_5)_2H_2]PF_6$ 3140 s, 2922 vw, 1451 m,sh, 1412 s, 1110 w, 1031 m, 1001 m, 784 sh]. The Tc–H vibration appears as a weak absorption at 1984 cm^{-1} [cf. Re–H 2058 cm^{-1}].

The NMR spectrum [6] of $[Tc(C_5H_5)_2H_2]PF_6$ in deuteroacetone shows a signal at $\tau = 4.11$ (triplet, splitting 0.2 Hz) and a barely recognisable signal in the hydride region at $\tau = 17.7$. [cf. $[Re(C_5H_5)_2H_2]PF_6$: $\tau = 4{,}17$ and $\tau = 24{,}6$].

We suggest that $Tc(C_5H_5)_2H$ has a bent structure similar to that of $Re(C_5H_5)_2H$.

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[*] Prof. Dr. E. O. Fischer and Dipl.-Chem. M. W. Schmidt
Anorganisch-Chemisches Laboratorium
der Technischen Hochschule
Arcisstr. 21
8 München (Germany)

[1] *D. K. Huggins* and *H. D. Kaesz*, J. Amer. chem. Soc. *83*, 4474 (1961).

[2] *G. Wilkinson* and *J. M. Birmingham*, J. Amer. chem. Soc. *77*, 3421 (1955); *M. L. H. Green*, *L. Pratt*, and *G. Wilkinson*, J. chem. Soc. (London) *1958*, 3916.

[3] Measurements by *P. Laubereau* and *B. Kannellakopulos*.

[4] vs = very strong, s = strong, m = medium, w = weak.

[5] *M. L. H. Green*, *J. A. McCleverty*, *L. Pratt*, and *G. Wilkinson*, J. chem. Soc. (London) *1961*, 4854; *E. O. Fischer* and *Y. Hristidu*, Z. Naturforschg. *15b*, 135 (1960).

[6] Measurements by *K.-E. Schwarzhans* (Varian A 60).

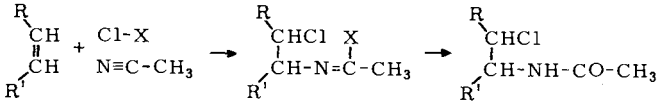
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[8] Measurements by *J. Müller* (Atlas CH 4).

Coupled Addition to the Carbon-Carbon Double Bond

By *W. Theilacker* [*]

In kinetic studies of the addition of HOCl to cyclohexene from aqueous solution with acetonitrile as co-solvent, it was found that the acetonitrile takes part in the reaction and *N*-(2-chlorocyclohexyl)acetamide *(2)* [R + R′ = $(CH_2)_4$; here X = OH] is formed in a coupled reaction.

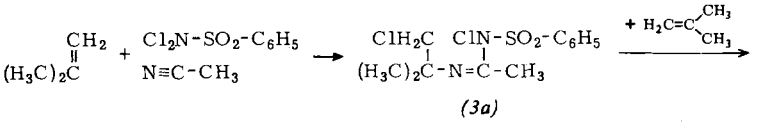


X = OH, Cl *(1)* *(2)*

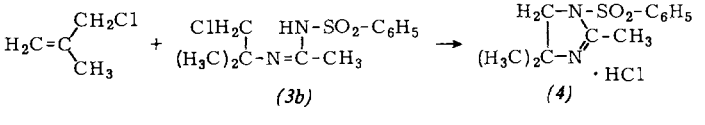
This reaction can be extended to other olefins and nitriles, and chlorine and water can be used in place of HOCl. *Cairns, Graham, Barrick,* and *Schreiber* [1] have added chlorine to olefin-nitrile mixtures with exclusion of water, obtaining imidoyl chlorides *(1)*, X = Cl, which can be converted into amides *(2)* by hydrolysis. The addition proceeds more smoothly and in better yield in the presence of water.

When α,β-unsaturated acids (R′ = COOH) are used in place of olefins, chlorine in aqueous acetonitrile affords, after hydrolysis, the β-amino-α-hydroxycarboxylic acids in yields of up to 70 % (*e.g.* isoserine, isothreonine, isoallothreonine, isohydroxyvaline).

Coupled addition also occurs with *N,N*-dichlorobenzenesulfonamide instead of HOCl or Cl_2. The amidines thus formed give imidazoline hydrochlorides *(4)* in yields of 30 to 90 %, sometimes spontaneously, sometimes when heated in solvents, sometimes under the influence of bases.



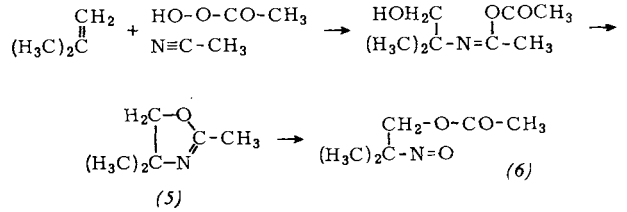
(3a)



(3b) *(4)*

The olefin and the nitrile components may be varied within wide limits; *N,N*-dichlorobenzenesulfonamide may be replaced by ring-substituted analogues or *N,N*-dichloromethanesulfonamide. Moreover, *N,N*-dichlorocarboxamides, if stable, may be used. Only one chlorine atom takes part in the addition, the second being used for chlorination of the olefin at the allyl position, whence a method for chlorination of olefins at the allyl position may be developed.

Olefins of the isobutene type also react with nitriles and peracetic acid, giving nitroso compounds such as *(6)* by way of oxazolines such as *(5)*.



(5) *(6)*

Since these nitroso compounds are further oxidized by peracetic acid, the reaction conditions must be closely controlled.

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[*] Prof. Dr. W. Theilacker
Institut für organische Chemie der Technischen Hochschule
Callinstr. 43
3 Hannover (Germany)

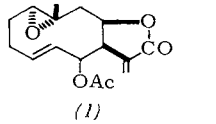
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Sesquiterpenoids with Ten-Membered Rings

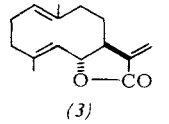
By *F. Šorm* [*]

Sesquiterpenoids are now known to include many diverse structures. Some sesquiterpenes, such as caryophyllene and humulene, also contain carbon rings of medium size, whose occurrence in nature was earlier considered unlikely. The most frequently encountered sesquiterpenoids are those with a ten-membered ring, which are derived from 4-isopropyl-1,7-dimethylcyclodecane (germacrane).

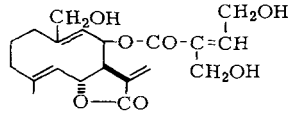
The presence of this ten-membered ring was first established in the lactone pyrethrosin *(1)* [1], and the first compound for which a complete determination of structure was presented was the ketone germacrone *(2)* [2]. Other lactones of this group were later isolated from plants of the family Compositae; they were named germacranolides. Together with the santanolides and the newly discovered guaianolides, ambrosanolides, and eremophylanolides they form an additional group of sesquiterpene lactones. The natural germacranolides are either simple unsaturated lactones such as costunolide *(3)*, or they contain an additional free (balchanolide, iosbalchanolide) or esterified hydroxyl group (acetylbalchanolide, eupatoriopicrin). Compounds containing two free or esterified hydroxyl groups have also been identified *e.g.* the bitter substances arctiopicrin *(4)*, cnicin *(5)*, scabiolide, and salonitolide.



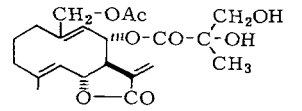
(1)



(3)

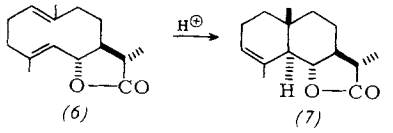


(4)



(5)

The structure and stereochemistry of all the germacranolides named above have been elucidated and it has been shown that they are closely related to the santanolides and guaianolides. It is noteworthy that the germacranolides are readily converted into compounds of the santonin series by stereospecific transannular ring closure; for instance, dihydrocostunolide *(6)* yields santenolide *(7)* in an acid medium.



(6) *(7)*

The cyclodecadiene system of natural germacranolides also undergoes other interesting chemical changes: thus β-elemenone *(8)* is formed on pyrolysis of germacrone *(2)*.



(2) *(8)*

Analogous changes presumably take place in nature and compounds of the germacrane type may well be precursors of the santanolides and guaianolides, and perhaps of the elemane type. The elemane series have an irregular linkage of isoprene residues that is difficult to explain in any other way.

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[*] Prof. Dr. F. Šorm
Institute for Organic Chemistry in the University
Flemingovo náměstí 2
Praha 6 (CSSR)

[1] *D. H. R. Barton* and *P. de Mayo*, J. chem. Soc. *1957*, 150; *D. H. R. Barton, O. C. Böchmann*, and *P. de Mayo, ibid. 1960*, 2263.

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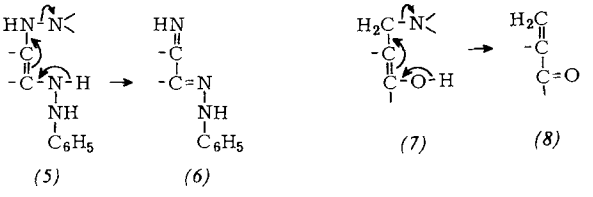
Recent Studies of Mechanism in the Carbohydrate Field

By *H. Simon*[*]

In connection with the Amadori rearrangement[1] and the hydrolysis of glycosylamines[2] we have studied transglycosidation by measuring the exchange rate of an *N*-glucoside with a free amine. This free amine was labeled with tritium and was chemically identical with that bound to the glycoside.

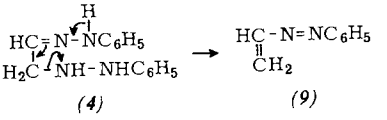
Reaction of *N-p*-nitrophenyl- *(1)*, *N-p*-tolyl- *(2,)* and *NN*-pentamethylene-D-glucosides *(3)* with the corresponding amines obeys second-order kinetics. The rate shows the same strong dependence on pH as that of the hydrolysis. Maximum rates are: for *(1)* in the strongly acidic region; for *(2)* at pH 1.5; and for *(3)* at pH 5.0. The mechanistic conclusions drawn for hydrolysis[2] can thus be extended to the present reactions.

Kinetic and tracer experiments have been made on glycolaldehyde and six of its derivatives, particularly on phenylhydrazinoacetaldehyde phenylhydrazone *(4)*, a type of compound not yet studied, although it is postulated as an intermediate in osazone formation. The hydrazone *(4)* cannot be dehydrogenated to the osazone by iodine, 2,6-dichlorophenolindophenol, oxygen, or Fe^{3+} ions; thus it is very improbable that phenylhydrazine can effect dehydrogenation in an intermolecular reaction; kinetic experiments have also provided evidence against such a supposition. The aniline eliminated during osazone formation also plays no decisive role; it is split off in an azaallyl elimination *(5)* → *(6)* which has parallels in the easy loss of amine from derivatives of an aminopropenol *(7)* → *(8)*[3]. A corresponding elimination of aniline occurs if glycoaldehyde is treated under osazone formation conditions.



(5) *(6)* *(7)* *(8)*

Compound *(4)* undergoes elimination of phenylhydrazine *(4)* → *(9)* as well as the decomposition *(5)* → *(6)*:



(4) *(9)*

The very rapid osazone formation from *(4)* in an anhydrous medium without addition of phenylhydrazine is therefore explained by assuming the reaction *(5)–(6)* and formation of the osazone by *(6)* and the phenylhydrazine which is liberated *via (4)–(9)*. α,β-Unsaturated azo compounds of type *(9)* probably are also produced during osazone formation from aldoses. Mannose phenylhydrazone gives the azo compound *ca.* 10 times faster than glucose phenylhydrazone – at least in pyridine/acetic anhydride – as was ascertained on use of labeled material. In this way the large difference in osazone formation shown by epimeric aldoses can be explained.

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[*] Prof. Dr. H. Simon
Chemisches Institut der Fakultät für Landwirtschaft und Gartenbau der Technischen Hochschule München
8050 Weihenstephan b. Freising (Germany)

[1] *D. Palm* and *H. Simon*, Z. Naturforsch. *18b*, 419 (1963); *20b*, 32 (1965).

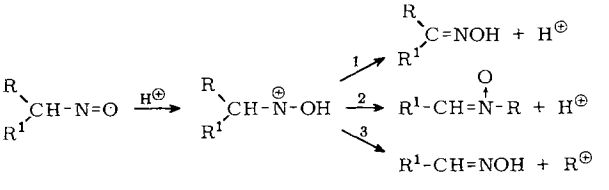
[2] *H. Simon* and *D. Palm*, Chem. Ber. *98*, 433 (1965).

[3] *H. Simon* and *G. Heubach*, Chem. Ber. *98*, 3703 (1965).

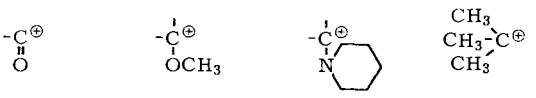
Acid-Catalysed Reactions of Aliphatic Nitroso Compounds

By *W. Pritzkow*[*]

Monomeric nitroso compounds may react with strong acids by prototropic rearrangement (route 1), by nucleophilic 1,2-migration of an organic group (route 2), or by fragmentation (route 3).



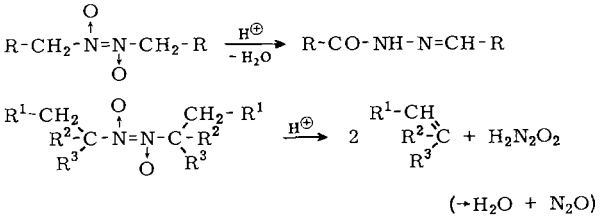
Reaction by route 1 is easily realized: it is the normal reaction of secondary nitroso compounds with acids. Route 3 is used when $R^{\oplus}$ is a relatively stable carbonium ion, *e.g.*:



In such cases prototropic rearrangement often takes second place to fragmentation.

No example has hitherto been found for route 2, nucleophilic 1,2-rearrangement, leading to nitrones.

For dimeric nitroso compounds with nitroso groups bound to primary carbon the reactions formulated above are accompanied by a disproportionating rearrangement, and for those with a nitroso group bound to tertiary C by an elimination:



(→H_2O + N_2O)

Lecture at Marl-Hüls (Germany), on November 2nd, 1966 [VB 29 IE]
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[*] Prof. Dr. W. Pritzkow
Institut für Chemie und Technologie
der Technischen Hochschule
Geusaer Strasse
X 42 Merseburg (Germany)

Substitution Effects in Organosilicon Compounds

By *G. Schott*[*]

After a review of the most important categories of substitution constants [*e.g.* σ^H(*Hammett*), σ^* (*Taft*), σ' (*Roberts*), σ^0 (*Taft*)] and a discussion of the relationships existing between them, the applicability was investigated of these parameters to compounds in which the reactive center constitutes a silicon atom carrying a reactive substituent. Various test reactions were carried out [*e.g.* a) to c)], partly of nucleophilic and partly of electrophilic nature, and of different orders. The results obtained for about 80 organosilicon compounds can therefore be considered as of a general nature.

a) $R_3Si{-}O{-}CO{-}R' + ROH \longrightarrow R_3Si{-}OR + R'{-}CO{-}OH$

b) $R_3Si{-}H + Br_2 \longrightarrow R_3Si{-}Br + HBr$

c) $R_3Si{-}H + H_2O \longrightarrow R_3Si{-}OH + H_2$

It was found that:

1. In substituted alkyl-Si compounds the σ^* constants (*Taft*) are experimentally confirmed; deviations were observed when the substituents were able to interact with the Si atom through $d\pi$-resonance.

2. In substituted phenyl-Si compounds, only the σ^0 constants (*Taft*) were applicable not the σ^H values of Hammet.

The conclusions made as to the bonding on Si atoms agree with the results obtained by spectrometry.

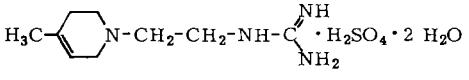
Lecture at Hamburg (Germany), November 11th, 1966 [VB 37 IE]
German version: Angew. Chem. 79, 65 (1967)

[*] Prof. Dr. G. Schott
Institut für Anorganische Chemie der Universität
Buchbinderstr. 9
X 25 Rostock (Germany)

Therapy Congress and Pharmaceutical Exhibition

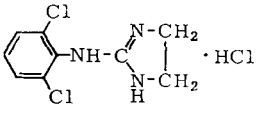
The 18th GermanTherapyWeek took place from August 27th to September 3rd, 1966 in Karlsruhe, in conjunction with an exhibition of drugs in which 285 firms participated. Examples of pharmaceuticals that contain new synthetic active components or components that are new to the German market, are described below; new combinations of known substances are not reported.

New antihypertonics were introduced by Farbenfabriken Bayer, Leverkusen, and by C. H. Boehringer, Ingelheim. Leron® from Bayer contains 1,2,3,6-tetrahydro-1-(2-guanidinoethyl)-4-methylpyridine sulfate dihydrate *(1)* (generic name: cyclazenin) as active component; it is a colorless, crystalline substance, m.p. 231–233 °C; the solution in water is neutral. Leron is suitable in particular for therapy of medium to severe hypertonicity when treatment with the usual antihypertonic drugs – even in combination with salidiuretics – is insufficient.



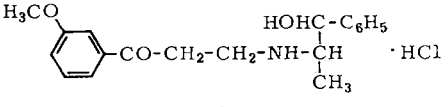
(1)

Catapresan® from C. H. Boehringer contains a new active component from the imidazoline group, namely 2-(2,6-dichloroanilino)-2-imidazoline hydrochloride *(2)*, which is readily soluble in water and alcohol. Catapresan differs both in its mode of action and in its structure from the imidazoline derivatives known hitherto, for the latter either decongest the mucous membranes (vasoconstrictors) or are strong vasodilators. It is suitable for treatment of pathological hypertension, even in advanced cases.



(2)

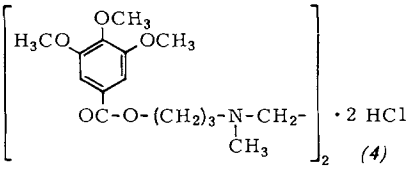
A new drug for treatment of coronary insufficiency, angina pectoris, myocardial infarction – particularly if there are also symptoms of cardiac weakness or incipient cardiac insufficiency and strengthening of the heart is desired – ildamen® from Chemiwerk Homburg, Frankfurt/M. contains as active component ω-[(β-hydroxy-α-methylphenethyl)-amino]-*m*-methoxypropiophenone hydrochloride *(3)* (generic name: oxyfedrin), m.p. 192–194 °C.



(3)

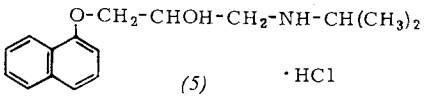
Ustimon® is a drug for strengthening the myocardium in treatment of coronary diseases; it was developed by Österreichische Stickstoffwerke, Linz, and introduced by Byk-

Gulden Lomberg GmbH., Constance. It contains *N,N'*-dimethyl-*N,N'*-bis-[3-(3,4,5-trimethoxybenzoyloxy)propyl]-ethylenediamine dihydrochloride *(4)* (generic name: hexobendin), a white, crystalline, water-soluble, bitter substance, m.p. 180 °C. Ustimon is suitable for treatment of circulatory disorders in the coronary vasicles and the myocardium, for prophylaxis and therapy of cardiac thrombosis, for treatment of postinfarction conditions, and for basic treatment of organic coronary diseases.



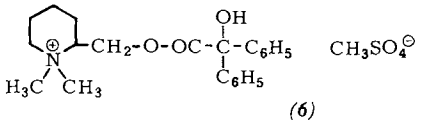
(4)

A novel product for the treatment of angina pectoris is Dociton®, produced by ICI Ltd., England, and marketed in Germany by Rhein-Pharma Arzneimittel GmbH., Heidelberg. Its active component is 1-(isopropylamino)-3-(1-naphthyloxy)propan-2-ol hydrochloride *(5)* (generic name: propanolol hydrochloride), a colorless substance, m.p. 163–164 °C, readily soluble in water and ethanol. Dociton acts by selective and reversible blocking of the β-receptors in the heart. In this way the heart is protected from the consequences of undesired sympathetic irritation (adrenalin and similar substances); the heart activity is thus economized by influencing the heart frequency, the myocardial tone, and the oxygen consumption.



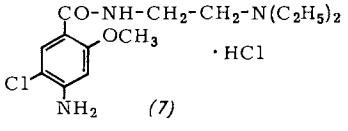
(5)

Acabel® from Chemie Grünenthal GmbH., Stolberg/Rheinland, is a new spasmolytic of the benzilic ester series. It consists of 2-(benziloylmethyl)-1,1-dimethylpiperidinium methyl sulfate *(6)* (generic name: piribenzil methylsulfate). Acabel is a parasympatholytic with marked musculotropic and neurotropic properties and is characterized by strong, rapid, and long-lasting spasmolysis and alleviation of pain with good tolerance and low dosage rates.



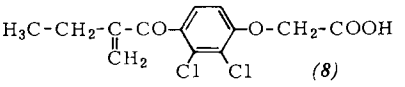
(6)

A new type of regulator for the motor function of the digestive tract, with simultaneous antiemetic action, has come on the market in the form of Paspertin® from Kali-Chemie AG., Hannover. The active component, 4-amino-5-chloro-*N*-[2-(dimethylamino)ethyl]benzamide hydrochloride *(7)* (generic name: metoclopramid), has no chemical relation to substances previously used for treatment of functional disturbances of the digestive tract and of nausea: it is a procaine amide derivative. Indications for Paspertin are nausea, vomiting, feeling of repletion, pressure on the stomach, epigastric pains, *etc.*



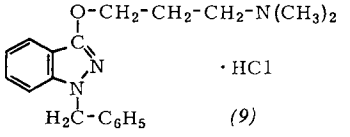
(7)

Hydromedin®, introduced by Sharp and Dohme GmbH., Munich, is a new sulfonamide-free diuretic suitable for treatment of edema at all stages and of the most varied origin. It contains [2,3-dichloro-4-(2-ethylacryloyl)phenoxy]-acetic acid *(8)* (generic name: etacrynic acid), a white, crystalline substance, m.p. about 122 °C, which is sparingly soluble in water.



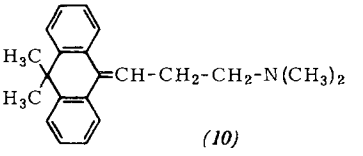
(8)

Kali-Chemie AG., Hannover, and Troponwerke, Cologne, jointly introduced the antiphlogistic tantum®. This preparation contains 1-benzyl-3-(3-dimethylaminopropoxy)-1*H*-indazole hydrochloride *(9)* (generic name: benzydamin hydrochloride) and has antiphlogistic, decongestive, and analgetic action on inflamed tissues. It is suitable for the treatment of postoperative or posttraumatic inflammations and swellings, inflammatory conditions of supporting and motor apparatus, and unspecific inflammation of the upper respiratory tract.



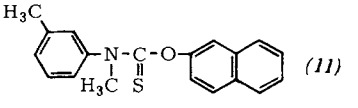
(9)

A new thymoleptic, Trausabun® from Byk-Gulden Lomberg GmbH., Constance, has both psychomotor stimulating and sedating components and consists of 9-[(3-dimethylamino)-propylidene]-9,10-dihydro-10,10-dimethylanthracene *(10)* (generic name: melitracen).



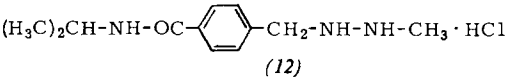
(10)

A new antimycotic has been introduced by Byk-Essex Pharmateuzische GmbH., Munich. Tonoftal® is a 1% solution of 2-naphthyl-*N*-methyl-*N*-(*m*-tolyl)thiocarbamate *(11)*, a colorless, odorless, oil-free liquid, suitable for local application in infections by *Trichophyton rubrum, Tr. mentagrophytes, Tr. tonsurans, Microsporon canis, M. audouini, Epidermophyton floccosum,* and *Malassezia furfur*; it is inactive against *Candida albicans.*



(11)

Natulan® belongs to a new class of cytostatics, the methylhydrazine derivatives. It is *N*-isopropyl-*p*-[(2-methylhydrazino)methyl]benzamide hydrochloride *(12)*, introduced by Hoffmann-La Roche AG., Grenzach/Baden. Natulan is

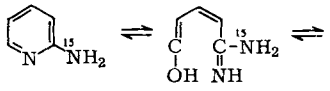


(12)

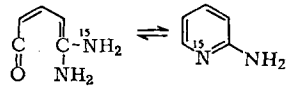
particularly suitable for treatment of lymphogranulomatosis, but successes have also been obtained against other malignant neoplasia. [VB 44 IE]

German version: Angew. Chem. 79, 102 (1967)

Reversible hydrolytic ring opening of 2-aminopyridine *(1)* was studied by *M. Wahren*. Prolonged heating of *(1)* with ^{15}N-labeled amino-nitrogen in hydrochloric acid or ammonium hydroxide results in hydrolysis to *(2a)*. Its tautomer *(2b)* provides the starting material *(1)*, with both nitrogens labeled.

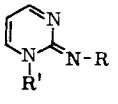


(1a) *(2a)*



(2b) *(1b)*

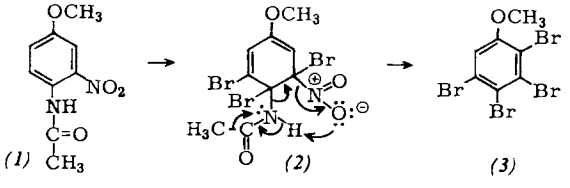
The exchange could be followed only up to about 4% of the expected equilibrium condition, because of the fast substitution of the amino group resulting in the formation of 2-hydroxypyridine. In the Dimroth rearrangement of iminodihydroheteroaromatic compounds to amino-heterocycles, an open-chain intermediate corresponding to *(2)* is also involved. For example, in aqueous sodium hydroxide 1-ethyl-1,2-dihydro-2-iminopyrimidine *(3a)* gives 2-ethylaminopyrimidine.



(3a): R = H; R' = C_2H_5
(3b): R = CH_3; R' = C_2H_5
(3c): R = C_2H_5; R' = CH_3

Interestingly, *(3b)* cannot rearrange to a stable aromatic structure, so that an equilibrium results between *(3b)* (40%) and *(3c)* (60%), as shown by *D. J. Brown, B. T. England*, and *J. S. Harper* on the basis of NMR studies. With different substituents R and R' the equilibrium lies on the side in which R in *(3)* is more bulky or a stronger electron attractant. / Z. Chem. *6*, 181 (1966); J. chem. Soc. (London) C *1966*, 1165 / –Bu. [Rd 543 IE]

The concerted elimination of an acetamido and a nitro group was observed by *C. R. Harrison* and *J. F. W. McOmie* when they brominated 4-acetamido-3-nitroanisole *(1)* in acetic acid in the presence of a little pyridine. The product, 2,3,4,5-tetrabromoanisole, m.p. 140–141 °C, previously unknown, can be isolated in 57% yield. 4-Amino-3-nitroanisole, however, is brominated as expected in the 5-position. The reaction mechanism clarifies some earlier reactions, *e.g.* the loss of an acetamido group during bromination of anilides in HBr/HNO_3.

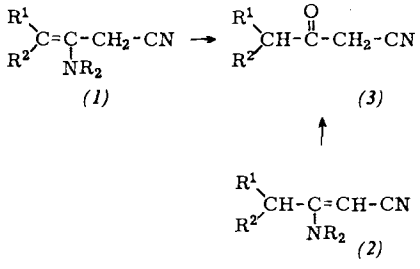


(1) *(2)* *(3)*

First *(1)* is brominated in 5-position followed by the addition of one molecule of bromine, resulting in *(2)*, which eliminates HNO_2 and methyl isocyanate and is again brominated to give *(3)*. / J. chem. Soc. (London) C *1966*, 997 / –Bu. [Rd 545 IE]

An alternative to the Sandmeyer synthesis of aromatic bromo-compounds is suggested by *J. I. G. Cadogan, D. A. Roy*, and *D. M. Smith*. Instead of adding the diazonium salt to a HBr/CuBr solution, substituted anilines can be diazotized with amyl nitrite in bromoform at 100 °C. This procedure is not suitable for chloro-compounds, as chlorine radicals are less easily abstracted. Examples: 4-bromoaniline gives 69% of 1,4-dibromobenzene; methyl 2-aminobenzoate yields 71% of methyl 2-bromobenzoate. / J. chem. Soc. (London) C *1966*, 1250 / –Bu. [Rd 546 IE]

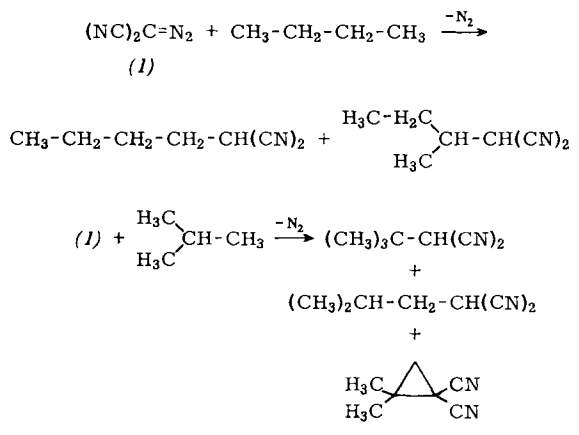
The synthesis of enamines from allenes was studied by *P. M. Greaves* and *S. R. Landor*. Amines add to 1-cyanoallenes with small alkyl substituents in a fast exothermic reaction. 1-Cyanoallenes with larger substituents must be heated with the amines. The enamines are formed in 80 to 90% yield. Addition takes place in the 1,2 or 2,3 position; diethylamine adds predominantly in the 1,2 position, and piperidine preferentially in the 2,3 position. The two types of enamines *(1)* and *(2)* do not isomerize, and evidently are formed by



(1) *(3)* *(2)*

two different routes. They can be quantitatively hydrolysed to the same β-oxonitriles *(3)*, so providing a new synthesis of these compounds. / Chem. Commun. *1966*, 322 / –Ma. [Rd 551 IE]

The reaction of dicyanocarbene, which is liberated from dicyanodiazomethane *(1)*, with alkanes, alkenes, and alkynes has been studied by *E. Ciganek*. The carbene is inserted into the primary, secondary, and tertiary C–H bonds of n-butane and isobutane in the relative ratios of 1:4.6:12. The addition of the carbene to *cis*- and *trans*-2-butenes is not stereospecific.

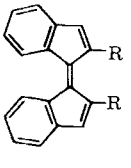


At high dilution, both isomers give a mixture of 70% of *trans*- and 30% of *cis*-2,3-dimethyl-1,1-dicyanocyclopropane. Compound *(1)* adds to alkynes to give 3,3-dicyanocyclopropenes. / J. Amer. chem. Soc. *88*, 1979 (1966) / –Ma. [Rd 552 IE]

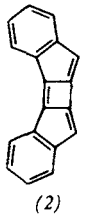
2-Pyridinecarbaldehyde oximes have been prepared by *F. A. Daniher, B. A. Hackley*, and *A. B. Ash* in a one-step reaction from 2-chloromethylpyridines and a buffered aqueous-ethanolic solution of hydroxylammonium chloride, using a method described by *S. Forman*. Examples: 5-chloro-2-chloromethylpyridine gave 63 % of 5-chloro-2-pyridinecarbaldehyde oxime (m.p. 194–195 °C); ethyl 6-chloromethyl-3-pyridinecarboxylate gave 72 % of ethyl 6-hydroxyiminomethyl-3-pyridinecarboxylate (m.p. 128–129 °C). These compounds, which could previously be obtained only by syntheses involving several steps, are precursors of *N*-methyl-2-hydroxyiminomethylpyridinium iodides, which are of interest as antidotes for poisoning by organic phosphines. / J. org. Chemistry *31*, 2709 (1966) / –Bu. [Rd 563 IE]

Trifluoromethylated and chlorodifluoromethylated 1,3,5-oxadiazines and 1,3,5-dioxazines can, according to *M. E. Hermes* and *R. A. Braun*, be obtained in good yields by condensation of hexafluoroacetone or 1,3-dichlorotetrafluoroacetone with cyanamides. For example, from hexafluoroacetone and an excess of dimethylcyanamide at 175 °C, these authors obtained 91 % of 4,6-bis(dimethylamino)-2,2-bis(trifluoromethyl)-2*H*-1,3,5-oxadiazine (m.p. 136 °C, b.p. 250 °C), while with an excess of hexafluoroacetone at 150 °C, 6-dimethylamino-2,2,4,4-tetrakis(trifluoromethyl)-4*H*-1,3,5-dioxazine is obtained as an unstable liquid in 96 % yield. The oxadiazines and dioxazines with unsubstituted amino groups (obtained from cyanamide) undergo thermal rearrangement to form dihydrotriazines and dihydrooxadiazines, e.g. 4,6-diamino-2,2-bis(chlorodifluoromethyl)-2*H*-1,3,5-oxadiazine → 4-amino-2,2-bis(chlorodifluoromethyl-1,2-dihydro-1,3,5-triazin-6-ol (m.p. 298 to 299 °C, λ_{max} = 212 mμ, ε = 2820). / J. org. Chemistry *31*, 2568 (1966) / –Bu. [Rd 564 IE]

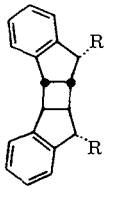
A symmetrical dibenzofulvalene (1a) was obtained by *A. G. Anastassiou, F. L. Setliff*, and *G. W. Griffin* in an (unsuccessful) attempt to prepare *(2)*. Indene was irradiated with long-wave UV light for 24 hours to obtain *syn,trans*-tuxane *(3a)*, which reacted with *N*-bromosuccinimide to form *(3b)*. Treatment of *(3b)* with potassium amide in liquid ammonia yields 27 % of biindenyl and about 2 % of *(1a)*, the structure of which was proved by analysis, NMR spectrometry, and comparison of the UV spectrum with that of *(1b)*, which was known. Unlike the parent compound fulvalene, *(1a)* is very



(1a) R = H
(1b) R = Br



(2)



(3a) R = H
(3b) R = Br

stable. (Calculated delocalization energy 6.73 β; m.p. of the gold-yellow leaflets > 300 °C). / J. org. Chemistry *31*, 2705 (1966) / –Bu. [Rd 565 IE]

L-Lysine oxygenase from *Pseudomonas fluorescens* has been crystallized by *H. Takeda* and *O. Hayaishi*. The enzyme, which catalyses the decarboxylation of lysine with oxidation, by atmospheric oxygen, to δ-aminovaleramide, has a mole-

$$NH_2-(CH_2)_4-CHNH_2-COOH + O_2 \rightarrow NH_2-(CH_2)_4-CONH_2 + CO_2 + H_2O$$

cular weight of 191 000; each molecule contains 2 molecules of flavin-adenine dinucleotide (FAD), which can be readily removed with ammonium hydrogen sulfate. The apoenzyme can be reactivated to the extent of 50 to 80 % by 10^{-6} M FAD. No iron or copper could be detected in the enzyme; the detection limits were 0.05 and 0.01 mole, respectively, per mole of FAD. / J. biol. Chemistry *241*, 2733 (1966) / –Hö. [Rd 567 IE]

Cytochrome C peroxidase from baker's yeast mitochondria has been obtained as crystals having maximum dimensions of 5×0.2×0.2 mm³ by *T. Yonetani, B. Chance*, and *S. Kajiwara*. These authors made use of the fact that the concentrated enzyme is much less soluble in distilled water than in buffer solutions. The crystallization took place during the dialysis of an approximately 0.2 mM solution in phosphate buffer against water, with the addition of seed crystals. The crystals showed no change in crystal form or loss of enzyme activity on storage for 5 hours at 23 °C in an atmosphere saturated with water vapor. Substrates such as H_2O_2, CH_3OOH, and C_2H_5OOH were absorbed by the crystals to form the enzyme-substrate complex, with no observable change in crystal form. The enzyme and the enzyme-substrate complex are isomorphous, the color merely changes from brown to red-brown. / J. biol. Chemistry *241*, 2981 (1966) / –Hö. [Rd 568 IE]

5'-Hydroxypolynucleotide kinase has been characterized and concentrated from phage-infected (T1 and T5) *Escherichia coli* by *A. Novogrodsky*. The enzyme catalyses the phosphorylation of free 5'-hydroxyl groups in polynucleotides. Nucleosides and 2'-substituted nucleosides are not phosphorylated. The phosphate donors are ATP, GTP, UTP, and CTP. The characterization of the enzyme is based on the following observations: 1. Micrococcus nuclease, an endonuclease, which produces fragments having free 5'-hydroxyl groups from DNA and RNA, increases the phosphate receptor activity of DNA and RNA. 2. Alkaline phosphatase and phosphomonoesterase split off ^{32}P-phosphate from polynucleotides that have been labeled with ^{32}P-phosphate in the 5' position by the kinase. 3. Polyriboadenylate and polyribocytidylate that have been labeled as in 2 give labeled 2'(3')-5'-adenosine diphosphate and 2'(3')-5'-cytidine diphosphate on alkaline degradation. 4. During the degradation of a polynucleotide from the 3' end (by snake venom phosphodiesterase), ^{32}P-phosphate is incorporated at the 5' end by the kinase. The kinase was also detected in rat liver cell nuclei, but not in uninfected *E. coli*. / J. biol. Chemistry *241*, 2923, 2933 (1966) / –Hö. [Rd 569 IE]

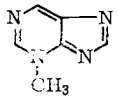
The conditions for the binding of mRNA on ribosomes have been studied by *P. B. Moore*. The experiments were carried out with ribosomes from *Escherichia coli* and with synthetic homopolynucleotides (poly-U and poly-C). The optimum magnesium ion concentration was 10^{-2} M, but Mg^{2+} could be replaced by Ca^{2+} and Mn^{2+}, and even by spermidine (polycation, 10^{-3} M). It is therefore unlikely that the cations act as complex formers. Each ribosome can bind only poly-U or poly-C, pointing to the existence of only one mRNA-binding site per ribosome. The binding of mRNA never required the presence of other cofactors such as tRNA, GTP, or the transferases. In view of the pretreatment of the ribosomes, it is very unlikely that these factors could still have been bound. / J. molecular Biol. *18*, 8 (1966) / –Hö. [Rd 570 IE]

Desensitization of fructose-1,6-diphosphatase by chemical modification has been achieved by *O. M. Rosen* and *S. M. Rosen*. The enzyme catalyses the dephosphorylation of fructose-1,6-diphosphate. It is reversibly and non-competitively inhibited by AMP, whereas the enzyme phosphofructokinase, which catalyses the reverse reaction, is activated by AMP. The inhibition by AMP is hindered (desensitization) if the enzyme is treated with 1-fluoro-2,4-dinitrobenzene in the presence of fructose-1,6-diphosphate. This is not accompanied by any

loss of activity. The desensitization is irreversible. The enzyme is irreversibly deactivated when it is treated with the fluorodinitrobenzene in the absence of fructose-1,6-diphosphate. On total hydrolysis of the enzyme after treatment with fluorodinitrobenzene, *o*-dinitrophenyl-tyrosine and ε-dinitrophenyllysine were found in equal quantities. The enzyme can be reversibly desensitized by *p*-chloromercuribenzoate or urea. / Proc. nat. Acad. Sci. USA *55*, 1156 (1966) / –Hö. [Rd 577 IE]

Evidence of the interaction between aminoacyl-tRNA and transferase I has been obtained by *F. Ibuki, E. Gasior,* and *K. Moldave.* The transfer of amino acids from aminoacyl-tRNA to peptides requires the presence, not only of ribosomes and mRNA, but also of guanosine triphosphate, a thiol, and the aminoacyltransferases I and II. The very labile transferase I is relatively stable in the reaction mixture. This stabilization is attributed entirely to the interaction with aminoacyl-tRNA, whose influence is lost on removal of the amino acid. No specificity for the tRNA species can be detected. Conversely, transferase I protects the aminoacyl-tRNA against hydrolysis. It appears that a transferase I-aminoacyl-tRNA complex is formed, in which the components stabilize each other. / J. biol. Chemistry *241*, 2188 (1966) / –Hö. [Rd 578 IE]

3-Methylpurine *(1)*, the only *N*-methyl isomer of purine that had not previously been described, has been synthesized by *B. Townsend* and *R. K. Robins.* 3-Methylpurine is of interest as a model substance for a series of naturally occurring 3-substituted purines. (Thus glycosidization of synthetic 6-dimethylaminopurine nucleosides, which are related to puromycin, takes place, not in position 7, but in position 3 of the purine). The compound *(1)* is prepared by desulfuration of 3-methyl-6-methylthiopurine in hot methanol with Raney nickel. 3-Methylpurine forms crystals having m.p. 184–185 °C (from n-heptane/benzene) and is stable for several months, but is rapidly decomposed by 1 N alkalis.



(1)

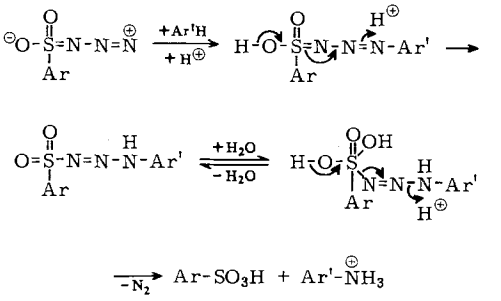
3-Methylpurine and its derivatives are more reactive than the other methylpurines, this is due to the possibility of formation of many polar structures. / J. heterocyclic Chem. *3*, 241 (1966) / –De. [Rd 590 IE]

Lean $H_2/N_2/O_2$ flames containing alkali metal have been studied spectrophotometrically at about 2000 °K by *M. J. McEwan* and *L. F. Phillips.* These authors found that considerable quantities of NaO_2 are formed as a result of the reaction

$$Na + O_2 + M = NaO_2 + M \qquad M = \text{Collision partner}$$

By measurement of the equilibrium constants of this reaction, the dissociation energy $D^0_{Na-O_2}$ was found to be 65 ± 3 kcal/mole. Potassium behaves similarly but, owing to the greater stability of KO_2, the dissociation energy could not be determined in this case. / Trans. Faraday Soc. *62*, 1717 (1966) / –Hz. [Rd 593 IE]

Acid-catalysed amination of aromatic compounds can be achieved with arenesulfonylazides, according to *G. S. Sidhu, G. Thyagarajan,* and *U. T. Bhalerao.* (The synthesis was discovered in the study of the Schmidt reaction on chromones). The following reaction proceeds in good yield (see Table) in concentrated H_2SO_4 even below 25 °C:



Ar	Ar'–NH_2	Yield (%)
C_6H_5	C_6H_5–NH_2	60–65
p-CH_3–C_6H_4	C_6H_5–NH_2	60–65
C_6H_5	*o*- and *p*-CH_3–C_6H_4–NH_2	55–60
p-CH_3–C_6H_4	*o*- and *p*-Cl–C_6H_4–NH_2	35–40

Since substituents in the nucleus of the arenesulfonylazide evidently have no influence, the authors conclude that the reaction involves direct electrophilic substitution of the substrate Ar'H by the azide $ArSO_2N_3$. / Chem. and Ind. *1966*, 1301 / –Jg. [Rd 594 IE]

BOOK REVIEWS

Gmelins Handbuch der anorganischen Chemie (Gmelin's Handbook of Inorganic Chemistry), 8th completely revised edition. Published by the Gmelin-Institut für anorganische Chemie und Grenzgebiete in der Max-Planck-Gesellschaft zur Förderung der Wissenschaften. Initiated by *R. J. Meyer*, continued by *E. H. Erich Pietsch*. Verlag Chemie GmbH., Weinheim/Bergstr.

The output of "Gmelin" for 1964 amounted to seven volumes containing a total of 3521 pages and 1078 illustrations at a total price of DM 2898; these are impressive figures, both editorially and from the point of view of price.

System No. 3: Oxygen. Vol. 6: Ordinary Water (electrochemical behavior, systems with organic solvents), isotopic varieties of water, ions of water. 1964, iv, xxiii, 364 pp. with 60 illustrations. Cloth DM 278.–. Revised by *Anna Bohne-Neuber, Erna Brennecke, P. Koch, Margarete Lehl-Thalinger, Gertrud Pietsch-Wilcke.*

The present Vol. 6 continues the description of the compounds of oxygen started in Vol. 5 (1963) [*]. In accordance with the "Gmelin principle", the only compounds of oxygen are water and hydrogen peroxide.

The chapter on ordinary water is first concluded with two sections "Electrochemical behavior" (17 pp.) and "Systems with organic solvents" (70 pp.). In the former, particular attention is given to the specific conductance of natural and distilled water and to the electro-kinetic phenomena occurring in liquid water. The second presents a general review of the behavior of mixtures of organic solvents with water, particularly from the point of view of phase theory, the discussion being confined to a few particularly important solvents (benzene, methanol, ethanol, diethyl ether, dioxane, acetic acid).

Most (about $^2/_3$) of this volume deals with the isotopic varieties of water (237 pp.). Corresponding to the three hydrogen isotopes ^1H = H, ^2H = D, and ^3H = T and the three oxygen isotopes ^{16}O, ^{17}O, and ^{18}O, there are 18 possible varieties of water. Of these, only "heavy water" D_2O (O =

[*] Cf. Angew. Chem. *76*, 930 (1964).; Angew. Chem. internat. Edit. *3*, 710 (1964)

natural mixture of oxygen isotopes), together with HDO, which is always present in mixtures with H_2O but is unstable in the pure liquid phase, is of any practical importance; consequently, 205 pages (more than $^6/_7$) of this chapter are devoted to D_2O and HDO, while the remaining 32 pages deal with the other varieties of water, special attention being given to the heavy water $H_2{}^{18}O$ and the super-heavy (radioactive) water T_2O. Special mention should be made of the data on the formation of D_2O (and HDO) from H_2O by nuclear reaction, by synthesis from the elements, and by isotope exchange between water and hydrogen and between water and hydrogen compounds, on the concentration and purification of D_2O on the laboratory and industrial scales – electrolytic dissociation of water, fractional distillation of water and of hydrogen, isotope exchange between hydrogen, hydrogen compounds (hydrogen sulfide, mercaptans, ammonia, cyclohexane, benzene) and water, with discussion of the fundamental principles and illustrations of apparatus –, on the physical and chemical properties of D_2O and HDO, on the behavior of heavy water as a solvent, and on the analysis of heavy water.

The last chapter, "Ions of water" (40 pp.) deals with the H_3O^+ and OH^- ions, including their hydrated and deuterated forms.

The literature is fully covered up to the end of 1949, and further references are cited to bring the literature up to the present, though these references are not exhaustively utilized in every case. The System No. "Oxygen", including the present volume, now covers 2096 pages and contains 372 illustrations (total price DM 1311.–).

System No. 16: Phosphorus. Part B: Technology, physiological damage, the element. 1964, iv, xxx. 458 pages with 32 illustrations. Cloth DM 350.–. Revised by *M. Atterer, Vera Haase, G. Hantke, A. Hirsch, G. Kirschstein, H. K. Kugler, A. Kunze, Gertrud Pietsch-Wilcke, K. Rumpf, F. Seuferling, Ph. Stiess, Hildegard Wendt.*

The present Part B is the first volume of the 8th edition on the important element phosphorus, which has not been revised since the (385 pp.) corresponding volume of the last edition (1911). It deals with the technology of phosphorus and phosphoric acid (86 pp.), physiological damage due to phosphorus and its compounds (11 pp.), and elementary phosphorus (361 pp.).

The chapter "Technology" is concerned in particular with the methods for the wet decomposition and thermal reduction of crude phosphates, and for the oxidation of phosphorus, the working-up (purification, concentration) of technical phosphoric acid, the production of white phosphorus, and its conversion into the red form.

The section "Physiological damage" deals with damage (*e.g.* burns, poisoning) by white phosphorus and phosphorus compounds (phosphine, phosphoric acids, phosphorus halides, phosphorus sulfides, radioactive phosphorus).

Most (80 %) of the volume is devoted to elementary phosphorus. Following a brief note (6 pages) on general properties, position in the periodic table, valence, and atomic weight, the formation and preparation of the element in the laboratory are d scussed (4 pp.). In view of the growing scientific and practical importance of the radioactive isotopes ^{32}P (half-life 14.3 days) and ^{33}P (half-life 25.0 days) over the last few decades, the formation, concentration, and separation of these isotopes, as well as the classification of the phosphorus isotopes in general, are reported at length (53 pp.). The sections on the atom and atom-ions, molecules and molecule-ions, and forms of phosphorus report in detail (72 pp.) on the properties of the atom in the ground and excited states (optical spectra, X-ray spectra, absorption and scattering of X-rays and γ-rays), the interactions in the valence activity of phosphorus, the P_2 and P_4 molecules, and the transitions between the white, red, violet, and black forms of phosphorus. In the chapter on physical properties (26 pp.), the macrophysics of elementary phosphorus is subdivided in the usual manner according to physical states and modifications. The chapter on chemical behavior (80 pp.), contains particularly interesting notes on the behavior of white phosphorus towards light, heat, and oxygen, on the reactions of phosphorus with acids, non-metals, compounds of non-metals, metals, and compounds of metals, and on the solutions of phosphorus in inorganic and organic solvents. Detailed data are also given in the chapter "Detection and determination" (120 pp.). Since the volumes of *Fresenius-Jander*'s handbook of analytical chemistry dealing with the qualitative (1956) and quantitative (1953) analysis of phosphorus have already been published, this chapter is confined to period between about 1950 and the end of 1960.

The present Part B, which contains numerous illustrations and (in keeping with the practice followed for some years) has German/English indices and marginal notes in English, was followed by two further volumes in 1965; these will be reviewed in the future.

System No. 19: Bismuth. Supplement 1964, iv, lviii, 866 pages with 212 illustrations. Cloth DM 652.–. Revised by *Hildegard Banse, Elisabeth Bienemann-Küspert, G. Czack, H. Engst, Inge Flachsbarth, H. Golder, Eleonore Kirchberg, G. Kirschstein, Marie-Luise Klaar, K. Koeber, Imberta Leitner, Ellen von Lindeiner-Schön, Wolfgang Müller, Gertrud Pietsch-Wilcke, N. Polutoff, H. Rieger, K. Rumpf, W. Schaffernicht, P. Schubert, F. Seuferling, Hildegard Wendt.*

The present supplement to the 229-page principal volume "Bismuth", which appeared in 1927, covers literature published up to the end of 1960, and deals in the usual manner with the occurrence of bismuth, physiological damage due to bismuth, elementary bismuth, and the compounds of bismuth.

The occurence of bismuth, which covers only a few pages in the principal volume, is now subjected to a new and lengthy discussion (153 pp.), which is subdivided as usual into the sections extraterrestrial occurrence, geochemistry, topography, and minerals.

Following a few data on physiological damage due to elementary bismuth and its compounds (8 pp.), the main chapter (more than half of the text) contains a description of elementary bismuth (460 pp.). This part begins with short discussions (3 pp.) on the position of bismuth in the periodic table, its valence, and its atomic weight, and then goes into details of the formation and preparation of the element (46 pp.). This section deals with the technology of bismuth (working-up of the crude material, isolation of the metal from bismuth ores, purification of crude bismuth and reactor bismuth, preparation of pure bismuth, purity testing, use) as well as with the preparation of special forms of bismuth (particularly colloidal solutions, thin layers and films, single crystals). In the discussion of the physical properties (251 pp.), the handbook takes the modern development into account, and deals with the properties of the atomic nucleus, the atom, the atom-ions, the molecule and the molecule ions (total 98 pp.) separately from those of the bulk metal (153 pp.). Thus this chapter begins with a description of the 18 known bismuth isotopes (the natural isotopes ^{209}Bi, ^{210}Bi (RaE), ^{211}Bi (AcC), ^{212}Bi(ThC), and ^{214}Bi (RaC) being discussed together with all the other nuclides, in contrast to the principal volume), and the formation, concentration and separation, the decay and nuclear reactions of the bismuth isotopes, and the behavior of Bi activities in practically weightless quantities are discussed. This is followed by data on the arc and X-ray spectra of the bismuth atom, the absorption, scattering, and reflection of X-rays and γ-rays, positive and negative bismuth ions, and the Bi_2 molecule and the Bi_2 anion. The section on bulk bismuth begins with data on the one-component system bismuth (constitution diagram, vaporization and condensation, latent heats), and then proceeds in the usual manner with a discussion of the macrophysics of bismuth, which concentrates largely on the structural-crystallographic, mechanical-thermal, and electric-magnetic properties, and on

the electrochemical behavior (potentials, cells, behavior as electrode, electrolytic deposition of bismuth from solutions and melts).

The chapter on the chemical behavior (40 pp.) also takes into account the investigations (behavior of the melt towards metals, alloys, and other reactor materials) carried out in recent years in connection with the use of molten bismuth in reactor technology. The survey of the chemical behavior of the bismuth ion is also valuable. The chapter on the detection and determination of bismuth (99 pp.) follows the chapters on the qualitative (1956) and quantitative (1951) analysis of bismuth in *Fresenius-Jander*'s handbook of analytical chemistry, and deals mainly with the literature published between 1950 and the end of 1960. In accordance with the Gmelin principle, the only alloys of bismuth discussed are the Bi/Sb alloys (21 pp.).

In accordance with the same principle, the bismuth compounds discussed (245 pp.) are those with hydrogen, oxygen, nitrogen, halogens, chalcogens, boron, carbon, silicon, phosphorus, arsenic, and antimony. The sections on bismuth halides and chalcogenides are particularly detailed, and account for 80 % of the chapter.

With the present bismuth volume, there is now available a complete, up to date description of the elements of Group V of the periodic system.

System No. 21: Sodium. Supplement, Vol. 1: Technology of sodium and its compounds. 1964. iv, xxiv, 399 pages with 35 illustrations. Cloth DM 304.–. Revised by *K. Beeker, E. Best, H. Bitterer, G. Hantke, A. Hirsch, H. K. Kugler, A. Kunze, F. Plessmann.*

The present Vol. 1 of the supplement to the 992-page principal volume "Sodium", which appeared in 1928, deals with the technology of sodium and its compounds, the literature up to and including 1960 being fully covered. The volume clearly shows the development trends during this period.

In the isolation of metallic sodium, the transition from the electrolysis of molten sodium hydroxide (Castner method) to that of molten sodium chloride (Downs method) has been almost completed: in 1925, 75 % of the world production (15240 t) were still produced by the Castner method, while in 1957, 98 % of the world production, which had increased in the meantime by a factor of more than ten (203708 t) were produced by the Downs method.

The process that was formerly almost exclusively used for the preparation of sodium hydroxide solution, *i.e.* the calcination of soda, has been largely replaced by the electrolysis of sodium chloride solutions, particularly by the amalgam process; the chlorine, which was occasionally regarded as an undesirable by-product, is steadily becoming the principal product (with a resulting over production of NaOH).

The section on the production of sodium nitrate deals *inter alia* with the Guggenheim process of cold-leaching of caliche, which had to be adopted during the 1930's because of competition from synthetic saltpeter.

The description of the production of sodium chloride contains interesting sections on modern flotation processes, advances in the preparation, purification, and concentration of brines, and controlled crystallization. The section on sodium salts of the oxo acids of chlorine reports *inter alia* on the production of dilute sodium hypochlorite solutions (mainly used for the bleaching of paper and textiles), the preparation of sodium chlorite (introduced around 1940 as a bleach for fibers and textiles), and progress in the electrochemical isolation of sodium chlorate (which is important as an oxidizing agent) and of sodium perchlorate (used as an intermediate in industrial inorganic chemistry).

Most of the section on sodium sulfide is devoted to the classical method of reduction of sodium sulfate with coal. In the section on sodium salts of oxo-acids of sulfur, mention should be made of the notes on the regeneration of sodium sulfite from cellulose brines, on the production of sodium sulfate from brines, and on the technology of sodium thiosulfate and sodium dithionite.

The description of the large-scale production of $NaBH_4$, which is finding increasing use as a selective reducing agent and as a starting material for the production of boranes, is particularly interesting.

The discussion of the production of soda shows the extensive development, both theoretical and practical, of the Solvay process. The section on the technology of sodium cyanide deals mainly with progress in the Castner process (preparation from ammonia, sodium, and coal) and in the Bucher process (preparation from atmospheric nitrogen, soda, and coal).

The section on the preparation of sodium silicate (water glass) describes, not only the method normally used at present, *i.e.* fusion of the raw materials and dissolution of the product, but also the numerous suggestions for production by a wet process.

An important section in the description of the technology of sodium phosphates deals with the condensed sodium phosphates, which have grown in importance since about 1925, and which now account for more than 75 % of the total phosphate output.

The section on the peroxo compounds of sodium deals in particular with sodium peroxide, sodium peroxosulfate, and the peroxohydrates of sodium borate, carbonate and phosphate.

A final section discusses physiological damage due to sodium and sodium compounds (working hazards in the production and use of metallic sodium, sodium hydride, oxide, peroxide, hydroxide, amide, *etc.*, radioactive sodium). Volume 2, which was published in 1965, will be reviewed later.

System No. 58: Cobalt. Supplement, Part B, Vol. 2: Complex compounds of trivalent cobalt. 1964, iv, xxxix, 507 pages with 71 illustrations. Cloth DM 471.–. Revised by *K.-Chr. Buschbeck, H. Feicht, R. Gagarin, Ursula Hettwer, G. Krause, Irmingard Kreuzbichler, H. Lehl, W. Schaffernicht, (the late) G. Schleitzer, Edith Schleitzer-Steinkopf.*

The present Vol. 2 completes the supplement to the principal Vol. B of the System No. "Cobalt", the 314-page Vol. 1 (Complex compounds of mono- and bivalent cobalt) having appeared a year earlier.

The volume is divided into two parts: Part 1 (317 pp.) deals with the complex Co(III) compounds with normal bonding of the ligands, and Part 2 (142 pp.) with complex Co(III) compounds with inner-orbital bonding of the ligands. The volume is introduced by three pages on taxonomy, configuration notation, and the *trans*- and *cis*-effect, and concludes with a 45-page appendix containing addenda, a list of abbreviations for commonly-occurring ligands, and a particularly welcome formula and alphabetic index of the organic complex formers occurring as ligands and addends in the principal volumes Cobalt A (1931/32) and Cobalt B (1930) and in the two corresponding supplements A (1961) and B (1963/64).

Part 1 of the text, which is divided into mononuclear and polynuclear complexes, begins the section on mononuclear complexes (297 pp.) with compounds of the hexammine type $[CoA_6]^{3+}$ (86 pp.) having six (similar or dissimilar) neutral ligands A. Corresponding to the coordination number 6 of cobalt, this is followed by complexes of the pentammine type $[CoXA_5]^{2+}$ (74 pp.) having one acid ligand X, the tetrammine type $[CoX_2A_4]^{+}$ (108 pp.) having two, the triammine type $[CoX_3A_3]$ (14 pp.) having three, the diamminecobaltate(III) type $[CoX_4A_2]^{-}$ (14 pp.) having four, and the monoamminecobaltate(III) type $[CoX_5A]^{2-}$ (1 p.) having five (similar or dissimilar) acid ligands X[**]. In the section on polynuclear complexes (20 pp.), the discussion starts with dinuclear cobalt(III) compounds having one, two, and three bridge

[**] The cobaltates(III) of the type $[CoX_6]^{3-}$ having six acid ligands X were described earlier in Supplement A (1961).

bonds, and then proceeds *via* the tri- and tetranuclear complexes to the polymeric polynuclear compounds. The discussion covers not only the preparation and the physical and chemical properties of the various complexes, but also questions relating to the stereoisomerism of such compounds with optically inactive and optically active ligands; very complicated situations occasionally arise in the latter case (*e.g.* eight stereoisomeric forms of tris(propylenediamine)-cobalt(III) complexes $[Copn_3]^{3+}$).

Part 2 deals with cobalt(III) complexes with inner-orbital bonding of the complex formers, (*e.g.* porphyrins, amino acids, ethylenediaminetetraacetic acid, dimethylglyoxime), *i.e.* simultaneous bonding to the cobalt by neutral and acid groups of the ligands. The complexes in this part are grouped, not according to complex types, as in Part 1, but according to ligands, by analogy with the arrangement of Vol. 1 of Supplement B. Special mention should be made of the cobalt complexes with α-amino acids and peptides (with their isomerism and optical activity), the complexes with ethylenediaminetetraacetic acid (which have recently been studied to an increasing extent, and in which the ligand may be hexa- and pentadentate), and the complexes with Schiff bases, with dimethylglyoxime (*Chugaev*'s reagent), with biguanide and its derivatives, and with cysteine.

The literature is fully covered up to the end of 1949, with extensive supplements for the period 1950 to 1960 taking into account developments up to the present time. With the present volume, the System No. "Cobalt" now contains 2585 pages and 342 illustrations, and costs a total of DM 1718.–. Alloys containing cobalt are described in System No. 59 "Iron", Part D, 2nd Supplement (magnetic materials).

System No. 59: Iron. Gmelin-Durrer: Metallurgy of iron, 4th completely revised edition, Vol. 1: Historical, definitions, general physicochemical principles, thermal pretreatment of iron ores (at the same time supplement to the principal volume "Iron", Part A, Vols. 3 to 5). Vol. 1a: 1964, iv, vii, xxii, 583 pages; Vol. 1b: 1964, iv, 344 pages with 668 illustrations. Cloth, total DM 843.–. Revised by *F. Cappel, E. Franke, B. Ilschner, W. John, H. Meiler, K. Meyer, H. Rausch, F. Rex, Brigitte Schenkel, G. von Struve, H. Viereck, Hertha Winkler.*

With the present Vol.1 of the 4th edition of "Gmelin-Durrer", the Gmelin-Institut resumes the discussion of the wide topic of the metallurgy of iron, which was started in the 1st edition in 1933, and which has now been expanded to four volumes. The work also represents a supplement to Vols. 3 (1930), 4 (1932), and 5 (1933) of Part A of the Gmelin principal volume "Iron", which also deals with the metallurgy of iron. As a deviation from the practice previously followed, each of the four volumes planned is subdivided into a text volume (a) and an illustration volume (b), since the number of illustrations is so large (in Vol. 1, for example, there are 668 illustrations to 583 pages of text) that they could not be conveniently arranged in the text.

Vol. 1, in which the state of knowledge is described by four Gmelin authors and eight outside experts, is characterized in that each complete field is preceded or followed by a survey containing no references, so that this work is not simply an exhaustively revised handbook, but also an orientating textbook.

Following short general notes (13 pp.) on the history and definitions of "iron" and "steel", a 16 page chapter first discusses the physicochemical principles of the processes used in ironworks, dealing on the one hand with the "states" (thermodynamic concepts and designations, thermochemical values relating to the metallurgy of iron, the structure of the liquid metals and slags, phase-boundary equilibria), and on the other with "processes" (fundamentals of the kinetics of metallurgical processes, diffusion in liquid metals and slags, viscosity of liquid metals and slags, special problems in reactions with porous solids and in reactions of gases with solid fuels and reducing agents). In this discussion, the special case of iron often takes second place to the general problem, *e.g.* of the liquid state, the binary system, the diffusion-controlled process, since wherever data for iron are not yet available, results obtained with other substances and systems are considered.

The following 405-page main part (70 % of the text volume) is devoted to the thermal pretreatment and the lumping of ores. The thermal pretreatment is deliberately restricted to preparation in the narrower sense, *i.e.* to the drying of ores and their calcination and magnetizing roasting; the general principles, the furnaces and equipment, their operation, the operating data, and the thermal energy balances are discussed in all three cases. The subsequent discussion of the lumping of ores deals with briquetting (general considerations, briquettes with and without fuel and binder, industrial briquetting procedure), extrusion (fundamental data, extrusion procedure), sintering (processes in sintering, influence of variables, behavior of the accessory elements, additives, special processes, sintering apparatus), pelletizing (general principles, production of pellets, firing of the pellets, fire aggregates), and the binding of iron ore by coking with coal (production of iron coke, other binding processes).

The text volume 1a is accompanied by an illustration volume 1b, the figures of which impressively illustrate the discussions in the text volume. This Volume 1b, contrary to the usual practice, contains a detailed subject index in German and English covering 166 pages, and including about 7000 subjects, as well as the 22-page content index. This is particularly useful, since the extremely wide range of aspects considered cannot be presented to the user by the content index. The next three volumes will also contain a subject index of this type.

On the whole, the seven volumes of "Gmelin 1964" reviewed here again represent an imposing output by the Gmelin editorial staff, which is attempting to increase the speed of reporting in future by new information methods. We must await with keen anticipation the planned "Rapid Information", which will analyse the original publications for all substances and subjects mentioned in the original (and not only in its title), and make these available to the user a few weeks after its publication. *E. Wiberg* [NB 537 IE]

Katalytische Hydrierungen im Organisch-Chemischen Laboratorium (Catalytic Hydrogenation in the Organic Chemistry Laboratory). By *F. Zymalkowski.* Ferd. Enke Verlag, Stuttgart 1965. 1st ed., viii, 360 pp., 15 illustrations, paper DM 80.–, cloth DM 86.–.

The book provides a survey of the methods of catalytic hydrogenation. The first, general section contains a detailed description of the methods and of hydrogenation catalysts, the industrial processes being deliberately excluded. The comprehensive special section deals with the use of catalytic hydrogenation, the material being arranged according to reduction steps. The possibilities and limitations of the method are illustrated with the aid of numerous characteristic examples. Considerable space is given to the discussion of the sterio course of the hydrogenation. Numerous procedures are interspersed in the text, so that this book is a particularly successful combination of a monograph and a laboratory handbook. The value of the book is enhanced by more than 1000 well-chosen references. The book fills a gap in the German literature, and should be of great value to all preparative organic chemists. Its purchase can be wholeheartedly recommended. *H. Stetter* [NB 513 IE]

Analgetics, Chemistry and Pharmacology. Vol. 5 of the series: Medicinal Chemistry. Edited by *G. de Stevens.* Academic Press, New York-London 1965. 1st edit., viii + 475 pp., numerous figs., $17.–.

Three years have elapsed since the appearance of the first volume in this series, and during that time it has earned a

secure place in the technical literature. In distinction from other series, the individual volumes treat large areas of drug research in the form of monographs and offer the reader a comprehensive review. The fifth volume is also written in this way: eight chapters deal with an introduction (I), the physiology and pharmacology of pain and its treatment (II), clinical measurement of pain (III), morphine and its derivatives (IV), synthetic analgetics with morphine-like action (V), isoquinoline analgetics (VI), pyrazole derivatives (VII), and synthetic analgetics in general (VIII), as well as the most important aspects of analgetics in respect of general relationships.

In an introduction *A. Burger* gives an excellent review of the historical development and present trends of analgetics research.

The second chapter (*C. A. Winter*) gives a clear and comprehensive account of the physiology and pharmacology of pain. The pharmacological and clinical testing of analgetics continues to pose numerous problems; *Winter*'s review and the next chapter by *R. W. Houde, S. L. Wallenstein,* and *W. T. Beaver* on the clinical apprehension of pain provide the active researcher with valuable help towards further progress.

The other five chapters deal with chemical aspects of the individual groups of analgetics. *E. L. May* and *L. J. Sargent* treat morphine and its derivatives; in this, the oldest area of analgetics research, the repetition of much that has been included in other reviews was unavoidable. Synthetic analgetics with morphine-like action (*R. A. Hardy jr.* and *M. G. Howell*) and isoquinoline analgetics (*A. Brossi, H. Besendorf, L. A. Pirk,* and *A. Rheiner*) form topical subjects whose presentation is very welcome. *W Krohs*, the author of the monograph "Pyrazolone und Dioxopyrazolidine gives a very good, brief survey of pyrazole derivatives which however could be equally ob ained from his book. Finally, the editor treats synthetic compounds with analgetic action in general at the end of the special part of the book. This last chapter gave the reviewer particular pleasure; it is brief and clear, introduces much new material, and will certainly be stimulating to those working in the field.

In summarizing, it may be stated that the monograph "Analgetics" is successful. Pharmacological, physiological, clinical, and chemical aspects are equally well treated, and the book will surely remain the best review of analgetics for a long time. The reviewer warmly recommends it to all interested chemists, biochemists, pharmacologists, physiologists, and clinicians, congratulates the editor on a valuable contribution to the literature on drug research, and wishes this series the success that it deserves.

E. Jucker [NB 502 IE]

Modern Textbook of Organic Chemistry. By *G. P. Ellis.* Butterworth & Co. Ltd., London 1966. 1st Edit., xii + 466 pp., numerous illustrations, bound, £ 2/17/6.

The aim of the present textbook is to point out the relationships in organic chemistry and reduce the amount of pure learning involved.

An introduction deals with chemical bonds, the principal types of reactions, and the fundamentals of spectroscopy (UV, IR). In the subsequent chapters, the usual subdivision of material into aliphatic and aromatic compounds is dropped in favor of subdivision by functional groups. The book starts with hydrocarbons, grouped into alkanes, cycloalkanes, alkenes, cycloalkenes, alkynes, and aromatic hydrocarbons, then proceeds to halogen compounds, alcohols and phenols, ethers, and aldehydes, emphasis being placed on the influence of the ligand (*e.g.* aliphatic and aromatic) on the functional group. This is followed by chapters on stereochemistry, carboxylic and sulfonic acids and their derivatives, nitro and nitroso compounds, amines and diazo compounds, amino acids, carbohydrates, and heterocyclic compounds.

Each chapter is subdivided into a general introduction and sections on nomenclature, bonding problems, UV and IR spectra (with illustrations), general reactions, and methods of preparation, as well as a discussion of some important specific compounds. Problems are given at the end of each chapter. A pleasing feature, particularly in the case of heterocycles, is the inclusion of summaries of the reactions of various compounds.

As a whole, the book gives a very unfinished impression and contains many errors. On page 14, for example, enolization is indicated as a hydride shift, and on page 229 the author describes a mechanism for the Cannizzaro reaction that corresponds to the fourth-order rate equation, which is observed in only a few cases. The aldehyde group here carries a dot whose meaning is obscure. The use of symbols, in fact, is somewhat confusing throughout. A dot is used in one case for a single electron in free radicals (p. 19), and then a few pages later for a pair of electrons (p. 21, chloroacetic acid). The manner in which, *e.g.*, the nitration of benzene is represented on p. 17 is questionable. An entire side chain is omitted from vitamin B on page 405.

A book claiming to be modern should discuss nuclear magnetic resonance spectra as well as IR and UV spectra. Mention of the Cahn-Ingold-Prelog rules in the discussion of stereochemistry would also have been desirable. As would the use of more energy-level diagrams in the discussion of reaction mechanisms.

The overall approach of the book is very welcome, but it would have to be thoroughly revised before it could really be recommended.

H. J. Bestmann [NB 541 IE]

Sulfonation and Related Reactions. By *E. E. Gilbert.* Interscience Publishers, a Division of John Wiley & Sons Ltd., London 1965. 1st ed., xi, 530 pp., 1 illustration, 71 tables, cloth, £6.6.0.

The author, *E. E. Gilbert*, an employee of Allied Chemical Corp., has for some time been well known to those interested in this field as a result of his experimental papers and reviews (cf., *e.g.*,"The Reactions of Sulfur Trioxide and of its Adducts with Organic Compounds" in Chemical Reviews *62*, 549 (1962)). The book is intended to follow on from *C. M. Suter*'s book "The Organic Chemistry of Sulfur", which covers the literature in this field up to 1941.

The book is divided into eight chapters. The first describes the reagents used for the sulfonation and sulfation of organic compounds, while the second chapter deals with the sulfonation of aliphatic, aromatic, and heterocyclic compounds with the compounds described in the first chapter.

The introduction of the sulfo group into organic compounds of various classes by means of sulfur dioxide, *e.g.* in the sulfochlorination and sulfoxidation of aliphatic compounds, or by means of bisulfites, *e.g.* in the Strecker synthesis or the addition of bisulfites to olefins, is reported in the third chapter.

The next chapter deals with the oxidation of organic compounds containing sulfur with formation of sulfo compounds. Indirect methods for the sulfonation of organic compounds, such as sulfoalkylation or sulfoarylation, are described in Chapter 5. The sixth chapter is concerned with sulfation, *i.e.* the preparation of compounds with sulfur joined to carbon *via* oxygen (esters of sulfuric acid and their derivatives). *N*-Sulfonation and desulfation, *i.e.* the reverse of sulfonation, are described in the last two chapters.

The individual sections of the book are characterized by a clear presentation of the material discussed. Evidently, this work was written by an outstanding authority with very wide knowledge and great practical experience. The literature (up to mid-1964) is adequately covered by about 3000 references. The book, which closes a gap in the literature on sulfonation and related reactions, can be wholeheartedly recommended to all those interested in this field.

F. Asinger [NB 510 IE]

The Structure of Small Molecules. By *W. J. Orville-Thomas.* Series of monographs: Principles of Modern Chemistry. Elsevier Publishing Company, Amsterdam-New York 1966. 1st ed., vii, 189 pp., 55 illustrations, bound, Dutch fl. 26.–

This book is the first of a series of monographs intended to serve as a basis for a one-semester course of two lectures a week.

The volume is specially concerned with the use of quantum-chemical concepts to obtain an understanding of the electronic structure and bonds in "small" polyatomic molecules, *i.e.* those containing up to about 5 atoms. Though this is a very narrow selection from the entire field of application of quantum chemistry, it is justified methodically. The models suitable for these molecules, with their wide range mcom position and geometry, indeed are different from those used *e.g.* for the rather uniform group of the planar aromatic hydrocarbons.

The treatment is aimed at chemists. The *Hückel* version of the molecular orbital method (HMO method) is used. A short introduction is followed by sections on the basic concepts of the chemical bond and the properties of such bonds (bond lengths, angles, and energies, force constants, and bond moments) and another section giving a survey (though only rudimentary) of quantum mechanics. This is followed by a section on stereochemistry and its quantum-chemical interpretation, and a final chapter (which in the reviewer's opinion is the most interesting) on the electronic structures of a large number of individual molecules, organized on the basis of a theoretical ordering principle. The substance index is also very useful.

The book is not very suitable as an introduction to quantum chemistry as a whole, nor is it intended as such. However, it does provide a source of information on the numerous molecules with which it deals.

W. A. Bingel [NB 521 IE]

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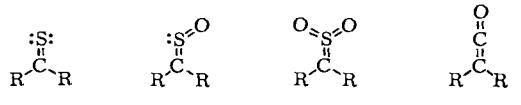
Sulfines and Sulfenes — the *S*-Oxides and *S,S*-Dioxides of Thioaldehydes and Thioketones

BY G. OPITZ [*]

Four sulfines have so far been prepared by elimination of HCl from sulfinyl chlorides with triethylamine and by oxidation of diaryl thioketones with peracid. They are colored, crystalline compounds, which slowly decompose at room temperature. Attempts to prepare sulfenes have not yet been successful, but mesylsulfene [1] has been isolated as the trimethylamine adduct. It can be shown by interception reactions that sulfenes are formed as intermediates by the action of trialkylamines on aliphatic sulfonyl chlorides and by the action of sulfur dioxide on diazoalkanes. They react with ROD to form monodeuterated sulfonates, with diazoalkanes to give three-membered rings, with enamines, dienamines, ketene O,O-, O,N-, and N,N-acetals, and chloral, and in some cases with vinyl ethers, to give four-membered rings. They also react with nitrones to give five-membered rings, and with β-aminovinyl ketones and dienamines to give six-membered rings.

A. Introduction

Sulfines are the *S*-oxides and sulfenes [2] the *S,S*-dioxides of thioaldehydes and thioketones. They are formally the inner anhydrides of sulfinic and sulfonic acids respectively, just as ketenes are inner anhydrides of carboxylic acids. *S*-oxides and *S,S*-dioxides of thiocarboxylic acid derivatives such as chlorides or amides are not regarded as sulfines or sulfenes.



Alkylidene	sulfide	sulfoxide	sulfone	ketone
Inner anhydride of a	sulfenic acid	sulfinic acid	sulfonic acid	carboxylic acid
Usual name	thioketone (or thioaldehyde)	sulfine	sulfene	ketene

Sulfines (like sulfinic acids and dialkyl sulfoxides) have a lone pair of electrons on the S atom, whereas in the sulfenes (as in sulfonic acids and dialkylsulfones), all the electrons of the S atom are involved in bonding. Sulfenes are derivatives of sulfur trioxide, and sulfines are derivatives of sulfur dioxide, one O atom in each case being replaced by an alkylidene group.

Wedekind and *Schenk* [3] first used the name sulfenes to express the relationship [4] to the ketenes. This was formally logical, but it precluded the possibility of using endings to indicate the state of oxidation, as is usual with the acids (sulfenic, sulfinic, sulfonic acids). Nevertheless, *Sheppard* and *Diekmann* [5] chose the name sulfines for alkylidene sulfoxides [6].

[*] Prof. Dr. G. Opitz
Chemisches Institut der Universität Tübingen
Wilhelmstrasse 33
74 Tübingen (Germany)

[1] The following abbreviations are used: mesyl chloride/NEt_3 = methanesulfonyl chloride in the presence of triethylamine; tosyl = *p*-toluenesulfonyl; NMe_3–HCl = trimethylammonium chloride; THF = tetrahydrofuran; DMF = dimethylformamide.

[2] *T. J. Wallace*, Quart. Rev. (chem. Soc., London) *20*, 67 (1966).

[3] *E. Wedekind* and *D. Schenk*, Ber. dtsch. chem. Ges. *44*, 198 (1911).

[4] *H. Staudinger*: Die Ketene. F. Enke, Stuttgart 1912, pp. 92, 129.

[5] *W. A. Sheppard* and *J. Diekmann*, J. Amer. chem. Soc. *86*, 1891 (1964).

[6] In this paper sulfines and sulfenes are named generally as derivatives of sulfine (CH_2=SO) and sulfene (CH_2=SO_2), by analogy with the ketenes, and occasionally as oxides or dioxides of thioaldehydes or thioketones. If the C atom of the CH_2 group forms part of a ring, the groups =SO and =SO_2 should be designated by the prefixes "sulfinyl" and "sulfonyl", respectively. Thus *(5)* is called 9-sulfinylfluorene. This suggestion is based on the rule for ketenes (=CO = carbonyl when the CH_2 group forms part of a ring).

The differences between carbonyl and thiocarbonyl groups are explicable on the basis of differences in polarizability, size, and electronegativity of the heteroatoms [7] (Table 1).

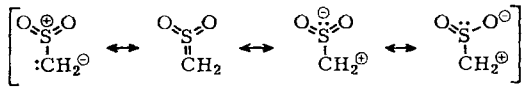
Table 1. Electronegativity according to

	Pauling	*Mulliken*	*Allred* and *Rochow* [8]
C	2.60	2.63	2.50
O	3.50	3.17	3.50
S	2.60	2.41	2.44

With its relatively strong 2p-2p π bond the carbonyl group is strongly polar but difficult to polarize; most aldehydes and ketones are stable in the monomeric form. The thiocarbonyl group with its more diffuse 2p-3p π bond is weakly polar, but easily polarizable; all thioaldehydes and most thioketones are unstable, mainly because of their pronounced tendency to di-, tri-, and polymerize. That carbonyl and thiocarbonyl groups react differently with sodium hydrogen sulfite, zinc and hydrochloric acid, diazomethane, and sodium acetylide [9] suggests that the S atom may even carry a partial positive charge:

$R_2C^{\delta\oplus}=O^{\delta\ominus}$; $R_2C^{\delta\ominus}=S^{\delta\oplus}$

What effect does *S*-oxidation have on the reactivity of the CS double bond? It might be thought that the presence of the more electronegative O atoms on the S atom would increase the carbonyl reactivity, particularly since, in addition to the "carbonyl" canonical structure *(1c)* of sulfene, a 1,3-dipolar formulation such as *(1d)* is possible, in which the oxygen has taken over the negative charge [10].



(1a) ylide like; *(1b)* cumulative; *(1c)* carbonyl like; *(1d)* 1,3-dipolar

Canonical structures of sulfene

If we imagine *(1d)* to be cyclized to *(2)*, the sulfur clearly has assumed the same oxidation state as in a sulfinic acid.



(2) hydroxymethanesulfinic acid — inner ester of — *(3)* hydroxymethanesulfenic acid

In the "ylide" canonical structure *(1a)*, on the other hand, the oxidation state of the S atom is the same as in a sulfonic acid. Thus the cumulative formulation *(1b)*, which is neutral locally as well as overall, conceals the ability to react in two directions, on the one hand to form derivatives of methanesulfonic acid, and on the other to give derivatives of hydroxymethanesulfinic acid. We shall see that both types of reaction do occur.

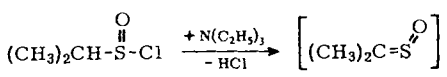
However, by far the most common mode of reaction is that corresponding to the "ylide" structure *(1a)*. Thus, the sulfonyl group exhibits electrophilic and the methylene nucleophilic character; the sulfenes consequently resemble the ketenes in their reactions. The question of whether the sulfines behave analogously cannot be answered until further reactions are known. No evidence of the existence of the three-membered rings *(2)* and *(3)* has been found as yet.

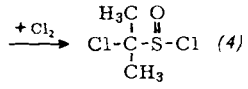
The fact that no sulfenes, and only four sulfines, have so far been isolated clearly shows that the instability of the thiocarbonyl compounds is further increased by *S*-oxidation. The relationship between structure and stability probably follows the same rules as for the thiocarbonyl compounds. Thus it is no accident that the *S*-oxides of thioamides [11] were discovered before the sulfines, whereas no *S*,*S*-dioxides of thioamides are known at present, and that three of the four sulfines that have been isolated are diarylsulfines. An interesting but as yet unanswered question is that of the extent of the similarity of the sulfenes to the ketenes, *e.g.* whether the sulfenes exhibit differences in dimerization properties and in sensitivity to oxygen such as exist between aldoketenes and ketoketenes.

B. Sulfines

I. Elimination of HCl from Sulfinyl Chlorides

Attempts to prepare the simplest sulfine, thioformaldehyde *S*-oxide, by the action of triethylamine on methanesulfinyl chloride or to intercept it by cycloaddition to ketene acetals [12] or to enamines [13] have been unsuccessful. The report [5] that NEt_3 forms a salt with methanesulfinyl chloride, but does not split off HCl, is in marked contrast to the vigorous reaction of NEt_3 with 2-propanesulfinyl chloride in dichloromethane at −20 °C, in which NEt_3–HCl is reported to be precipitated in quantitative yield [5] (according to the author's observations, 5.6 g of NEt_3–HCl dissolve in 100 ml of CH_2Cl_2 at −20 °C). Dimethylsulfine (thioacetone *S*-oxide) could not be detected either directly or by interception with reactive olefins or dienes. However, its presence in the filtrate, which undergoes an exothermic reaction on warming to room temperature, is indicated by the presence of NMR signals of chemically non-equivalent methyl groups, and by the formation of 2-chloro-2-propanesulfinyl chloride *(4)* on addition of chlorine [5].





(4)

[7] *R. Mayer, S. Scheithauer,* and *D. Kunz,* Chem. Ber. *99,* 1393 (1966).

[8] *F. A. Cotton* and *G. Wilkinson*: Advanced Inorganic Chemistry. Interscience Publishers, New York 1962, pp. 88–93.

[9] *A. Schönberg, E. Singer, E. Frese,* and *K. Praefcke,* Chem. Ber. *98,* 3311 (1965).

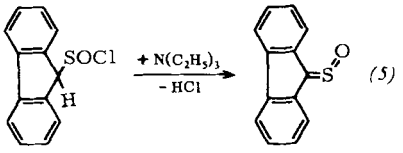
[10] The resonance behavior of the S=O double bond will not be discussed here.

[11] *W. Walter* and *H. P. Kubersky,* Liebigs Ann. Chem. *694,* 70 (1966) and literature cited there.

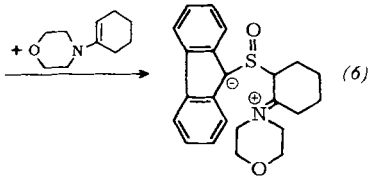
[12] *W. E. Truce* and *J. R. Norell,* J. Amer. chem. Soc. *85,* 3231 (1963).

[13] *S. Schüring,* Diploma Thesis, Universität Tübingen, 1963.

The first thioketone *S*-oxide was prepared by *Sheppard* and *Diekmann*[5] by the addition of NEt_3 to the unstable 9-fluorenesulfinyl chloride in ether at room temperature. NEt_3–HCl was precipitated immediately, and thiofluorenone *S*-oxide (9-sulfinylfluorene) *(5)* was isolated from the filtrate in a crude yield of 75%.



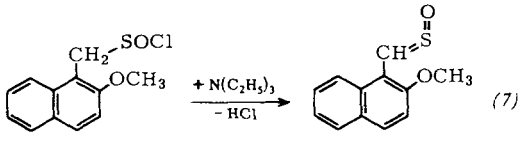
(5)



(6)

The sulfine *(5)* (orange-red needles, m.p. 111–112 °C) shows an additional fine structure of the aromatic signals in the NMR spectrum as compared with fluorene. This is to be expected, since the CSO group, which lies in the plane of the ring, forms an angle at the sulfur atom, so that the protons in the two benzene rings experience different levels of magnetic shielding. The UV spectrum is similar to that of fluorenone, but the bands show a slight hypsochromic shift. *(5)* decomposes slowly at room temperature and rapidly at its melting point, with loss of SO_2 and formation of a brown mass, from which 48% of bifluorenylidene and a few percent of fluorenone have been isolated. However, it does not appear to be affected by boiling benzene, THF, or cyclohexene, even when heated in these liquids for days. It reacts with *N*-(1-cyclohexenyl)morpholine to form a crystalline adduct which is assumed to have the zwitterion structure *(6)*[5] because of its strong IR absorption at 1710 cm^{-1}.

Barely eight weeks later, *Strating*, *Thijs*, and *Zwanenburg*[14] reported the preparation of the first thioaldehyde *S*-oxide, the brilliant yellow 2-methoxy-1-naphthylsulfine *(7)*, by the same method.

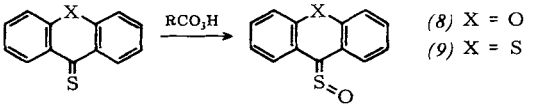


(7)

The anisotropy of the magnetic shielding by the sulfine group is shown in the NMR spectrum by a strong displacement of the aldehyde proton signal to lower fields (in $CHCl_3$, $\Delta\tau = -0.53$). *(7)*, which melts at about 90 °C with decomposition, reacts with a sulfuric acid solution of 2,4-dinitrophenylhydrazine to form the 2,4-dinitrophenylhydrazone of 1-formyl-2-methoxynaphthalene with liberation of H_2S, and on UV irradiation in CH_2Cl_2 it gives the aldehyde itself together with sulfur.

II. Oxidation of Thioketones

Strating, *Thijs*, and *Zwanenburg*[15] also prepared the diarylsulfines *(5)*, *(8)*, and *(9)* in yields of 97, 84, and 83% respectively, by oxidation of the thioketones with monoperoxyphthalic acid in ether or methylene chloride. The reaction proceeds very rapidly at room temperature, the color of the thioketones disappearing almost instantaneously.



(8) X = O
(9) X = S

Whenever the thiocarbonyl compound is obtainable in the monomeric form, as it is in these cases, then this should be the best method for the preparation of sulfines. *(8)* and *(9)*, like *(5)*, form orange-red needles which slowly decompose at room temperature. Treatment of *(9)* in ethanol with a trace of sulfuric acid gives thioxanthone in 81% yield and hydrogen sulfide, showing that the oxygen has added to the thione sulfur, and not to the sulfide sulfur.

Some IR and UV data for *S*-oxides of thioaldehydes, thioketones, thioacyl chlorides, and thioamides are given in Table 2. The sulfines give two strong IR bands at 1019–1078 and 1065–1128 cm^{-1} which are assigned to the C=S=O grouping. Owing to the variation in the position of the thiocarbonyl vibration, it is probable that these ranges will later prove to be too narrow.

Table 2. IR and UV absorptions of sulfines and related compounds.

Compound	IR (cm^{-1})	UV (mμ (log ε))
(5) [5]	1019, 1120	362 (4.18) in dioxane
(7) [14]	1040, 1065	398 (4.16) in dichloromethane
(8) [15]	1068, 1128	410 (4.02) in cyclohexane
(9) [15]	1078, 1093	420 (3.85) in cyclohexane
cis-Thiobenzoylchloride-*S*-oxide [16, 22]	1025, 1145	229 (3.90), 323 (3.95)
trans-Thiobenzoylchloride-*S*-oxide [16, 22]	1005, 1120	226 (3.90), 328 (4.10)
Thioamide-*S*-oxides [11]	900–1100	
Thioacetamide-*S*-oxide [11]	916	290 (3.95) in water

C. Sulfenes

I. Elimination of HCl from Sulfonyl Chlorides (Sulfonyl Chloride Acting as Sulfene Interceptor)

1. Elimination of HCl from 2,6-Dibromophenol-4-sulfonyl Chloride

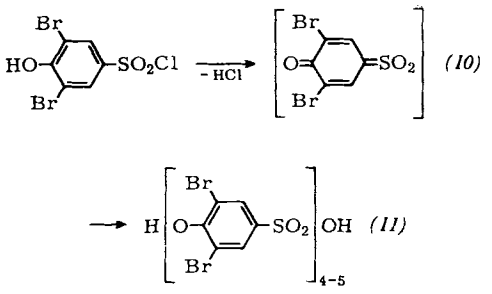
In 1908, *Zincke* and *Brune*[17] observed that 2,6-dibromophenol-4-sulfonyl chloride loses HCl when treated with soda or potassium acetate in aqueous acetone. They attributed the transient intense yellow coloration to the formation of quinoid sulfene *(10)*, and assumed the colorless precipitate that gradually separates to be a dimer or trimer of *(10)*.

[14] *J. Strating*, *L. Thijs*, and *B. Zwanenburg*, Recueil Trav. chim. Pays-Bas *83*, 631 (1964).

[15] *J. Strating*, *L. Thijs*, and *B. Zwanenburg*, Tetrahedron Letters *1966*, 65.

[16] *J. F. King* and *T. Durst*, Canad. J. Chem. *44*, 819 (1966).

[17] *T. Zincke* and *R. Brune*, Ber. dtsch. chem. Ges. *41*, 902 (1908).



(10)

(11)

According to *Hall*[18], the yellow color is due to the phenoxide anion of the sulfonyl chloride. It is possible that the phenoxide anion is converted into the precipitate, which according to *Oae* and *Kiritani*[19] has the constitution *(11)*, without initial formation of the sulfene.

2. Elimination of HCl from Primary Sulfonyl Chlorides and Mesyl Chloride

While the proton of the phenolic hydroxyl group is easily removed in the formation of *(10)*, which in the light of the vinylogy principle is reminiscent of the reaction $HO-SO_2Cl \rightarrow HCl + SO_3$, it is necessary in the case of the aliphatic sulfonyl chlorides to remove the much more firmly bound α-CH proton. This is achieved with trialkylamines under conditions that lead to ketene secondary products in the reaction of carboxylic acid chlorides[20]. The real incentive in the search for sulfenes was provided in 1911 by the discovery, by *Wedekind* and *Schenk*[3], that triethylamine removes HCl from phenylmethanesulfonyl chloride, even in cold benzene. These authors obtained NEt_3–HCl, SO_2, and stilbene, and concluded that the phenylsulfene intermediate (thiobenzaldehyde *S,S*-dioxide) had lost SO_2 and that the resulting phenylcarbene had dimerized. In a repetition of this work, *King* and *Durst*[21] also isolated triethylammonium phenylmethanesulfonate and thiobenzoyl chloride *S*-oxide *[(14)*, R = C_6H_5], which they resolved into its geometric isomers by chromatography[22,16].

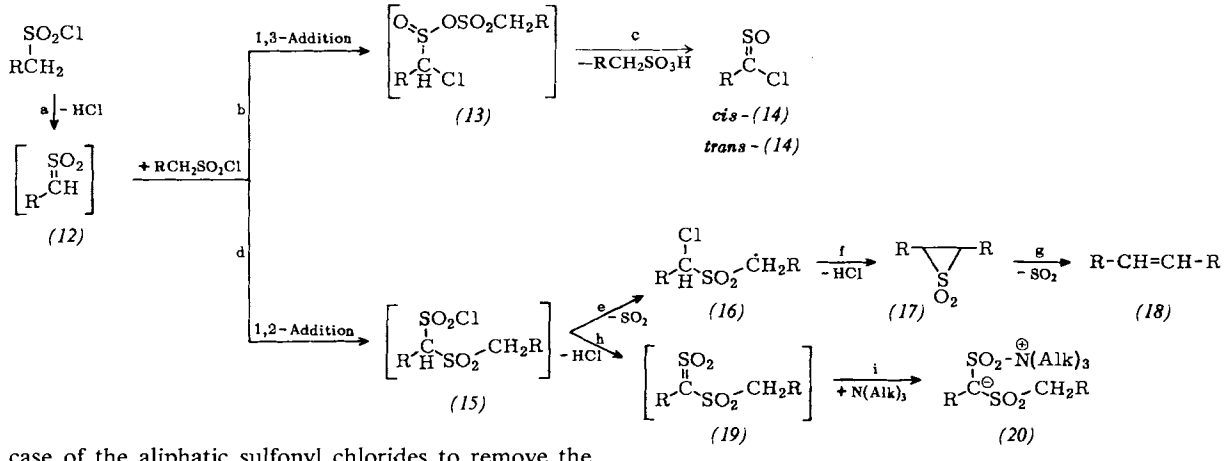
This reaction shows a peculiar dependence on the solvent (Table 3). In ether or dichloromethane it yields stilbene, but no thiobenzoyl chloride *S*-oxide, while in cyclohexane it gives thiobenzoyl chloride *S*-oxide, but no stilbene.

Table 3. Products of the reaction of phenylmethanesulfonyl chloride with triethylamine [16] (+ present — absent).

Solvent	NEt_3–HCl	SO_2	*trans*-Stilbene	*cis*-Stilbene episulfone	NEt_3–$C_6H_5CH_2SO_3H$	$C_6H_5C(Cl)=SO$
Ether	+	+	+	+	trace	trace
CH_2Cl_2	+	+	+	+	trace	trace
Benzene	+	+	+	+	+	+
Cyclohexane	+	trace	trace	—	+	+

The dependence on the structure of the primary sulfonyl chloride is also surprising. Whereas *p*-nitrophenylmethanesulfonyl chloride in cold ether gives *trans-p,p'*-dinitrostilbene (44%)[12,23], the reaction of 10-camphorsulfonyl chloride with triethylamine or pyridine yields the thiocarbonyl chloride *S*-oxide *(24)*, but no olefin[24]. Other primary sulfonyl chlorides and bromides of the camphor series react in a similar manner[25,27].

The products obtained can be explained by the assumption that the sulfene *(12)*, liberated by dehydrochlorination of the sulfonyl chloride, immediately adds to unreacted sulfonyl chloride either in the 1,3-position (route b) or in the 1,2-



Scheme 1. Reaction of primary sulfonyl chlorides with trialkylamine.

[18] *W. L. Hall*, J. org. Chemistry *31*, 2672 (1966).

[19] *S. Oae* and *R. Kiritani*, Bull. chem. Soc. Japan *38*, 1543 (1965).

[20] *E. Wedekind* and *W. Weißwange*, Ber. dtsch. chem. Ges. *39*, 1631 (1906).

[21] *J. F. King* and *T. Durst*, Tetrahedron Letters *1963*, 585.

[22] *J. F. King* and *T. Durst*, J. Amer. chem. Soc. *85*, 2676 (1963).

[23] *R. Fusco, S. Rossi*, and *S. Maiorana*, Chim. e Ind. (Milano) *44*, 873 (1962).

[24] *E. Wedekind, D. Schenk*, and *R. Stüsser*, Ber. dtsch. chem. Ges. *56*, 633 (1923).

[25] *E. Wedekind* and *R. Stüsser*, Ber. dtsch. chem. Ges. *56*, 1557 (1923).

[26] *H. Burgess* and *T. M. Lowry*, J. chem. Soc. (London) *127*,271 (1925).

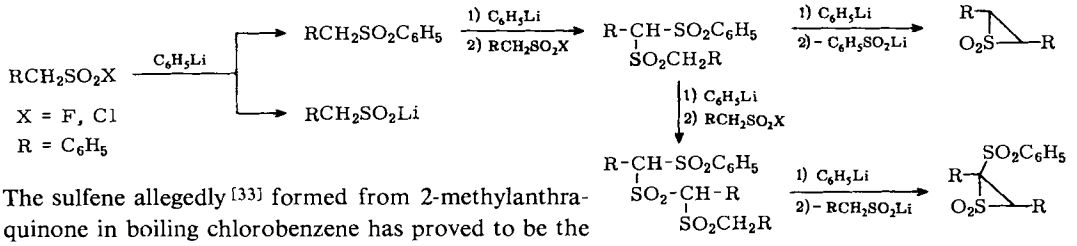
[27] *T. Hasselström* and *D. Hedman*, Ann. Acad. Sci. Fennicae Ser. *A 30*, No. 12, 3–9 (1930); *1931* II, 1412.

position (d) (Scheme 1). *Strating*[28] explains the formation of the thiocarbonyl chloride *S*-oxide *(14)* by 1,3-addition to the mixed anhydride *(13)* of a sulfonic acid and an α-chlorosulfinic acid, followed by 1,2-elimination (c) of the sulfonic acid. The olefin *(18)* is formed by 1,2-addition (d) of the sulfonyl chloride to the sulfene to form an α-sulfonylsulfonyl chloride *(15)*, elimination of SO_2 to form the α-chlorosulfone *(16)*, and a Ramberg-Bäcklund reaction *via* the three-membered ring sulfone *(17)*[29]. Carbenes are not involved in the formation of the olefins[30,12,16].

a) *Step a*

When triethylamine is used as halogen hydride acceptor, step a proceeds rapidly for sulfonyl chlorides and bromides[16,27,28]. With sulfonyl fluorides, however, the reaction is so slow[16,31] under these conditions that it is of no preparative value.

Although phenylmethanesulfonyl fluoride and chloride are converted into mono-, di-, and trisulfones, as well as olefines[32], by the base phenyl-lithium, it is conceivable that such products are produced *via* α-metalated sulfones, phenylsulfenes playing no part in this reaction.



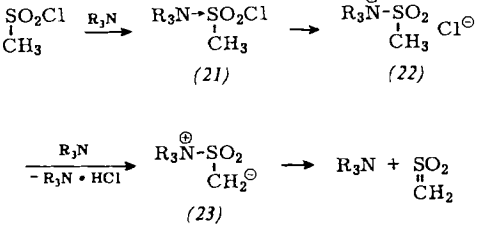
The sulfene allegedly[33] formed from 2-methylanthraquinone in boiling chlorobenzene has proved to be the sulfonic acid[34].

Dehydrohalogenation can best be carried out by means of trialkylamines in most[24,26,28,35,36], but not in all, cases[24,37,38] pyridine and similar cyclic imines are also suitable reagents. Triethylamine is most commonly used for this purpose and has many advantages; it is easy to purify and to add to, and to remove from, the reaction mixture. Its hydrochloride is easily separable since it is not hygroscopic, and is only sparingly soluble in petroleum, ether, benzene, ether, THF and at −40 °C, in acetonitrile.

Remarkable differences in behavior with aliphatic[39] and aromatic[40,41] sulfonyl chlorides exist between trimethyl- and triethylamine in spite of their having almost the same basicity. Thus, mesyl chloride adds to NMe_3, in ether at −20 °C, to give a sparingly soluble adduct (presumably *(21)*, R = CH_3), which with aniline yields *N*-mesylaniline and with enamines, sulfones having four-membered rings (cf. Section C V 1). The IR spectrum and the formation of mesyl chloride and NMe_3–DCl on treatment of this compound with DCl demonstrate that the mesyl group has remained intact. Elimination of HCl, accompanied by formation of NMe_3–HCl as well as various unidentified secondary products, occurs when the labile adduct is allowed to stand.

With NEt_3, however, no adduct can be detected and elimination of HCl starts immediately. The precipitate formed in ether reacts neither with aniline[42] nor with enamines[42]. No experimental evidence exists for the suggested[43,16] presence of a polysulfene. On the contrary, it is typical of the sulfenes that they react with one of the reaction components from which they are formed, in this case with sulfonyl chloride, instead of di-, tri- or polymerizing as do ketenes. Time will show whether the short lifetime of sulfenes is an adequate explanation.

The formation and reactions of the mesyl chloride-trimethylamine adduct would suggest that the 1,2-elimination of HCl with other amines proceeds *via* a labile sulfonyl chloride-amine adduct *(21)* or an acylammonium salt *(22)*.



This is not supported by the fact[31] that enamines also react with primary and secondary sulfonyl chlorides to give sulfones with four-membered rings in good yields when ethyldiisopropylamine is used in place of trimethylamine. The only observable effect is that the reaction proceeds more slowly. The formation of adducts analogous to *(21)* or *(22)* can be excluded on steric grounds.

The question of whether the sulfene is liberated or remains attached to the amine as in *(23)*[23] cannot be answered at present. In our opinion, the formation of trialkylammonium salts of the sulfonyl chlorides

[28] *J. Strating*, Recueil Trav. chim. Pays-Bas *83*, 94 (1964).

[29] *R. Fusco, S. Rossi*, and *S. Maiorana*, Chim. e Ind. (Milano) *45*, 564 (1963); *R. Fusco, S. Rossi, S. Maiorana*, and *G. Pagani*, Gazz. chim. ital. *95*, 774 (1965).

[30] *G. Opitz, H. Schempp*, and *H. Adolph*, Liebigs Ann. Chem. *684*, 92 (1965).

[31] *G. Opitz* and *K. Rieth*, unpublished.

[32] *Y. Shirota, T. Nagai*, and *N. Tokura*, Bull. chem. Soc. Japan *39*, 405 (1966).

[33] *A. Locher* and *H. E. Fierz*, Helv. chim. Acta *10*, 642 (1927).

[34] *J. F. King, P. de Mayo, E. Morkved, A. B. M. A. Sattar*, and *A. Stoessl*, Canad. J. Chem. *41*, 100 (1963).

[35] *J. F. King* and *T. Durst*, J. Amer. chem. Soc. *86*, 287 (1964).

[36] *J. F. King* and *T. Durst*, J. Amer. chem. Soc. *87*, 5684 (1965).

[37] *W. E. Truce, R. W. Campbell*, and *J. R. Norell*, J. Amer. chem. Soc. *86*, 288 (1964).

[38] *G. Opitz* and *D. Bücher*, unpublished.

[39] *G. Opitz* and *K. Fischer*, Z. Naturforsch. *18b*, 775 (1963).

[40] *W. Loop* and *E. Lührs*, Liebigs Ann. Chem. *580*, 225 (1953).

[41] *L. Horner* and *B. Nickel*, Liebigs Ann. Chem. *597*, 20 (1955).

[42] *N. Fischer*, Dissertation, Universität Tübingen, 1965.

[43] *I. J. Borowitz*, J. Amer. chem. Soc. *86*, 1146 (1964).

$(Alk)_3NH^{\oplus}\ {}^{\ominus}CR_2-SO_2Cl$, as formulated by *Fusco* [29] and *King* [21], is unlikely. The smooth elimination of HCl from secondary sulfonyl chlorides by NEt_3 in acetonitrile at −40 °C is important in view of the complications encountered in cycloaddition experiments under other conditions [44].

A convincing argument for the occurrence of sulfenes as intermediates is the formation of monodeuterated sulfonates in the presence of deuterated alcohol.

$$RCH_2-SO_2Cl + AlkOD \xrightarrow[-HCl]{NEt_3} RCH_2-SO_2OAlk + R-CHD-SO_2OAlk$$

R = H, CH_3, C_2H_5, CH_2=CH, C_6H_5, *p*-$O_2N-C_6H_4$; Alk = CH_3, C_2H_5 [37,45]

R = C_6H_5; Alk = CH_3, $CH(CH_3)_2$, $C(CH_3)_3$ [35,36]

If the deuterium were incorporated at the sulfonyl chloride or ester stage by base-catalysed H,D exchange, the other α-H atoms would also be replaced to some extent. However, as was shown independently by *King* and *Durst* [35,36] for phenylmethanesulfonyl chloride and by *Truce, Campbell,* and *Norell* [37,45] for a series of primary sulfonyl chlorides, mesyl chloride, mesyl bromide, methanesulfonic anhydride, and 2-propane- and 1-propene-1-sulfonyl chloride, the products appear to contain only undeuterated and monodeuterated esters, but no polydeuterated esters. Phenylmethanesulfonyl chloride and an excess of CH_3OD or the dideuterated sulfonyl chloride and an excess of CH_3OH give only monodeuterated esters at 25 °C (within a minute), but only in the presence of a base such as NEt_3. In the absence of a base, the esterification proceeds much more slowly ($t_{1/2}$ = 90 min at 50 °C) and without H,D exchange [36].

$$C_6H_5-CH_2-SO_2Cl \xrightarrow[\text{in } CH_3OD]{+NEt_3}$$

$$C_6H_5-CHD-SO_2OCH_3 \xleftarrow[\text{in } CH_3OH]{NEt_3} C_6H_5-CD_2-SO_2Cl$$

It must be concluded from the above findings that, in the presence of NEt_3, the monodeuterated ester is formed by the elimination-addition mechanism *via* the sulfene. According to *Truce* [45], the normal product results from an S_N2 reaction *via* a sulfonyltriethylammonium salt, which could also be formed by "collapse" [45] of the sulfene with the NEt_3–HCl.

$$RCH_2-SO_2Cl + N(C_2H_5)_3 \xrightarrow{E2} RCH{=}SO_2 + \overset{\oplus}{N}H(C_2H_5)_3Cl^{\ominus} \xrightarrow{+AlkOD} RCHD-SO_2OAlk$$

$$RCH_2-SO_2Cl + N(C_2H_5)_3 \xrightarrow{S_N2} RCH_2-SO_2-\overset{\oplus}{N}(C_2H_5)_3Cl^{\ominus} \xrightarrow{+AlkOD} RCH_2-SO_2OAlk$$

This hypothesis would explain the isotope distribution in the case of 1-propene-1-sulfonyl chloride and the migration of the double bond can be explained by preferential 1,2-addition to the vinylsulfene that is liberated as an intermediate.

$$CH_3-CH{=}CH-SO_2Cl + Alk\ OD \xrightarrow[-H(D)Cl]{+NEt_3} CH_3-CH{=}CH-SO_2OAlk + CH_2{=}CH-CHD-SO_2OAlk$$

(a) *(b)*

Alk = CH_3; ratio *(a)*:*(b)* = 33:67

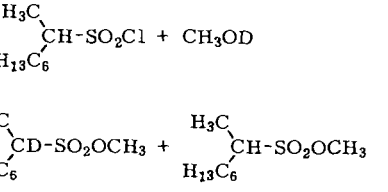
Alk = C_2H_5; ratio *(a)*:*(b)* = 9:91

Further evidence opposing a 1,4-addition, which is hindered by the inductive effect of the sulfonyl group, is provided by the uniform product obtained with 2-propene-1-sulfonyl chloride.

$$CH_2{=}CH-CH_2-SO_2Cl \xrightarrow[-HCl]{N(C_2H_5)_3} \left[CH_2{=}CH-\overset{\ominus}{C}H-\overset{\oplus}{S}O_2 \leftrightarrow \overset{\ominus}{C}H_2-CH{=}CH-\overset{\oplus}{S}O_2 \right]$$

$$\xrightarrow{+AlkOD} CH_2{=}CH-CHD-SO_2OAlk$$

Secondary sulfonyl chlorides such as 2-octanesulfonyl chloride show less readiness to undergo an elimination-addition type of reaction (ratio of deuterated: normal ester = 87:13 where the total yield is 40%).



2-Octanesulfonyl azide does not react under the above conditions. The elimination of HN_3 is, however, initiated by the addition of potassium methoxide and the deuterated ester is produced in 61% yield after a reaction time as short as 5 min. The degree of the participation of the sulfene mechanism in amide formation from [2-D]-(+)-2-octanesulfonyl chloride may be assessed from the amount of deuterium lost; dimethyl amine 46%, aniline 8%, *N*-methylaniline 0% D loss [46].

The mild and rapid introduction of sulfonyl groups into hydroxy and amino compounds *via* sulfenes is of preparative interest, at least when this cannot be achieved with aromatic sulfonyl chlorides, as is the case with some oximes [47] and with *N*-t-butoxycarbonylsedridine [48] [*N*-t-butoxycarbonyl-2-(2-hydroxypropyl)-piperidine].

In the synthesis of cephalosporin C, *Woodward* [49] accomplished the *O*-acylation of a sensitive 5-hydroxythiazolidine by using mesyl chloride/ethyldiisopropylamine.

b) *Steps b and c*

Steps b and c are supported by reactions in the presence of tosyl chloride [28]. Since the sulfonyl chloride that adds to the sulfene in the 1,3 position is "lost" as the sulfonic acid in step c, it can in principle be replaced by another sulfonyl chloride. If this replacement is successful, more thiocarbonyl chloride *S*-oxide *(14)* must be formed. In fact, the yield of *(24)* in the reaction of 10-camphorsulfonyl chloride with pyridine can be increased from 38 to 70% by the addition of an equimolar quantity of tosyl chloride. When 10-camphorsulfonyl bromide

[44] *G. Opitz* and *K. Rieth*, Tetrahedron Letters *1965*, 3977.

[45] *W. E. Truce* and *R. W. Campbell*, J. Amer. chem. Soc. *88*, 3599 (1966).

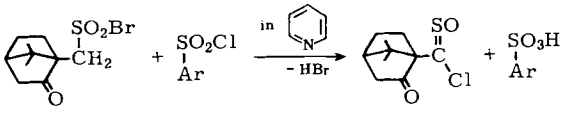
[46] *D. J. Cram, R. D. Trepka,* and *P. S. Janiak*, J. Amer. chem. Soc. *88*, 2749 (1966).

[47] *W. E. Truce* and *A. R. Naik*, Canad. J. Chem. *44*, 297 (1966).

[48] *G. Fodor*, lecture at Tübingen on July 20th, 1966.

[49] *R. B. Woodward*, Angew. Chem. *78*, 557 (1966).

reacts with tosyl chloride in pyridine, only the chlorine compound *(24)* is obtained.



(24)

This shows that a halogen-free intermediate must be involved, and so disproves *Wedekind*'s hypothesis [24] that the sulfene removes water from the sulfonyl halide in the formation of *(24)*.

It has not yet been proved that the 1,3 addition (b) does in fact take place, but if so, it is the only known reaction in which the sulfenes react as expected from the 1,3-dipolar resonance structure *(1d)*.

c) *Steps d, e, f, and g*

Step d, which should also take place with any other sulfonyl chloride, leads by a 1,2 addition to an α-sulfonylsulfonyl chloride *(15)*. The corresponding addition of carbonyl chlorides to ketenes is apparently possible only in a few cases [4]. Like all sulfonyl chlorides having unsaturated groups (vinyl, aryl, acyl) on the α-C atom, *(15)* tends to lose SO_2.

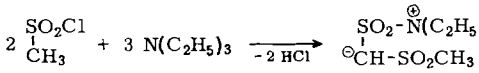
Mesylmethanesulfonyl chloride [*(15)*, R = H, m.p. = 106–108 °C], which has been known for only a short time [50], is relatively stable, but unsuccessful attempts [3, 25] to prepare diphenylmethanesulfonyl chloride and 9-fluorenesulfonyl chloride show that two phenyl groups in the α position cause SO_2 to be eliminated from a sulfonyl chloride, even at room temperature. The combination phenyl + sulfonyl in *(15)* [R = C_6H_5] probably has a similar effect.

After the elimination of SO_2 (e), the presence of the α-chlorosulfone [*(16)*, R = C_6H_5] and the trialkylamine satisfies the conditions for the Ramberg-Bäcklund reaction [51,52], *i.e.* the 1,3 elimination of HCl (f) to give the three-membered ring sulfone *(17)* with subsequent loss of SO_2 (g) to give the olefin *(18)*.

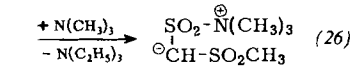
More recent work shows that the reaction has a wide range of application [53–56]. NEt_3 is satisfactory as the base for bis-(α-bromobenzyl)sulfone [57]; it is not yet known whether this is also true of purely aliphatic α-halogenosulfones. In boiling D_2O/NaOD, the H/D exchange of the α-protons in α-chlorodiethylsulfone [*(16)*, R = CH_3] is faster than the formation of 2-butene (97% of olefinic D), but slower in the case of the three-membered ring sulfone [*(17)*, R = CH_3] (5% of olefinic D) [54]. The proportion of the *cis*-olefin formed with 2N KOH increases with decreasing size of the group R in the α-chlorosulfone *(16)* (CH_3 78, C_2H_5 56, C_3H_7 53% of the *cis*-olefin). The values show practically no change when the Cl atom is replaced by Br or I. This can be explained by step f, which involves anionization on the halogen-free side and intramolecular nucleophilic substitution analogous to the cyclopropanone ring closure in the Favorskii reaction, since the elimination of SO_2 (g), which is slow at room temperature and fast at high temperatures, is stereospecific [16,52], even in the presence of 2N KOH [54].

d) *Steps h and i*

The α-position of the original sulfonyl chloride is strongly activated by conversion into the α-sulfonylsulfonyl chloride *(15)*. This must facilitate the elimination of HCl (h) to form the α-sulfonylsulfene *(19)*. In view of the relatively high acidity (1,3-disulfones dissolve in dilute alkali), it seems surprising that the elimination of SO_2 (step e) can compete with the elimination of HCl (step h) at low temperatures, and the latter step has never been discussed until now. The first sulfene was recently isolated as the trimethylamine adduct *(26)* by the route a, d, h, i [58,59].



(25)



(26)

When NEt_3 is added to mesyl chloride in acetonitrile at −40 °C, NEt_3–HCl is precipitated quantitatively, and on filtering the mixture the mesylsulfene-triethylamine adduct *(25)* is present in the filtrate; this can be isolated as a colorless powder by freeze-drying, but it is preferentially converted into the much more stable NMe_3 adduct *(26)*, which is sparingly soluble in acetonitrile. If NMe_3 is used in the initial reaction, a mixture of *(26)* and NMe_3–HCl is precipitated.

The secondary reactions of the simple sulfene when mesyl chloride reacts with NEt_3 in ether or petroleum ether at −10 to +20 °C are unknown. However, it is certain that neither a polysulfene nor thiiran dioxide is formed. In aqueous solution, the precipitate gives an acid reaction and evolves SO_2, and when heated with PbO it forms PbS. The formation of SO_2 suggests route d, e, and the formation of H_2S suggests route b, c; the latter route should lead to the thioformyl chloride *S*-oxide [*(14)*, R = H], which is presumably unstable. The probability of side reactions occurring is very high in the case of mesyl chloride. Thus the sulfonyl chloride *(15)* and mesyl chloride must be expected to add on in both the 1,3- and the 1,2-position in the sulfenes *(12)* and *(19)*. In this way the groups R=CH_3–SO_2 and CH_3–SO_2–CH_2–SO_2 can be introduced into thioformyl chloride *S*-oxide [*(14)*, R = H] and into mesylsulfene [*(19)*, R = H]. Other reactions may follow.

3. Elimination of HCl from Secondary Sulfonyl Chlorides

Fusco et al. [29] have studied tne reaction of 2-propanesulfonyl chloride with NEt_3. For secondary sulfonyl chlorides, Scheme 1 can be simplified by the omission of

[50] *G. Opitz* and *G. Walz*, unpublished.

[51] *L. Ramberg* and *B. Bäcklund*, Ark. Kem., Mineralog. Geol., Ser. *A 1*, 1 (1940); Chem. Abstr. *34*, 4725 (1940).

[52] *N. P. Neureiter* and *F. G. Bordwell*, J. Amer. chem. Soc. *85*, 1209 (1963).

[53] *N. P. Neureiter*, J. org. Chemistry *30*, 1313 (1965).

[54] *N. P. Neureiter*, J. Amer. chem. Soc. *88*, 558 (1966).

[55] *L. A. Paquette*, J. Amer. chem. Soc. *86*, 4383 (1964).

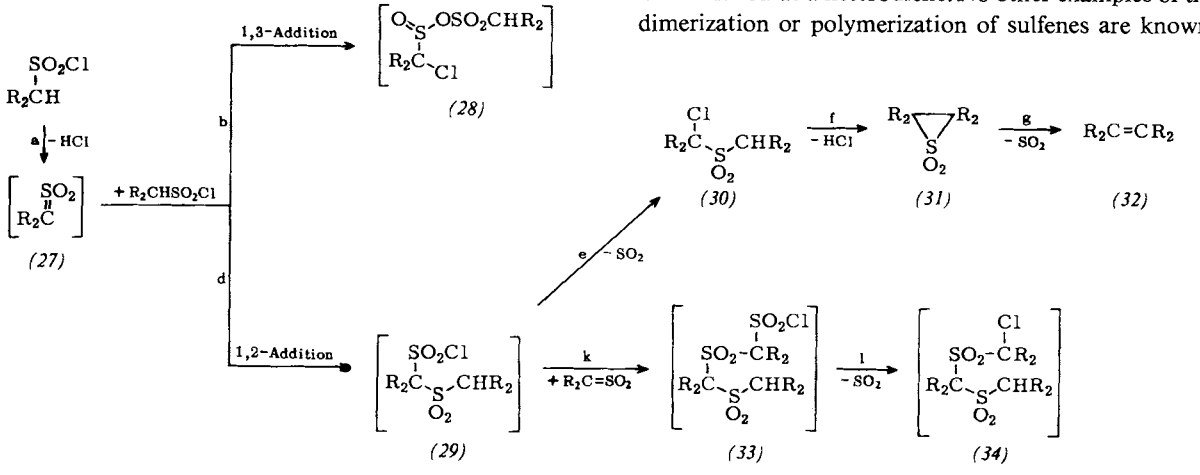
[56] *L. A. Paquette* and *L. S. Wittenbrook*, Chem. Commun. *1966*, 471.

[57] *L. A. Carpino* and *L. V. McAdams III*, J. Amer. chem. Soc. *87*, 5804 (1965).

[58] *G. Opitz, M. Kleemann, D. Bücher, G. Walz*, and *K. Rieth*, Angew. Chem. *78*, 604 (1966); Angew. Chem. internat. Edit. *5*, 594 (1966).

[59] *G. Opitz* and *D. Bücher*, Tetrahedron Letters *1966*, 5263.

steps c, h, and i (Scheme 2 with secondary reactions). Nothing is known about step b. The formation of the α-sulfonylsulfonyl chloride *(29)* can be deduced from two secondary reactions. On the one hand *(29)* is a tertiary sulfonyl chloride, and so very readily loses SO_2 (e) to form the α-chlorosulfone *(30)* (t-butylsulfonyl chloride loses SO_2 at 35 °C with $t_{1/2}$ = 34 hours [60]). On the other hand, 1,2-addition (k) of *(29)* to the sulfene *(27)* yields the new α-sulfonylsulfonyl chloride *(33)*. This in turn forms the α-chlorodisulfone *(34)* by loss of SO_2 (l), and the α-chlorotrisulfone *(36)* by 1,2-addition (m) to the sulfene *(27)* followed by loss of SO_2 (n). The reaction can clearly continue with formation of $R_2CH(SO_2CR_2)_nSO_2Cl$ and $R_2CH(SO_2CR_2)_nCl$.



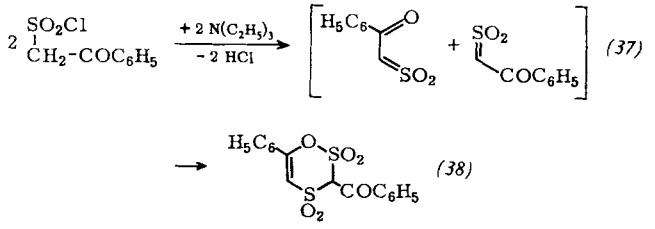
Scheme 2. Reaction of secondary sulfonyl chlorides with trialkylamine

(30), *(34)*, and *(36)* were isolated from the reaction products of 2-propanesulfonyl chloride (R = CH_3). With 2-butanesulfonyl chloride and cyclohexanesulfonyl chloride, on the other hand, only the sulfones [*(30)*, R_2 = CH_3, C_2H_5 or $(CH_2)_5$] were isolated; these did not give the olefin *(32)* (route f, g) under the conditions of the reaction (cold ether or boiling dioxane), but did so on subsequent heating with 2N NaOH.

Though it is still largely unknown how the secondary reactions of the sulfenes depend on the structure of the sulfonyl chloride and the reaction conditions, it may be assumed that the formation of products having low molecular weights will be favored by heat, unsaturated substituents, and a high degree of branching in the α position, all of which promote the elimination of SO_2. In any case, it can be seen from Schemes 1 and 2 that the elimination of SO_2 terminates the reaction sequences. The assumption [29] that the chlorodisulfone *(34)* can also be formed by addition of the α-chlorosulfone *(30)* to the sulfene *(27)* is opposed by the inertness of α-halogenosulfones [61].

4. Elimination of HCl from Benzoylmethanesulfonyl Chloride

The long sought dimerization of a sulfene was finally observed by *Fusco et al.* [29] in the reaction of NEt_3 with benzoylmethanesulfonyl chloride.



The triethylammonium salt of the dimer *(38)* is obtained in 45% yield in chloroform [29] and in 60% yield in acetonitrile [62]. The above authors formulated the cyclization as a Diels-Alder reaction of the benzoylsulfene *(37)*. This, like all sulfenes, can act as a dienophile [63,64], and by invocation of the keto group, it can also function as a heterodiene. No other examples of the dimerization or polymerization of sulfenes are known.

II. Reaction of Diazoalkanes with Sulfur Dioxide (Diazoalkane or SO_2 Acting as Sulfene Interceptors)

A second method for the production of sulfenes *in situ* was discovered by *Staudinger* and *Pfenninger* [65] during an attempt to prepare diphenylsulfene [*(42)*, R = C_6H_5, Scheme 3] from diphenyldiazomethane and sulfur dioxide. The sulfene is formed very rapidly at −20 to +20 °C, with evolution of N_2; the diazonium sulfinate *(39)* would appear to be a more probable intermediate than the cyclic azo compounds *(40)* and *(41)*. However, the sulfene again escapes direct detection by immediate reaction with one of the starting materials.

[60] *R. T. v. Aller, R. B. Scott jr.*, and *E. L. Brockelbank*, J. org. Chemistry *31*, 2357 (1966).

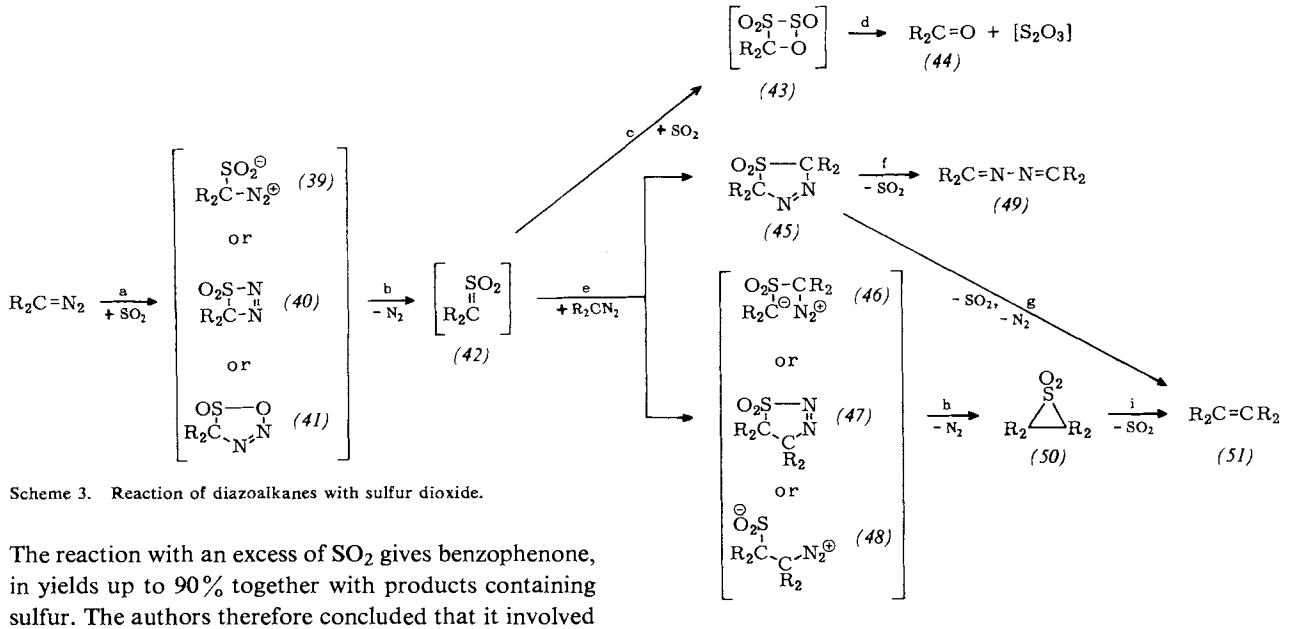
[61] *F. G. Bordwell* and *G. D. Cooper*, J. Amer. chem. Soc. *73*, 5184 (1951).

[62] *G. Opitz* and *H.-R. Mohl*, unpublished.

[63] *G. Opitz* and *E. Tempel*, Angew. Chem. *76*, 921 (1964); Angew. Chem. internat. Edit. *3*, 754 (1964).

[64] *G. Opitz* and *F. Schweinsberg*, Angew. Chem. *77*, 811 (1965); Angew. Chem. internat. Edit. *4*, 786 (1965).

[65] *H. Staudinger* and *F. Pfenninger*, Ber. dtsch. chem. Ges. *49*, 1941 (1916).



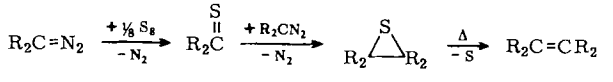
Scheme 3. Reaction of diazoalkanes with sulfur dioxide.

The reaction with an excess of SO_2 gives benzophenone, in yields up to 90% together with products containing sulfur. The authors therefore concluded that it involved a 2+2 cycloaddition (c) of the sulfene to SO_2 followed by cleavage of the four-membered ring (d) to form benzophenone *(44)* and S_2O_3 which decomposes into SO_2 and S.

If, on the other hand, SO_2 is passed into a solution of diphenyldiazomethane, the diazoalkane acts as a sulfene interceptor (e). The three-membered ring sulfone *(50)* is formed *via* an intermediate that was not isolated, but which Staudinger formulated as Δ^2-[1,2,3]-thiadiazoline-1,1-dioxide *(47)*. When *(50)* is heated, it partly loses SO_2 to form tetraphenylethylene *(51)*, and partly undergoes a rearrangement that is of no interest in this context, with formation of five-membered ring sulfones and other diphenylanthracene derivatives [65,66].

If the reaction is carried out in the presence of water, alcohols, ammonia, alkylamine, or dialkylamine, it yields diphenylmethanesulfonic acid or its esters or amides. Aniline, *p*-toluidine, and *p*-anisidine do not act as sulfene interceptors in this reaction [65,67,68].

The reaction sequence a, b, e, h corresponds to the reaction of diaryldiazomethanes with sulfur (or thioketones) to form episulfides [69,70], and steps e and h to the reaction of ketene



with diazomethane to form cyclopropanone [71], though in this case the ketene cannot be produced from diazomethane and CO [72].

The Staudinger-Pfenninger reaction for the synthesis of three-membered ring sulfones *(50)* or olefins *(51)* has now been applied to other diazo compounds: diazomethane [73,74], diazoethane [54], phenyldiazomethane [57,75], aryldiazoalkanes [73,76,77], and cycloalkyldiazoalkanes [78,79]. 2-Diazopropane gave only acetoneazine, while diazoacetic ester did not react with SO_2 [77]. With diazomethane as starting material, thiirane-*S*,*S*-dioxide [*(50)*, R = H, m.p. 19 °C, b.p. 64 °C/0.3 mm Hg] was isolated from the reaction products (yield 70%) and characterized. Diazoethane yields *cis*- and *trans*-2-butene in approximately equal amounts. The crystalline epithio dioxide of the *cis*-olefin can be separated from the oily *trans* derivative at low temperatures. On heating the former neat, in isopropanol, or in 2 N NaOD/D_2O, it is converted into *cis*-2-butene. The stereospecificity of the elimination of SO_2 is lost in the presence of potassium t-butoxide/$(CH_3)_3COD$, and H,D exchange takes place at the same time (20 parts of *cis*- to 80 parts of *trans*-H_5C_2–CD=CD–C_2H_5). The reaction of phenyldiazomethane with both liquid and aqueous SO_2, also afforded the epithio dioxide of *cis*-stilbene only, together with *trans*-stilbene and benzylidenazine. At 90 °C, the epithio dioxide gives pure *cis*-stilbene in 83% yield, whereas a mixture of 61 parts of *trans*- and 39 parts of *cis*-stilbene is formed when it is heated to 50 °C in 0.2N NaOH. The elimination of SO_2 is complete after 2 days at room temperature. The *trans*-stilbene is probably also formed *via* its epithio dioxide, without the participation of phenylcarbene [75].

While the reaction of diaryldiazomethanes and aryldiazoalkanes with SO_2 leads to three-membered ring sulfones *(50)* in good yields, or to olefins *(51)* and relatively small quantities of ketazine *(49)*, the ketazines predominate in the products obtained from cycloalkyldiazoalkanes. Cyclic azosulfones, which occur as pairs of

[66] *H. Kloosterziel* and *H. J. Backer*, Recueil. Trav. chim. Pays-Bas *71*, 1235 (1952).

[67] *H. Kloosterziel, M. H. Deinema*, and *H. J. Backer*, Recueil Trav. chim. Pays-Bas *71*, 1228 (1952).

[68] *S. T. Purrington* and *P. Wilder jr.*, J. org. Chemistry *30*, 2070 (1965).

[69] *M. Sander*, Chem. Reviews *66*, 297 (1966), pp. 318–326.

[70] *N. Latif, I. Fathy, N. Mishriky*, and *B. Haggag*, Canad. J. Chem. *44*, 629 (1966).

[71] *N. J. Turro* and *W. B. Hammond*, J. Amer. chem. Soc. *88*, 3672 (1966).

[72] *H. Staudinger*, Ber. dtsch. chem. Ges. *49*, 1884 (1916).

[73] *G. Hesse, E. Reichold*, and *S. Majmudar*, Chem. Ber. *90*, 2106 (1957).

[74] *G. Hesse* and *S. Majmudar*, Chem. Ber. *93*, 1129 (1960).

[75] *N. Tokura, T. Nagai*, and *S. Matsumura*, J. org. Chemistry *31*, 349 (1966).

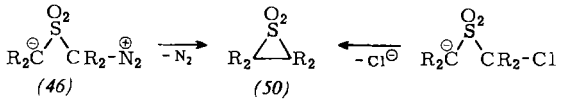
[76] *L. v. Vargha* and *E. Kovács*, Ber. dtsch. chem. Ges. *75*, 794 (1942).

[77] *E. Reichold*, Dissertation, Universität Erlangen, 1955.

stereoisomers and are regarded as Δ^3-[1,3,4]-thiadiazoline 1,1-dioxides *(45)*, are also formed, probably by 3+2 cycloaddition (e) of sulfenes and diazoalkanes. However, the isomeric Δ^2-[1,2,3]-thiadiazoline structure *(47)* can not yet be definitely ruled out. The best known product is the crystalline substance *(45)* with $R_2 = C_2H_5$, C_6H_{11}, which is obtained from 1-cyclohexyl-1-diazopropane and SO_2 [78,79]. The stereoisomers have identical UV and IR spectra, with sulfone bands at 1150 and 1300 cm^{-1}. When a solution of the isomers of *(45)* in petroleum ether is filtered through Al_2O_3, SO_2 is lost (f), whereby the ketazine *(49)* is formed.

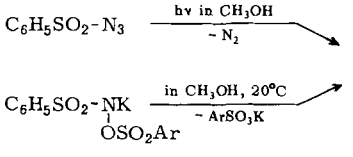
When the stereoisomers are heated slowly, the same reaction occurs at temperatures above 120 °C. Immersion of the reactants in a bath at 240 °C leads also to the liberation of nitrogen and formation of 3,4-dicyclohexyl-3-hexene *(51)* in 8% yield. In such cases the yield of olefin cannot be increased beyond 25% even when a special technique (flow pyrolysis) is used [79].

It may be assumed from these observations that the three-membered ring sulfones *(50)* are formed, not *via* the [1,3,4]-thiodiazolines *(45)*, but *via* the previously unknown Δ^2-[1,2,3]-thiadiazoline 1,1-dioxides *(47)* or *via* the zwitterions *(46)* or *(48)*. The elimination of N_2 from *(46)* to form the three-membered ring sulfone *(50)* would correspond to the elimination of the chloride ion in the Ramberg-Bäcklund reaction.



(46) *(50)*

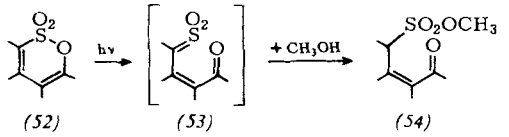
Neureiter [54] considers the variable steric course of the reaction to be incompatible with this mechanism [73,75,80]. Thus the preferential formation of the *cis*-olefin epithio dioxide is



not observed in the reaction of diazoethane with SO_2, as it is in the reaction of α-halogenated diethylsulfone with 2N KOH. However, this argument is not very convincing, in view of the great ease with which the diazonium group is split off.

III. Photochemical Ring Cleavage of Sultones

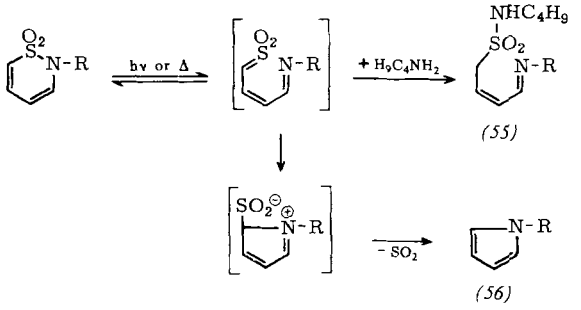
Doubly unsaturated δ-sultones *(52)* are converted into the sulfonates *(54)* on UV irradiation in methanol.



(52) *(53)* *(54)*

In the presence of benzylamine, the *N*-benzylsulfonamides are formed. Since these reactions do not take place in the dark, it is assumed that they proceed by photochemical ring cleavage to form the ketovinylsulfenes *(53)* [34].

The corresponding sultams react analogously when irradiated with UV light in the presence of butylamine.

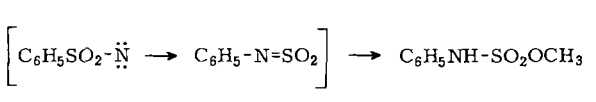


(55) *(56)*

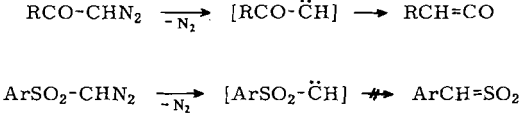
The reaction products are the *N*-butylsulfonamide *(55)* and the pyrrol *(56)* which is formed by loss of SO_2. *Durst* and *King* [81] interpret the formation of pyrrol, which is the main reaction in photolysis in cyclohexane, ether, or methanol, as well as in pyrolysis, as nucleophilic addition of the N atom of the imine on the C atom of the sulfene group and subsequent loss of SO_2. Nucleophilic addition can take place at the S atom (normal case, reversion to sultams) or at the C atom (exceptional case, reduction in ring size).

IV. Elimination of Nitrogen from α-Diazosulfones

Curtius and Lossen degradations can also take place in the sulfonic acid series [82] (23 and 67% yield respectively):



Similarly, the elimination of N_2 from α-diazosulfones could lead to sulfenes by a reaction akin to the Wolff rearrangement.



However, in the heat-, light-, or Ag_2O-induced decomposition of *p*-methoxybenzenesulfonyldiazomethane [83] and benzenesulfonyldiazomethane [84], only reactions of the arylsulfonylcarbene could be detected.

[78] *G. Hesse* and *E. Reichold*, Chem. Ber. *90*, 2101 (1957).

[79] *H. H. Inhoffen*, *R. Jonas*, *H. Krösche*, and *U. Eder*, Liebigs Ann. Chem. *694*, 19 (1966).

[80] *S. Rossi* and *S. Maiorana*, Tetrahedron Letters *1966*, 263.

[81] *T. Durst* and *J. F. King*, Canad. J. Chem. *44*, 1869 (1966).

[82] *W. Lwowski* and *E. Scheiffele*, J. Amer. chem. Soc. *87*, 4359 (1965).

[83] *A. M. v. Leusen*, *R. J. Mulder*, and *J. Strating*, Tetrahedron Letters *1964*, 543.

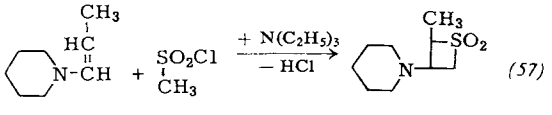
[84] *R. A. Abramovitsh* and *J. Roy*, Chem. Commun. *1965*, 542.

V. Cycloadditions with Sulfenes Produced *in situ*

Attempts to prepare sulfenes have resulted in interception by the sulfonyl chloride, diazoalkane, or SO_2. A component that is introduced deliberately can assume the role of interceptor only if the sulfene reacts more rapidly with this component than with sulfonyl chloride (*e.g.* with H_2O, D_2O, AlkOD, $(Alk)_2NH$, $ArNH_2$ [36,45], and tosyl chloride, but not with tosyl fluoride [28]) or than with diazoalkane or SO_2 (*e.g.* with H_2O [65,73], but cf. [75], and with AlkOH [65], NH_3, $AlkNH_2$, and $(Alk)_2NH$ [67], but not with $ArNH_2$ [67] or acetone [73]). Moreover, if the sulfene is produced from diazoalkane $+SO_2$, the intercepting component must not react with either of these components. The number of possible interceptors is therefore small, and it is at least partly understandable that unlike ketenes [85], sulfenes undergo cycloaddition only with strongly nucleophilic olefins and other very reactive partners. The high reactivity of the diazoalkanes is a great drawback and for this reason cycloadditions are generally carried out with sulfenes produced *in situ* from sulfonyl chloride and NEt_3.

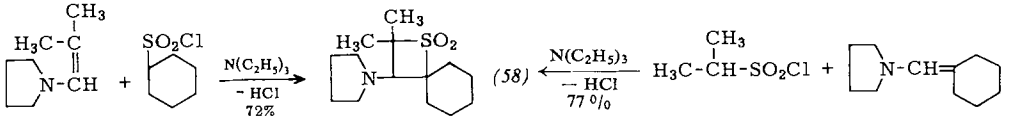
1. Enamines

The resumption of sulfene research in 1960 after a break of several decades was due to the observation [86,87] that *N*-(1-propenyl)piperidine is not *C*-acylated by mesyl chloride/NEt_3 in cold ether, but is converted into 2-methyl-3-piperidinothietane 1,1-dioxide *(57)* (yield 88%).



(57)

Mesyl chloride (methanesulfonic anhydride may also be used [38]) and primary sulfonyl chlorides react with enamines of aldehydes and ketones in the same orientation, and no obvious restrictions have been found regarding solvent and temperature [30,88,23,43,50,89–96]. Even more surprising is the fact that secondary sulfonyl chlorides do not react under a wide range of conditions, whereas the reaction proceeds smoothly in acetonitrile at −40 °C. The formation of the same product *(58)* from *N*-(2-methyl-1-propenyl)pyrrolidine and cyclohexanesulfonyl chloride and from *N*-(cyclohexylidenemethyl)pyrrolidine and 2-propanesulfonyl chloride proves the constitution of the fourmembered ring sulfones [44].

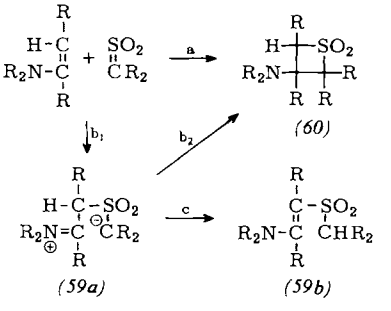


(58)

As in the analogous cycloaddition of enamines to ketenes [97] and isocyanates [98–100], high basicity of the enamine favors initiation of the reaction under mild conditions, while the formation of open-chain sulfones [*e.g. (59b)*] is favored by increasing α-substitution of the sulfonyl chloride and of the enamine. Thus the cycloaddition of dimethylsulfene to *N*-(2-methyl-1-propenyl)-pyrrolidine proceeds in 85% yield, whereas the yield in the cycloaddition to *N*-(2-methyl-1-propenyl)morpholine is only 10% [44]. *N*-Vinylcarbazole does not react with sulfene [96]. In general, open-chain sulfones are formed with sulfene and monosubstituted sulfenes only with enamines from ketones [30,95,23,101] and of disubstituted sulfenes with enamines from aldehydes and ketones [44].

In view of the difficulties encountered [102,103] in the conversion of enamines into open-chain sulfones by β-*C* acylation with aromatic sulfonyl chlorides, it may be assumed that cycloaddition and *C*-acylation proceed *via* sulfenes. Cycloaddition and subsequent ring opening can, however, be mistaken for direct *C*-acylation and this must be borne in mind when considering four-membered ring sulfones carrying substituents, such as vinyl, aryl, and aminomethyl groups, which are conducive to ring cleavage. The possibility that the four-membered ring is formed by addition of the sulfonyl chloride to the double bond of the enamine followed by dehydrochlorination, either directly or *via* the *C*-acylated enamine, has been ruled out experimentally [43,23,39].

It is unknown whether the cycloaddition is a one-step multicenter reaction (a) or a two-step addition (b).



(60)

(59a) *(59b)*

[85] *A. P. Krapcho* and *J. H. Lesser*, J. org. Chemistry *31*, 2030 (1966).

[86] *H. Adolph*, Dissertation, Universität Tübingen, 1959.

[87] *G. Opitz* and *H. Adolph*, Angew. Chem. *74*, 77 (1962); Angew. Chem. internat. Edit. *1*, 113 (1962).

[88] *G. Stork* and *I. J. Borowitz*, J. Amer. chem. Soc. *84*, 313 (1962).

[89] *D. C. Dittmer* and *F. A. Davis*, J. org. Chemistry *29*, 3131 (1964).

[90] *L. A. Paquette*, J. org. Chemistry *29*, 2851 (1964).

[91] *L. A. Paquette*, J. org. Chemistry *29*, 2854 (1964).

[92] *L. A. Paquette*, J. org. Chemistry *30*, 629 (1965).

[93] *L. A. Paquette* and *M. Rosen*, Tetrahedron Letters *1966*, 311.

[94] *W. E. Truce, J. R. Norell, J. E. Richman*, and *J. P. Walsh*, Tetrahedron Letters *1963*, 1677.

[95] *J. N. Wells* and *F. S. Abbott*, J. med. Chemistry *9*, 489 (1966).

[96] *G. Walz*, Diploma Thesis, Universität Tübingen, 1965.

[97] *J. Szmuszkovicz*, Advances org. Chemistry *4*, 1 (1963).

[98] *M. Perelman* and *S. Mizsak*, J. Amer. chem. Soc. *84*, 4988 (1962).

[99] *G. Opitz* and *J. Koch*, Angew. Chem. *75*, 167 (1963); Angew. Chem. internat. Edit. *2*, 152 (1963).

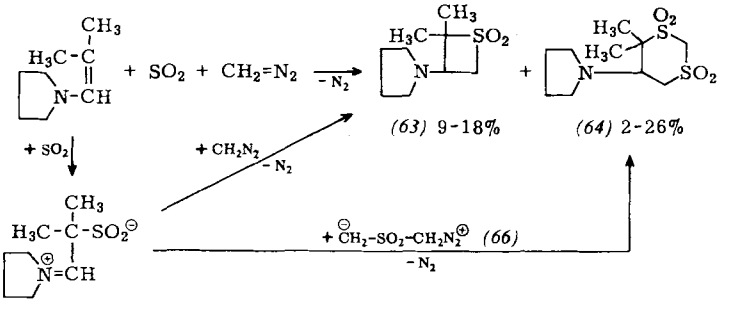
[100] *A. K. Bose* and *G. Mina*, J. org. Chemistry *30*, 812 (1965).

[101] *J. J. Looker*, J. org. Chemistry *31*, 2973 (1966).

[102] *M. E. Kuehne*, J. org. Chemistry *28*, 2124 (1963).

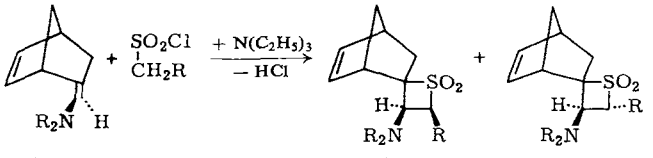
[103] *G. Opitz* and *F. Zimmermann*, unpublished.

Path b is probably preferred in view of both the selection rules [104] for multi-center cycloadditions and the observation [105] that even in the 2+2 cycloaddition to the non-polar cyclohexene, diphenylketene reacts rather more rapidly with the carbonyl group than with the diphenylmethylene group. This route provides a better explanation of the single orientation and of the fact that only strongly nucleophilic olefins are attacked by sulfenes. It also enables us to establish a relationship between the extent of *C*-acylation and the stabilization of the charges in the zwitterion *(59a)*. However, the expected solvent-dependence is lacking in the reaction of β-pyrrolidinostyrene with mesyl chloride/NEt_3. The yield of open-chain sulfone is the same (4%) in acetonitrile as in ether, though the yields of the cycloadduct are 75 and 35% respectively [95].



Route a should be stereospecific, while route b should be stereoselective only if the life of the zwitterion *(59a)* is very short. Owing to the lability of the *cis* enamines [106], it is more difficult to obtain any information in this case than in the stereospecific [107,108] cycloaddition of ketoketenes to vinyl ethers. Since the possibility of a *cis-trans* rearrangement of the enamine before addition cannot be ruled out, no conclusions can be drawn from the observation [109] that *trans-N*-(1-propenyl)morpholine yields only one four-membered ring sulfone on reaction with mesyl chloride/NEt_3, whereas the *cis*-enamine gives a mixture of two stereoisomers.

These experiments should be distinguished from the reactions of the bicyclic enamines *(61)* with CH_3SO_2Cl/NEt_3 and chloromethanesulfonyl chloride/NEt_3 [90,91]. The NMR spectra of these compounds show that they exist to the extent of 80–90% in the form shown.



(61) *(62a)* *(62b)*

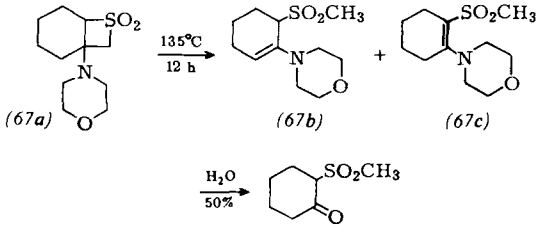
The cycloaddition of the sulfenes, which attack from the *exo* side, is stereoselective in that the amino group predominantly occupies the sterically favored position *(62a)*, *(62b)*, in which, unlike the H atom shown, it does not lie under the bicyclo system. The distance between the amino group and the olefinic protons, whose NMR signals appear as two doublets and not as a triplet, differs only in the stereoisomers shown. As expected, thioformyl chloride *S,S* dioxide gives two stereoisomeric cycloadducts [*(62a)* and *(62b)*, R = Cl] in which the Cl atom is *cis* and *trans* to the amino group respectively.

The enamine from pyrrolidine and isobutyraldehyde gives the same four-membered ring sulfone *(63)* with diazomethane/SO_2 as with mesyl chloride/NEt_3, as well as the disulfone *(64)* [39,42,110].

It seems doubtful, at least for *(64)*, whether the products in this case are formed by cycloaddition of the enamine to sulfene. It is possible that the reacting species is, not the enamine, but its SO_2 adduct *(65)*. This could react as an immonium sulfinate [111,112] with diazomethane to form the four-membered ring *(63)*, and with the adduct *(66)* of sulfene and diazomethane [cf. *(46)* in Scheme 3] to form the six-membered ring *(64)*.

The 3-aminothietane 1,1-dioxides are generally weakly basic compounds that crystallize well. Difficulties are sometimes encountered in their reduction with $LiAlH_4$ to form 3-aminothietanes [88,43,30,95] and in the elimination of amine [94,89,92,95] *via* the quaternary salt *(Hofmann)* or *via* the amine oxide *(Cope)* to form the 3-aminothietene 1,1-dioxide.

The thermal stability of the 3-aminothietane 1,1-dioxides depends on the nature and the number of substituents. 2-Ethyl-3-morpholinothietane 1,1-dioxide, 2-methyl-3-piperidinothietane 1,1-dioxide, and similar alkyl-substituted four-membered ring sulfones can be distilled or sublimed in a high vacuum. While ring cleavage takes place at room temperature [113] for the adduct of *N*-(1-cyclohexenyl)morpholine and ketene [*(67a)*, CO in place of SO_2], the sulfene cycloadduct *(67a)* must be heated for several hours at 135 °C [43]. *(67b)* and *(67c)* are formed in the ratio 67:33.



[104] *R. Hoffmann* and *R. B. Woodward*, J. Amer. chem. Soc. *87*, 2046 (1965).

[105] *T. J. Katz* and *R. Dessau*, J. Amer. chem. Soc. *85*, 2172 (1963).

[106] *J. Sauer* and *H. Prahl*, Tetrahedron Letters *1966*, 2863.

[107] *R. Huisgen*, *L. Feiler*, and *G. Binsch*, Angew. Chem. *76*, 892 (1964); Angew. Chem. internat. Edit. *3*, 753 (1964).

[108] *J. C. Martin*, *V. W. Goodlett*, and *R. D. Burpitt*, J. org. Chemistry *30*, 4309 (1965).

[109] *G. Opitz* and *G. Stephan*, unpublished.

[110] *S. Mächtle*, Diploma Thesis, Universität Tübingen, 1966.

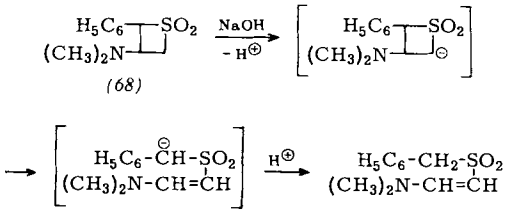
[111] *A. B. Burg*, J. Amer. chem. Soc. *65*, 1629 (1943).

[112] *G. Opitz*, *A. Griesinger*, and *H. W. Schubert*, Liebigs Ann. Chem. *665*, 91 (1963).

[113] *G. Opitz* and *F. Zimmermann*, Liebigs Ann. Chem. *662*, 178 (1963).

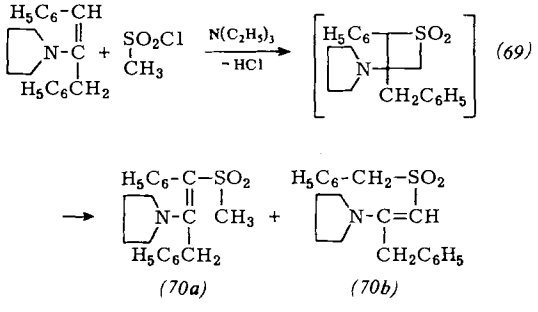
This reaction is of preparative interest, since the direct *C*-sulfonylation of *N*-(1-cyclohexenyl)morpholine with mesyl chloride is unsatisfactory even in the absence of NEt_3 [43].

Ring cleavage in 2-phenyl-3-dimethylaminothietane 1,1-dioxide has been achieved by heating with aqueous-methanolic sodium hydroxide solution [95]. The phenyl group probably promotes the reaction by delocalization of the negative charge.



(68)

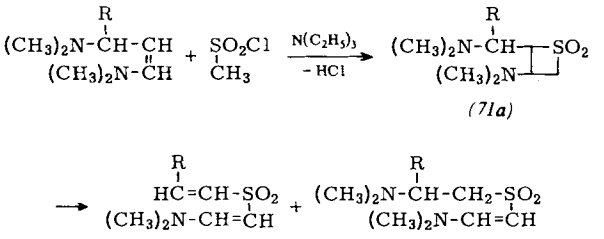
The enamine produced from dibenzyl ketone and pyrrolidine yields two open-chain sulfones *(70a)* and *(70b)*, and not the expected four-membered ring sulfone, when treated with mesyl chloride in ether.



(69)

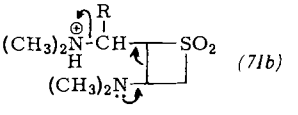
(70a) *(70b)*

Whereas the formation of the benzylsulfone *(70b)* is explicable only by assuming *(69)* to be intermediate, the isomeric methylsulfone *(70a)* can also be produced by direct *C*-sulfonylation of the enamine. Primary sulfonyl chlorides react analogously with this enamine [101]. Ring cleavage of the four-membered ring sulfones *(71a)*, which are obtained from γ-amino enamines, proceeds as readily (in THF at −20 °C) as for enolizable 3-amino-cyclobutanones [93].



(71a)

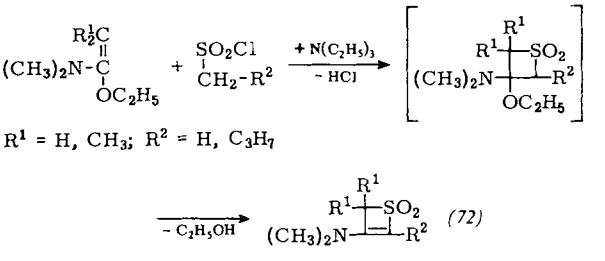
The reason for this probably lies in the ready fragmentation *(71b)* of the protonated diamine *(71a)* [93].



(71b)

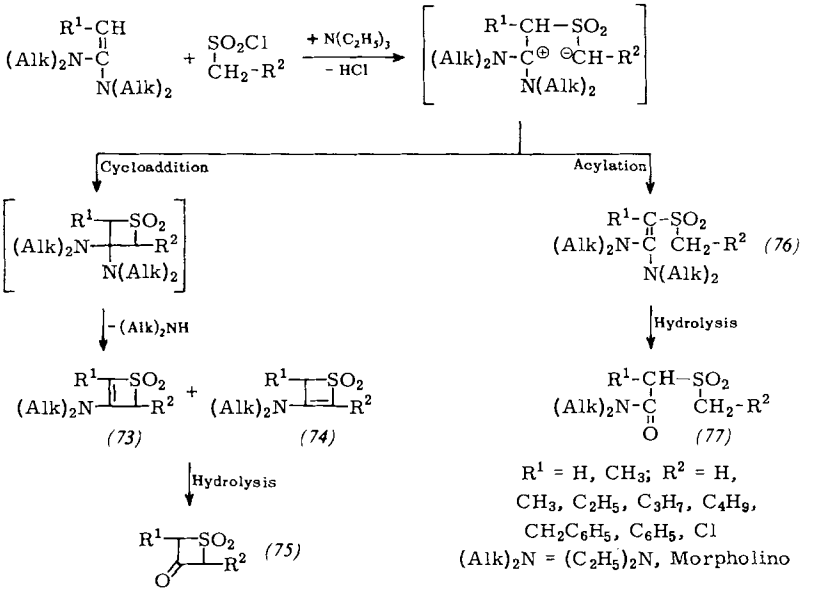
2. Ketene *O,N*- and *N,N*-Acetals

The cycloaddition of ketene *O,N*-acetals to sulfene is followed by spontaneous elimination of alcohol, leading to the formation of 3-dialkylaminothietene 1,1-dioxide *(72)* [114, 115].



(72)

Ketene *N,N*-acetals react similarly with elimination of dialkylamine, which reacts with part of the sulfonyl



(73) *(74)* *(75)* *(76)* *(77)*

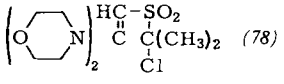
[114] *R. H. Hasek, P. G. Gott, R. H. Meen,* and *J. C. Martin,* J. org. Chemistry *28*, 2496 (1963).

[115] *R. H. Hasek, R. H. Meen,* and *J. C. Martin,* J. org. Chemistry *30*, 1495 (1965).

chloride. The unsaturated four-membered ring sulfones, which occur as mixtures of the isomers *(73)* and *(74)* when $R^1 \neq R^2$, are enamines, and can therefore be hydrolysed. The hydrolysis must be conducted carefully [114, 115], since 3-oxothietane 1,1-dioxide [*(75)*, $R^1 = R^2 = H$] is readily hydrolysed to mesylacetic acid [116]. The cycloaddition is accompanied by formation of open-chain sulfones; this is not surprising in view of the stabilization of the positive charge in the zwitterion [114–118] (with ketene instead of sulfene, only acylation is observed [119]). 1,1-Bis-(*N*-methylanilino)-2-methyl-1-propene is too inert for either reaction [116].

Since ketene *N,N*-acetals react with SO_2, the sulfenes cannot be produced from diazoalkane and SO_2 in this case [42].

The formation of open-chain sulfones is promoted by $R^1 = H$, by groups R^2 that, like C_6H_5, can accommodate the negative charge on the zwitterion, by substitution of the sulfene H atoms, as well as by polar solvents or solvents such as chloroform that dissolve the NEt_3–HCl. Thus the reaction of 1,1-dimorpholinoethylene and mesyl chloride/NEt_3 in ether, THF, or benzene gives 3-morpholinothietene 1,1-dioxide [*(73)*, $R^1 = R^2 = H$] in 69–92% yield, while in acetonitrile, DMF, or chloroform the same components give 1,1-dimorpholino-2-mesylethylene [*(76)*, $R^1 = R^2 = H$]. Primary sulfonyl chlorides, even in non-polar solvents, give open-chain sulfones as the main products, while these are the only products obtained with secondary sulfonyl chlorides. The formation of the very stable ketene *N,N*-acetal hydrochlorides [118, 103] gives rise to difficulties in the isolation of products, and in the hydrolysis of the sulfones *(76)* with hydrochloric acid to give the mesyl acetamides *(77)*.



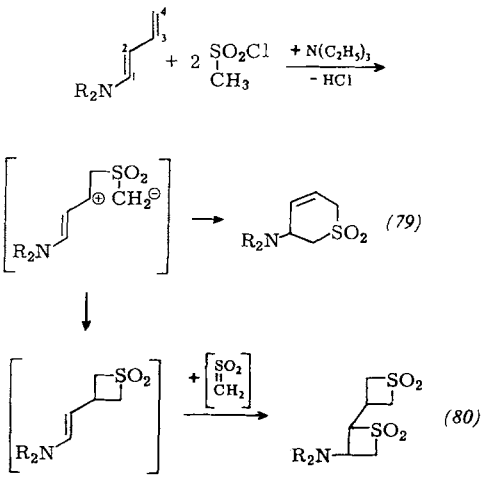
(78)

With 2-propanesulfonyl chloride the α-chlorosulfone *(78)* is formed as well as the normal product [*(78)*, H instead of Cl] [115]. According to recent observations [31], enamines can react analogously with secondary sulfonyl chlorides. Probably the zwitterionic primary adduct of olefin and sulfene is chlorinated by remaining sulfonyl chloride.

3. Dienamines

The butadienylamines, which give a Diels-Alder reaction even at 0 °C with ethyl acrylate, acrolein, acrylonitrile [120], and ketene [103], exhibit very interesting behavior on addition to sulfene. A 4+2 cycloaddition to give *(79)* competes fairly successfully with the double 2+2 cycloaddition leading to *(80)* [64, 93].

If electrophilic attack in position 4 is followed by ring closure in position 3, the product is an enamine, which reacts further with sulfene to form *(80)*. The cyclization in position 1, which is favored by a *cisoid* conformation

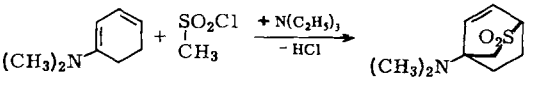


(79)

(80)

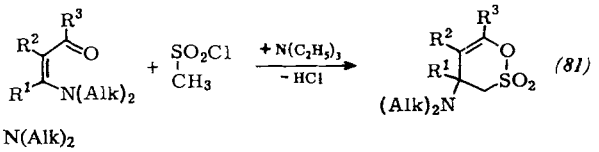
R_2N = Dimethylamino, diethylamino, pyrrolidino, piperidino, morpholino.

of the dienamine, leads to the stable allylamine *(79)*. If the cisoid structure is fixed, only the Diels-Alder reaction is observed [121].



4. β-Aminovinyl Ketones

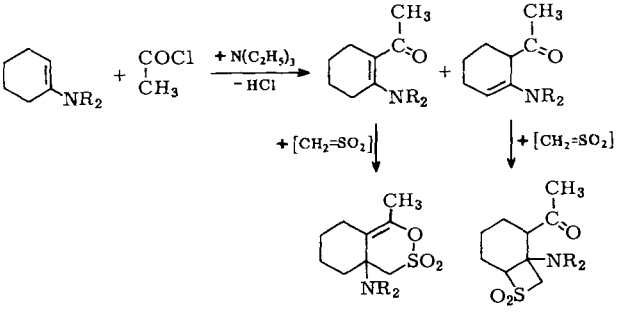
Sulfene acts as a dienophile toward β-aminovinyl ketones [63], giving good yields of the crystalline enol sultones *(81)*; the yield is low only when $R^1 = CH_3$, owing to side reactions [121]. The ring closure corresponds to the formation of α-pyrones with ketene [122].



(81)

$N(Alk)_2$				
Piperidino;	$R^1 = H$;	$R^2 = CH_3$;	$R^3 = CH_3$;	80%
Pyrrolidino;	$R^1 = H$;	$R^2 = H$;	$R^3 = CH(CH_3)_2$;	75%
Dimethylamino;	$R^1 = CH_3$;	$R^2 = H$;	$R_3 = CH_3$;	7%

With the aid of this 4+2 cycloaddition and the 2+2 cycloaddition of sulfene to enamines, it can be shown that the acetylation of cyclohexenylamines leads to mixtures of the vinylogous carbonamide and the unconjugated isomer [63].



NR_2 =			
Pyrrolidino	32%	8%
Piperidino	9%	57%
Morpholino	5%	66%

[116] *G. Opitz* and *H. Schempp*, Liebigs Ann. Chem. *684*, 103 (1965).

[117] *G. Opitz* and *H. Schempp*, Z. Naturforsch. *19b*, 78 (1964).

[118] *W. E. Truce* and *P. N. Son*, J. org. Chemistry *30*, 71 (1965).

[119] *G. Opitz* and *F. Zimmermann*, Chem. Ber. *97*, 1266 (1964).

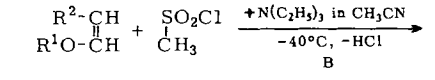
[120] *S. Hünig* and *H. Kahanek*, Chem. Ber. *90*, 238 (1957).

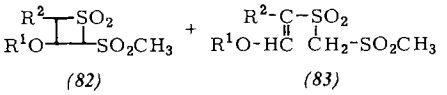
[121] *G. Opitz* and *F. Schweinsberg*, unpublished.

[122] *G. A. Berchtold*, *G. R. Harvey*, and *G. E. Wilson jr.*, J. org. Chemistry *26*, 4776 (1961).

5. Vinyl Ethers

Vinyl ethers undergo 2+2 cycloaddition with mesylsulfene to give the four-membered ring sulfones *(82)*, together with small quantities of the enol ethers *(83)* [123].



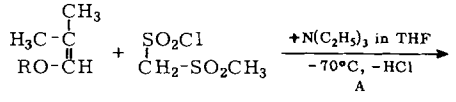


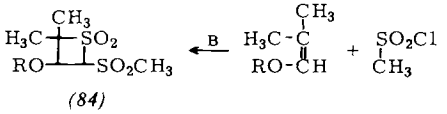
(82) *(83)*

$R^1 = C_2H_5$; $R^2 = H$	60%	22%
$R^1 + R^2 = (CH_2)_3$	70%	little

The fact that the mesylsulfene can be produced *in situ* either from mesylmethanesulfonyl chloride/NEt_3 in THF at −70 °C (route A) or from mesyl chloride/NEt_3 in acetonitrile at −40 °C (route B) shows that vinyl ethers do not react with simple sulfenes, since route B proceeds *via* sulfene (see Scheme 1). In the convenient and successful route B, the polar acetonitrile favors the formation of open-chain sulfones. This reaction is not so important in route A, which is little used at present.

With alkyl isobutenyl ethers, which cannot form open-chain sulfones, the cycloaddition by route B is almost quantitative, though the mesyl chloride must first be converted by at least three reaction steps into mesylsulfene.





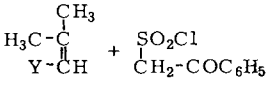
(84)

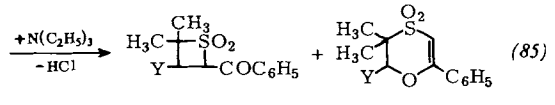
$R = CH_3$	A 75%; B 85%
$R = C_2H_5$	A – ; B 90%

The four-membered ring sulfones, which form beautiful crystals, are unstable to alkalis. 3-Ethoxy-2-mesylthietan 1,1-dioxide *[(82)*, $R^1 = C_2H_5$, $R^2 = H$], which is particularly sensitive to alkalis, is degraded to dimesylmethane $(CH_3{-}SO_2)_2CH_2$ by 2N NaOH.

Vinyl ethers evidently undergo cycloaddition with strongly electrophilic sulfenes only.

Methoxycarbonyl sulfene does not react [96]. Benzoyl sulfene undergoes 4+2 cycloaddition with the enol ether





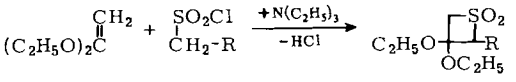
(85)

Y = 1-Pyrrolidinyl	40%	0%
Y = C_2H_5O	0%	42%

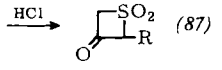
from isobutyraldehyde to give *(85)* [Y = alkoxy] and not 2+2 cycloaddition, as with the corresponding enamines [62].

6. Ketene Acetals

The more reactive ketene diethyl acetal adds to sulfene [124,43], which must be produced from mesyl chloride/NEt_3, since only thiirane dioxide is obtained when diazomethane/SO_2 is used [42]. The yield (24–68%) of 3,3-bis(ethoxy)thietane 1,1-dioxide *[(86)*, R = H], which is hydrolysed to 3-oxothietane 1,1-dioxide *[(87)*, R = H, yield 70%] by concentrated hydrochloric acid [125, 126], exhibits an unexpected dependence on the solvent [12]. In the absence of NEt_3 other products are formed [127].



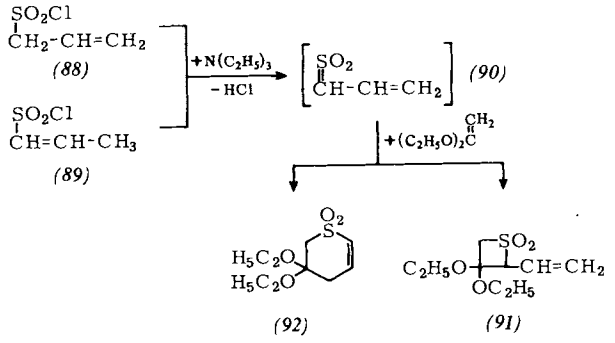
R = H, Ar, Cl, CF_3 *(86)*



(87)

Cycloaddition with primary sulfonyl chlorides occurs only if R is aromatic or electron-attracting [12, 118]. The particularly reactive *p*-nitrophenylmethanesulfonyl chloride gives 54% of the cycloadduct together with a little 4,4′-dinitrostilbene. Nothing is known about acylations.

An indication of the intermediate formation of sulfenes is provided by the observation by *Truce* and *Norell* [12] that the isomeric propenesulfonyl chlorides *(88)* and *(89)* give the four-membered ring sulfone *(91)* [46% from *(88)* and 51% from *(89)*] and the six-membered ring sulfone *(92)* [7% from *(88)* and 8% from *(89)*] in mixtures having almost the same composition.



(88) *(89)* *(90)* *(92)* *(91)*

Corresponding to its formation by 1,2- and 1,4-elimination, vinylsulfene *(90)* can undergo 1,2- and 1,4-cycloaddition. Its low tendency to enter into 1,4 addition with ketene acetal to form *(92)* and AlkOD (see Section C I 2a) is explained by the inductive effect of the SO_2 group.

[123] *G. Opitz, K. Rieth*, and *G. Walz*, Tetrahedron Letters *1966*, 5269.

[124] *W. E. Truce, J. J. Breiter, D. J. Abraham*, and *J. R. Norell*, J. Amer. chem. Soc. *84*, 3030 (1962).

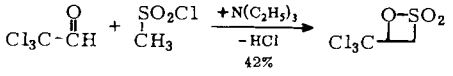
[125] *W. E. Truce* and *J. R. Norell*, Tetrahedron Letters *1963*, 1297.

[126] *W. E. Truce* and *J. R. Norell*, J. Amer. chem. Soc. *85*, 3236 (1963).

[127] *W. E. Truce, D. J. Abraham*, and *P. S. Radhakrishnamurti*, Tetrahedron Letters *1963*, 1051.

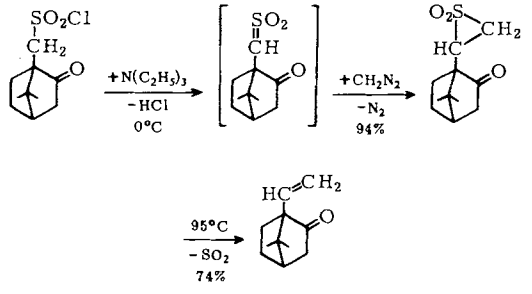
7. Chloral

The cycloaddition of sulfene to chloral corresponds to the formation of β-lactones from ketene and carbonyl compounds that undergo spontaneous hydration. In cold ether, the β-sulfone is obtained in 42% yield [128].



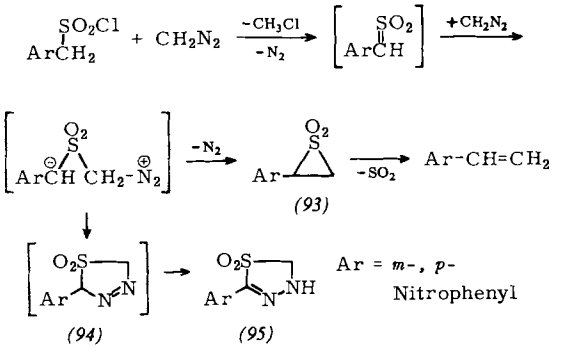
8. Diazoalkanes

The preparative disadvantage of the Staudinger-Pfenninger reaction (see Section C II), *i.e.* the fact that it yields only symmetrical olefins, can be overcome by the production of another sulfene from sulfonyl chloride and NEt_3 in the presence of a diazoalkane [129]. The sulfene is immediately intercepted by the diazoalkane, showing that diazoalkanes are much more reactive sulfene interceptors than sulfonyl chlorides.



Both symmetrical and unsymmetrical olefins, as well as their epithio *S,S*-dioxides, can be prepared in this way from mesyl chloride or primary sulfonyl chlorides and diazomethane, diazoethane, 1-diazo-2-methylpropane, and 2-diazobutane [39,129,130,42,56]. As in the reaction of diazoalkanes with SO_2, there appears to be no preference for the formation of the *cis*-olefin [130].

With *m*- and *p*-nitrophenylmethanesulfonyl chloride, the addition of triethylamine is unneccessary, since excess diazomethane acts as the HCl acceptor. In cold ether the reaction yields the epithio *S,S*-dioxide of nitrostyrene *(93)* and 2-nitrophenyl-Δ^2-[1,3,4]-thiadiazoline 1,1-dioxide *(95)*, which forms nitrobenzonitrile on hydrolysis [80].



[128] *D. Borrmann* and *R. Wegler*, Chem. Ber. *99*, 1245 (1966).

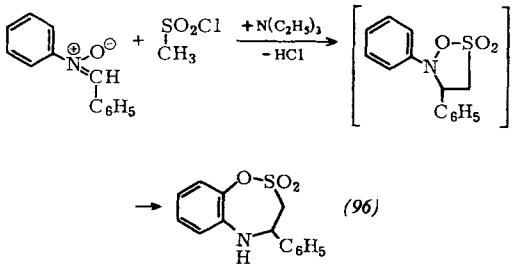
[129] *G. Opitz* and *K. Fischer*, Angew. Chem. *77*, 41 (1965); Angew. Chem. internat. Edit. *4*, 70 (1965).

[130] *G. Opitz* and *N. Fischer*, unpublished.

In view of the properties (see Section C II) of 2,5-diethyl-2,5-dicyclohexyl-Δ^3-[1,3,4]-thiadiazoline 1,1-dioxide [*(45)*, $R_2 = C_2H_5$, C_6H_{11}], it is unlikely that *(94)* can be converted into the three-membered ring sulfone *(93)* before isomerization to form *(95)*. This reaction therefore provides a further argument in favor of the view that the olefin *(51)* (Scheme 3) is not formed *via* the Δ^3-[1,3,4]-thiadiazoline 1,1-dioxide *(45)*.

9. Nitrones

Sulfene acts as a dipolarophile toward *N*-benzylideneaniline *N*-oxide. This can be deduced from the formation of the [1,2,5]-oxathiazepine *S,S*-dioxide derivative *(96)* in 63% yield [131].

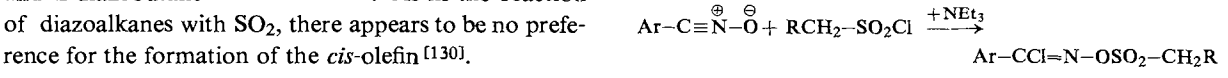


(96)

The migration of a sulfonyloxy group from the N atom of aniline into the *o* position following the 3+2 cycloaddition has also been observed with the benzoyloxy group [132].

10. Unsuccessful Interception Attempts

The reaction of nitrile oxides with methane- or phenylmethanesulfonyl chloride/NEt_3 leads to sulfonates of hydroxamyl cnlorides. No 1,3-dipolar cycloadditions have been achieved [47,133,134].



The structure of the products obtained with Schiff bases [42] has not yet been estaolished. Attempted cycloadditions of sulfenes produced *in situ* with anthracene and cyclohexene [43], with acrolein, ethyl acrylate, hexachlorobutadiene, trifluorochloroethylene, 1-ethoxy-1-ethylthioethylene, 1,1-bis-(*p*-methoxyphenyl)ethylene, 1,1-bis-(*p*-dimethylaminophenyl)ethylene, and phenylimino diethyl carbonate [12], with diphenylketene, 1,1-bis-(ethylthio)ethylene, 1,1-dichloroethylene, cyclopentadiene, and *p*-tolylthioethylene [124], with phenylacetylene, 1-methoxy-1-buten-3-yne, and 1,2-bis(ethoxy)ethylene [42], and with benzylideneaniline [12,42], vinyl ethyl ether [124,42], ethoxyacetylene [43,124], and tetramethoxyethylene [135] were unsuccessful.

[131] *W. E. Truce, J. R. Norell, R. W. Campbell, D. G. Brady*, and *J. W. Fieldhouse*, Chem. and Ind. *1965*, 1870.

[132] *L. Horner* and *H. Steppan*, Liebigs Ann. Chem. *606*, 47 (1957).

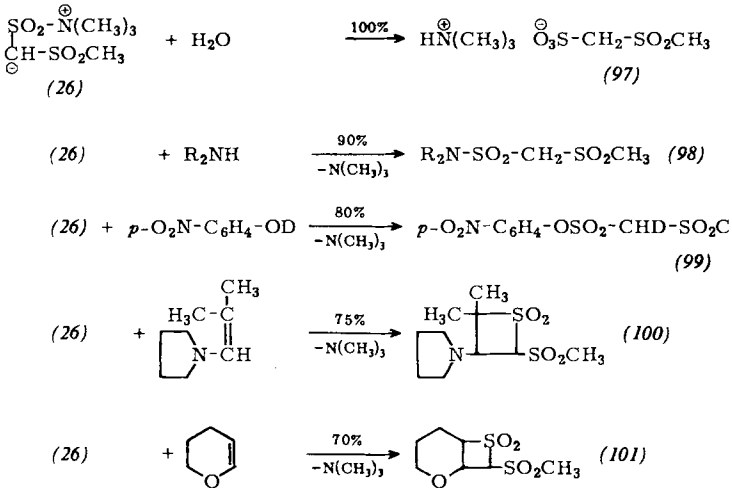
[133] *J. F. King* and *T. Durst*, Canad. J. Chem. *44*, 409 (1966).

[134] *P. Rajagopalan* and *C. N. Talaty*, Tetrahedron Letters *1966*, 2101.

[135] *R. W. Hoffmann* and *H. Häuser*, Angew. Chem. *76*, 346 (1964); Angew. Chem. internat. Edit. *3*, 380 (1964).

VI. Reactions of the Mesylsulfene-Trimethylamine Adduct

As was described in Section C I 2d, mesylchloride reacts with trialkylamines in acetonitrile at −40 °C to form mesylsulfene, which adds on to an excess of amine [58,59]. Trimethylamine stabilize the mesylsulfene to such an extent that the adduct *(26)* can be isolated at room temperature in air as a white, finely crystalline powder (yield 60%) which decomposes at 126–130 °C. The NMR spectrum, with singlets at $\tau = 5.6$ (CH), 6.9 (CH_3SO_2), and 7.0 [$N(CH_3)_3$] in the ratio 1:3:9, shows the ammonium character of the adduct [$N(CH_3)_3$:τ = 7.9; $^{\oplus}N(CH_3)_4$:τ = 6.7] and the small influence of the negative charge on the chemical shift of the methine proton [$CH_3SO_2\underline{C}H_2SO_2N(CH_3)_2$:$\tau$ = 5.6]. The hydrolysis with water to form trimethylammonium mesylmethanesulfonate *(97)* is complete only after about 5 hours at 36 °C, so that the reaction can be conveniently followed by IR and NMR spectroscopy.



(26), and the analogous mesylsulfene-triethylamine adduct, react with aniline, dimethylamine, and pyrrolidine to form the amides *(98)*. The reaction of *(26)* with p-O_2N–C_6H_4–OD gives the ester *(99)* of mesylmethanesulfonic acid, which is monodeuterated in the methylene group, and with *N*-(2-methyl-1-propenyl)-pyrrolidine and 2*H*-dihydropyran to give the fourmembered ring sulfones *(100)* and *(101)* respectively. The same compounds are formed when the mesylsulfene-amine adducts are replaced by CH_3SO_2–CH_2–SO_2Cl/NEt_3 [50].

VII. Future Prospects

56 years after the first experiments by *Wedekind* and *Schenk* [3], the concept of the formation of sulfenes from sulfonyl chlorides by dehydrochlorination with trialkylamine may be assumed to have been vindicated. The indirect proof of the existence of sulfenes by interception reactions has now been followed by direct proof in the isolation of a sulfene as the trimethylamine adduct. The next step must be the detection and isolation of free sulfenes. Only then will it be possible to answer the questions that still remain open: How does the life of free sulfenes depend on structure and temperature? What is the nature of the bonding? Why do sulfenes fail to polymerize? Do simple sulfenes also form amine adducts?

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Nickel-Catalysed Reactions of Allyl Halides and Related Compounds

BY G. P. CHIUSOLI AND L. CASSAR [*]

Allyl compounds react with carbon monoxide, or with carbon monoxide and acetylene, in the presence of tetracarbonylnickel as catalyst. These catalysts are involved also in coupling reactions and addition reactions of activated olefins and ketones. Reactions of this type can be used for the preparation of unsaturated aliphatic acids, esters, nitriles, hydrocarbons, alicyclic ketones, keto acids, keto esters, diketones, lactones, phenols, and other compounds. The reactions proceed via π-allylnickel complexes.

1. Preparation of Unsaturated Acids and Esters from Allyl Compounds, Acetylene, and Carbon Monoxide

a) Reaction of Allyl Halides

In earlier publications [1,2] we described two reactions for the preparation of unsaturated acids or esters by "carbonylation" with tetracarbonylnickel as the catalyst:

$$RCH{=}CH{-}CH_2X + CO + R'OH \xrightarrow[Ni(CO)_4]{} RCH{=}CH{-}CH_2{-}COOR' + HX \quad (a)$$

$$RCH{=}CH{-}CH_2X + HC{\equiv}CH + CO + R'OH \xrightarrow[Ni(CO)_4]{} RCH{=}CH{-}CH_2{-}CH{=}CH{-}COOR' + HX \quad (b)$$

R = alkyl, aryl, H; R' = alkyl, aryl, H; X = Cl, Br, I; some of the hydrogen atoms in the allyl group may be replaced by alkyl groups.

Reaction (a) gives β,γ-unsaturated compounds, while reaction (b) yields compounds with double bonds in both the α,β and δ,ε positions, the α,β substituents being *cis* to each other.

Reaction (a) is carried out at room temperature and at 2–3 atm pressure. The reaction is suppressed at higher pressures unless the temperature is also raised, whereas lower pressures favor dimerization of the allyl groups. Generally the yields do not exceed 50%. Reaction (b) is best carried out at room temperature and at atmospheric pressure (yield up to 80%). In both cases, the start of the reaction is characterized by a strong reddish coloration of the reaction mixture, which changes to green toward the end of the reaction.

If the compound is a secondary halide that can rearrange to a primary halide, it reacts in the primary form; *e.g.* $CH_3{-}CHCl{-}CH{=}CH_2$ reacts as $CH_3{-}CH{=}CH{-}CH_2Cl$ [2a]. The same is true of tertiary halides, which do not react as such, even under the usual mild conditions (0–50 °C), but rearrange first to give secondary halides.

When inert solvents (*e.g.* ethers or aromatic hydrocarbons) are used, the products are acyl halides [2a, 3b]. Reactions (a) and (b) are best carried out in dilute solution in the presence of an excess of tetracarbonylnickel (more than 1 mole per mole of allyl compound). Table 1 shows some methyl esters obtained *via* equation (b). No attempt was made to determine the optimum conditions for their syntheses.

Table 1. Methyl esters of 2-*cis*-5-dienoic acids obtained at 20 °C in methanol in accordance with eq. (b).

R''CH=CH–COOCH$_3$ R''– =	B.p. (°C/mm)	Yield (%)
$CH_2{=}CH{-}CH_2{-}$	62–63/28	70
$CH_3{-}CH{=}CH{-}CH_2{-}$	73–75/20	81
$CH_2{=}C(CH_3)CH_2{-}$	62–63/16	80
$CH_3{-}CH{=}CH{-}CH(CH_3){-}$	75–78/20	40
$CH_3{-}C(CH_3){=}CH{-}CH_2{-}$	85–86/12	35
$CH_3{-}(CH_2)_2{-}CH{=}CH{-}CH_2{-}$	69–70/2	62
$CH_3{-}(CH_2)_4{-}CH{=}CH{-}CH_2{-}$	68–70/0.4	73
$CH_3{-}(CH_2)_6{-}CH{=}CH{-}CH_2{-}$	103–104/1	64
$CH_3{-}(CH_2)_{14}{-}CH{=}CH{-}CH_2{-}$	150–156/0.2	48
$CH_3{-}C(CH_3)_2{-}CH_2{-}CH{=}CH{-}CH_2{-}$	97–100/8	55
$H_3COCO{-}CH{=}CH{-}CH_2{-}$	79–81/1	40
$H_3COCO{-}CH_2{-}CH{=}CH{-}CH_2{-}$	126–130/6	32
$H_3COCO{-}CH{=}CH{-}CH_2{-}CH{=}CH{-}CH_2{-}$	140–141/5	80
$H_3COCO{-}CH{=}C(CH_3){-}CH_2{-}$	81–82/1	45
$H_3C{-}COO{-}CH_2{-}CH{=}CH{-}CH_2{-}$	115–117/5	35
$NC{-}CH_2{-}CH{=}CH{-}CH_2{-}$	133–134/7	79
2-Cyclopenten-1-yl	92–96/12	50
2-Cyclohexen-1-yl	105–108/12	50
$C_6H_5{-}CH{=}CH{-}CH_2{-}$	155–160/5	54
$H_3COCO{-}CH{=}CH{-}CH_2{-}CH{=}CH{-}CH_2{-}CH_2{-}CH{=}CH{-}CH_2{-}$	150–155/0.3	19

Part of the tetracarbonylnickel enters into non-catalytic side reactions in which it is converted into nickel halide, *e.g.* with dimerization [eq. (c)], or hydrogenation [eq. (d)] of the allyl group.

$$2\,RCH{=}CH{-}CH_2X + Ni(CO)_4 \longrightarrow RCH{=}CH{-}CH_2{-}CH_2{-}CH{=}CHR + NiX_2 + 4\,CO \quad (c)$$

$$RCH{=}CH{-}CH_2X + Ni(CO)_4 + H_2O \longrightarrow RCH_2{-}CH{=}CH_2 + NiOHX + 4\,CO \quad (d)$$

Reaction (b) may also yield by-products, such as acrylic acids or esters, from acetylene and carbon monoxide; however, the formation of these products can be suppressed by neutralization of the hydrogen chloride liberated.

[*] Priv.-Doz. Dr. G. P. Chiusoli and Dr. L. Cassar
Instituto di Ricerche "G. Donegani",
Società Montecatini-Edison,
4 Via del Lavoro, Novara (Italy)

[1] *G. P. Chiusoli*, Angew. Chem. *72*, 74 (1960).

[2] a)–d): *G. P. Chiusoli*, Chim. e Ind. (Milano) *41*, 503, 506, 512, 762 (1959); e) *G. P. Chiusoli* and *S. Merzoni*, *ibid*, *43*, 259 (1961); f) *G. P. Chiusoli*, *G. Bottaccio*, and *A. Cameroni*, *ibid. 44*, 131 (1962); g) *G. P. Chiusoli* and *S. Merzoni*, *ibid. 45*, 6 (1963); h) *G.P. Chiusoli*, *S. Merzoni*, and *G. Mondelli*, *ibid. 46*, 743 (1964); i) *G. P. Chiusoli* and *G. Bottaccio*, *ibid. 47*, 165 (1965).

3-Chloro-1-propyne (propargyl chloride) reacts with carbon monoxide, water, and tetracarbonylnickel to give 2,3-butadienoic acid and itaconic acid. The similarity between this and the reaction of allyl chloride is, however, purely formal. *Jones et al.* interpreted this reaction as a variant of the oxo synthesis [3].

Generally allyl halide groups can be produced easily in olefins *e.g.* by "substitutive chlorination" with chlorine. An atom of bromine can be introduced into the allyl position in an olefin by means of *N*-bromosuccinimide, while an allyl H atom can be replaced by a hydroxyl or acetoxy group on oxidation with air in the presence of *e.g.* $PdCl_2$ [51] or cobalt acetate [52].

b) Reactions of Other Allyl Compounds

Unsaturated acids and esters [2d, 2g] can also be synthesized by reaction (b) when allyl alcohols, ethers, and esters [eq. (e)] are used, *e.g.*

$$RCH{=}CH{-}CH_2OH + CH{\equiv}CH + CO \xrightarrow[HCl]{Ni(CO)_4} RCH{=}CH{-}CH_2{-}CH{=}CH{-}COOH \qquad (e)$$

($RCH{=}CH{-}CH_2{-}CH{=}CH{-}COOCH_2{-}CH{=}CHR$ is a by-product in water/acetone).

These reactions are carried out in the presence of less hydrogen chloride than is required for the formation of allyl chlorides. The yields ($\approx$ 80–85%) are generally higher than when allyl chlorides are used [eq. (b)], since the latter reaction is impeded by the nickel chloride which is formed in the side reaction (c).

If higher temperatures ($\approx$ 130 °C) are used, allyl esters react with tetracarbonylnickel, even in the absence of hydrogen chloride, to form allyl groups, carbon monoxide, and nickel salts [3a]. An example of the use of allyl esters is the reaction of 4-chloro-2-butenyl acetate. When *cis*-1,4-dichloro-2-butene is treated with tetracarbonylnickel, carbon monoxide, and acetylene in methanol it decomposes, mainly into *cis*-2-butene and butadiene; if one of the chlorine atoms is replaced by an acetoxy group, the resulting compound reacts with acetylene, carbon monoxide, and methanol (with careful neutralization of the hydrogen chloride liberated) to form methyl 7-acetoxy-2,5-heptadienoate *(1a)* [catalyst $Ni(CO)_4$].

$$H_3C{-}CO{-}O{-}CH_2{-}CH{=}CH{-}CH_2{-}CH{=}CH{-}COOCH_3 \quad (1a) \quad + HC{\equiv}CH + CO \xrightarrow[HCl]{Ni(CO)_4} H_3COOC{-}CH{=}CH{-}CH_2{-}CH{=}CH{-}CH_2{-}CH{=}CH{-}COOCH_3 \quad (1b)$$

The "acetoxyallyl" group (of 1a) can then be made to react in the presence of hydrogen chloride to give dimethyl 2,5,8-decatrienedioate *(1b)*, which forms dimethyl sebacate on hydrogenation [4]. A further example is the use of allyl acrylate instead of allyl halides. Allyl acrylate can be obtained directly from two molecules of acrolein; it reacts with carbon monoxide, methanol and acetylene in the presence of hydrogen chloride and tetracarbonylnickel to give methyl acrylate and methyl 2,5-hexadienoate [5].

c) Catalysis under Pressure

The use of acetylene and carbon monoxide under pressure permits catalysts to be employed which do not decompose in secondary reactions. Using salts such as nickel benzenesulfonate, and complexes such as that of nickel bromide with acetylacetone, 2,5-dienoic acids can be prepared from allyl halides, alcohols, ethers, and esters. According to *Reppe*, esters of acrylic acid are formed under these conditions from acetylene and carbon monoxide [5a]. However, this reaction can be suppressed by the use of low partial pressures of acetylene [2h, 6].

For example, allyl alcohol in methanol (previously saturated with 8 atm of C_2H_2 and 38 atm of CO at 15 °C) at 170 °C is converted into methyl 2,5-hexadienoate (16% conversion) in 4 hours; the product is partly isomerized to methyl 3,5- and 2,4-hexadienoate. The yield is 80% if methyl allyl ether and diallyl ether are recycled in the system.

d) New Catalysts

A new method which we have developed, and in which finely divided nickel and thiourea or iron powder, nickel chloride, and thiourea is used as catalyst, seems even more advantageous [2e, 2h]. With these systems the reaction can be carried out at or even below room temperature (−30 °C with Raney nickel/thiourea) and at atmospheric pressure in the absence of tetracarbonylnickel. This new method is useful for the preparation of esters according to equation (b); on the other hand, tetracarbonylnickel is recommended for the synthesis of acids (equation (b) where R′ = H). Tetracarbonylnickel can be conveniently prepared from carbon monoxide, iron powder, nickel chloride, and sulfides in water [2e, 2h, 7]:

$$Fe + NiCl_2 + 4\,CO \longrightarrow Ni(CO)_4 + FeCl_2$$

2. Properties of the 2,5-Dienoic Acids and their Esters

a) Isomerization

The 2,5-dienoic acids and esters obtained according to equation (b) have the *cis* configuration about the α,β double bond. On treatment with cold alkalis the compounds rearrange, first into the less stable, and then into

[3] *E. R. H. Jones, G. H. Witham,* and *M. C. Whiting,* J. chem. Soc. (London) *1957,* 4628.

[3a] *M. Dubini, G. P. Chiusoli,* and *F. Montino,* Tetrahedron Letters *1963,* 1591.

[4] *G. P. Chiusoli* and *G. Bottaccio,* Ital. Pat. 685450 (1965).

[5] *G. P. Chiusoli* and *S. Merzoni,* Ital. Pat. 665034 (1964).

[5a] *W. Reppe*: Neue Entwicklungen der Chemie des Acetylens und Kohlenoxyds. Springer, Berlin 1949; Liebigs Ann. Chem. *582,* 1 (1953).

[6] *G. P. Chiusoli* and *S. Merzoni,* Ital. Pat. 675616 (1964); Ital. Pat. Application 34997/63 (Milan).

[7] *G. P. Chiusoli* and *G. Mondelli,* Brit. Pat. 983221 (1965).

the more stable dienoic acids or esters [8]. (In the case of straight-chain compounds, the 3,5-isomers are the less stable and the 2,5-isomers the more stable compounds.) This agrees with the principle that the first product in kinetically controlled reactions is the thermodynamically least stable product [8a].

Investigation of the tautomerism of these "five-carbon systems" activated by carboxyl or alkoxycarbonyl groups, enabled us to isolate 3,5- and 2,4-dienoic acid derivatives. Some of these derivatives, *e.g.* sorbic acid (2,4-hexadienoic acid), are important commercial products.

Prolonged treatment of the 2,5-dienoic esters with an excess of ammonia yields tautomeric amides, generally the amides of the 3,5-dienoic acids [9]. The amides of the 2,5-dienoic acids are best prepared by careful reaction of the 2,5-dienoic ester with thionyl chloride and ammonia [9a]. The derivatives of the 3,5- and 2,4-dienoic acids give Diels-Alder adducts with maleic anhydride; with 3,5-dienoic acids such adducts are formed immediately the components are mixed.

2,5-Diene derivatives having a *cis* configuration about the α,β double bond can be converted into the *trans* form by treatment with sulfide radicals [10]. The properties of some *cis-trans*-isomeric methyl dienoates are listed in Table 2.

Table 2 Properties of *cis-trans*-isomeric methyl 2,5-dienoates [10]; for UV and IR absorptions of the 3,5 and 2,4 derivatives see [8, 50].

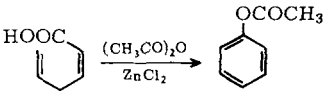
Methyl ester of	B.p. (°C/mm)	n_D^{20}	λmax [a] (mμ)	log ε	Characteristic IR frequencies (cm^{-1})		
					Stretching frequencies		Deformation frequencies
					>C=O	–C=C–	H–C=C–
2-*cis*-5-Hexadienoic acid	62—63/28	1.4483	205	4.12	1730	1652 1630 (vinyl)	818 995, 915 (vinyl)
2-*trans*-5-Hexadienoic acid	72—73/28	1.4510	206	4.16	1722	1655 1640 (vinyl)	985 995, 915 (vinyl)
2-*cis*-5-*trans*-Hepta-dienoic acid	73—75/20	1.4558	203	4.13	1730	1648	819 968
2-*trans*-5-*trans*-Hepta-dienoic acid	83—84/20	1.4575	203.5	4.18	1723	1655	985 968
5-Methyl-2-*cis*-5-hexa-dienoic acid	62—63/16	1.4529	203	4.12	1722	1650 1641 (vinylidene)	812 890 (vinylidene)
5-Methyl-2-*trans*-5-hexa-dienoic acid	70—72/16	1.4550	203.5	4.16	1722	1657 1641 (vinylidene)	980 894 (vinylidene)

[a] In n-hexane.

b) Cyclization

cis- or *trans*-Dienoic acids and their esters can be cyclized to form phenols by heating in acidic or alkaline media or preferably in acetic anhydride [11]. Phenols are also formed, generally in very small quantities, during the synthesis according to eq. (b) from allyl halides, acetylene, and carbon monoxide.

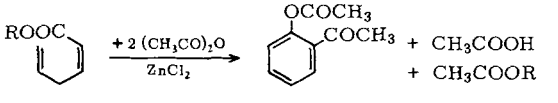
When 2-*cis*-5-hexadienoic acid, in the absence of solvent, is brought into contact with zinc or aluminum chloride or with other chlorides used as catalysts in the Friedel-Crafts reaction, a vigorous reaction, which is difficult to control, takes place and moderate quantities of phenol are formed. The reaction proceeds less vigorously in acetic anhydride and almost quantitative yields of phenol (as the acetate) are obtained.



3,5-Hexadienoic acid reacts in a similar manner, whereas 2,4-hexadienoic acid does not react under these conditions; 5-methyl-2-*cis*-5-hexadienoic acid yields *m*-cresol acetate in a remarkably pure state.

ω-Alkylhexadienoic acid derivatives do not react under these conditions to give phenols, whereas ω-carboxy derivatives do so. For example, salicyclic acid (as the acetate) can be obtained on treatment of 2,5- or 3,5-heptadiendioic acid with $ZnCl_2$ in acetic anhydride.

The system sodium acetate/acetic anhydride has been found suitable for the ω-alkyl compounds; it is possible in this way to obtain excellent yields of *o*-cresol by cyclization of 2,5- or 3,5-heptadienoic acid, and of 1,5-dihydroxynaphthalene by cyclization of 2,5,8- or 3,5,7-decatriendioic acid (products as acetates; catalyst: zinc chloride). The reaction of 2,5-hexadienoic esters in acetic anhydride leads to *o*-acetylation of the nucleus [12].



Phenols are formed when 2,5-dienoyl chlorides are allowed to react in the presence of finely divided metals, *e.g.* iron or palladium, in solvents such as benzene [12]. Thus, the reaction of 2,5-hexadienoyl chloride in the presence of palladium in boiling benzene yields phenol and HCl.

[8] *G. P. Chiusoli* and *S. Merzoni*, Chim. e Ind. (Milano) *43*, 256 (1961).

[8a] *C. K. Ingold*: Structure and Mechanism in Organic Chemistry. Cornell, New York 1953, p. 565.

[9] *G. P. Chiusoli*, Angew. Chem. *72*, 750 (1960).

[9a] *G. Agnès*, unpublished.

[10] *G. P. Chiusoli, G. Agnès, C. A. Ceselli*, and *S. Merzoni*, Chim. e Ind. (Milano) *46*, 21 (1964).

[11] *G. P. Chiusoli* and *G. Agnès*, Chim. e Ind. (Milano) *46*, 25 (1964).

[12] *G. P. Chiusoli* and *G. Agnès*, Chim. e Ind. (Milano) *46*, 548 (1964).

3. Substitutive Hydrogenation

Allyl halides with electron-attracting substituents such as $COOCH_3$, CN, or $CONH_2$ on the allyl carbon atoms [*] do not react with carbon dioxide in aqueous alcohol; instead, the halogen atom is replaced by a hydrogen atom from the solvent [2f]. Allyl rearrangement leads mainly to the less stable of the two tautomers. This is illustrated by reaction (f).

$$ClCH_2-CH=CH-CN + Ni + H_2O \longrightarrow CH_2=CH-CH_2-CN + NiOHCl \quad (f)$$

The reaction proceeds rapidly and the yields of $CH_2=CH-CH_2-CN$ are almost quantitative. The equilibrium between the two tautomers is established more quickly if the allyl carbon atoms carry alkyl substitutents.

2-Chloro-4-phenyl-3-butenonitrile gives the compound $C_6H_5-CH=CH-CH_2-CN$ almost quantitatively.

It is immaterial whether the halogen is attached to the C-1 or the C-3 carbon atoms of the allyl group; thus $CH_2=CH-CH(Cl)CN$ and $ClCH_2-CH=CH-CN$ [in eq. (f)] give the same product. This suggests the possibility of the following reaction:

$$RCH=CH-CHO \xrightarrow{HCN} RCH=CH-CHOH-CN \xrightarrow[Ni(CO)_4]{HCl} RCH_2-CH=CH-CN \text{ or } RCH=CH-CH_2-CN$$

4. Dimerization

Allyl halides form linear dimers on reaction with tetracarbonylnickel in alcohols. Allyl halides with electron-attracting substituents, however, do not form dimers in aqueous alcohol since the halogen is replaced by a hydrogen atom. If required, the dimers can be obtained in good yields in benzene, ether, *etc.* Irrespective of the steric nature of the allyl halide, the final product is predominantly *cis,cis* and *cis,trans* or *trans,trans* and *cis,trans*, depending on the nature of the electron-attracting substituents [13]. For example, when heated with tetracarbonylnickel in diethyl ether, 4-chloro-2-butenonitrile yields about 64% of *cis,cis*- and about 30% of *cis,trans*-2,6-octadienodinitrile, while methyl 4-chloro-2-butenoate yields about 38% of dimethyl *trans,trans*- and about 62% of dimethyl *cis,trans*-2,6-octadienoate *(2)*.

$$H_3COCO-CH=CH-CH_2-CH_2-CH=CH-COOCH_3 \quad (2)$$

For recent progress in this field see [13a,29a].

[*] The expression "allyl carbon atoms" refers to the atoms C-1, C-2, and C-3 (in the formula $-\overset{1}{C}H_2-\overset{2}{C}H=\overset{3}{C}H_2$).

[13] *G. P. Chiusoli* and *G. Cometti*, Chim. e Ind. (Milano) *45*, 404 (1963).

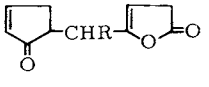
[13a] *E. J. Corey* and *M. F. Semmelhack*, Tetrahedron Letters *1966*, 6237.

5. Preparation of Derivatives of Cyclic Ketones and of Phenols

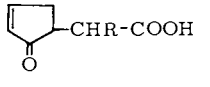
While the reaction of allyl halides having electron-attracting substituents with tetracarbonylnickel in benzene, ether, *etc.*, leads mainly to dimerization with very little uptake of carbon monoxide, direct carbonylation can be achieved, though in low yields (≈ 30–40% under CO at a high pressure and at 100 °C), in aliphatic, alicyclic, or aromatic ketones (water content < 1%) and even (though less satisfactorily) in esters. Side reactions include dimerization [14]. Dienoic acids are formed in the reaction with carbon monoxide and acetylene (yields of 40–50%) as well as cyclic compounds. In the reaction of nitriles coupling predominates. Thus from 4-chloro-2-butenonitrile with acetylene and carbon monoxide in ketones or esters, and in the presence of tetracarbonylnickel, 6-cyano-2,5-hexadienoic acid is formed in a yield of only 8–10%, the principal product being 1,6-dicyano-1,5-hexadiene.

Cyclic compounds are obtained as the main products when allyl halides, having no substituents or alkyl substituents on the allyl carbon atoms, are allowed to react with acetylene and carbon monoxide in inert solvents such as ketones, esters, or ethers. On the other hand, the formation of straight-chain acids (such as occurs in aqueous or alcoholic solution) becomes less important [15,16]. The initially formed acyl halides cyclize readily.

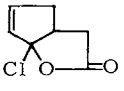
In the simplest case (allyl chloride), reaction with carbon monoxide and acetylene in moist acetone (0.5% water) leads to *(3)*, (which can isomerize to *(9)*) and *(4)* as well as *(26a)* and phenol. The acid *(4)* exists mainly in the form of the chlorinated lactone *(4a)*. Products such as *(7)* and *(8)* are also present.



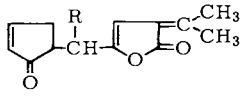
(3), R = H
(5), R = CH_3



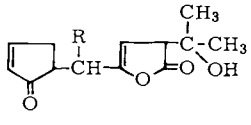
(4), R = H
(6), R = CH_3



(4a)

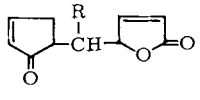


(7), R = H
(7a), R = CH_3



(8), R = H
(8a), R = CH_3

If the water content of the solvent is less than 0.1%, compounds of the type *(7)*–*(9)*, which result from a secondary reaction with the solvent, are the main products [16].



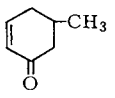
(9), R = H

[14] *L. Cassar* and *G. P. Chiusoli*, Ital. Pat. Application 54547/64 (Milan).

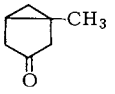
[15] *L. Cassar* and *G. P. Chiusoli*, Ital. Pat. Application 2758/65, 5845/65 (Milan).

[16] *L. Cassar* and *G. P. Chiusoli*, Tetrahedron Letters *1965*, 3295.

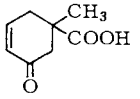
Crotyl chloride in moist acetone yields mainly *(5)* and *(6)*, while methallyl chloride gives mainly *m*-cresol together with the cyclic compounds *(10)–(12)*[16b].



(10)



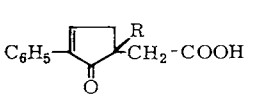
(11)



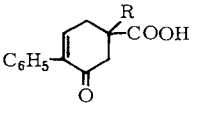
(12)

In diethyl ether or its homologues, the principal products of the reaction of allyl chloride with carbon monoxide and acetylene [in the presence of $Ni(CO)_4$] are *trans*-1-(2-oxo-3-cyclopentenyl)-3,6-heptadien-2-one *(24a)* [16a] and the acid *(4)*. An interesting by-product is the ketone *(24b)*. Ethyl acetate is intermediate between acetone and diethyl ether in its action.

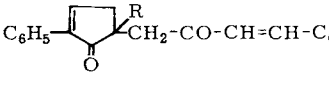
The stability of the complex formed from the alkyne and the nickel compound increases on going from acetylene to its higher homologues, and the use of anhydrous solvents is no longer necessary *e.g.* in the case of phenylacetylene. (Fewer side reactions take place in solvents containing water). The reaction of phenylacetylene, tetracarbonylnickel, carbon monoxide, and allyl chloride in acetone/water (4:1) yields *e.g.* the compounds *(13)–(16)* [17,21] [*(13)*, m.p. 110–111 °C; *(15)*, m.p. 104–105 °C]. Replacement of allyl chloride by methallyl chloride leads to the products *(13a)*, *(14a)*,



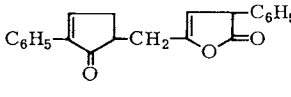
(13), R = H, 21%
(13a), R = CH_3



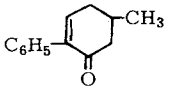
(14), R = H, 4%
(14a), R = CH_3



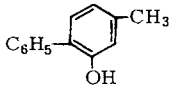
(15), R = H, 64%
(15a), R = CH_3, 37%



(16), 4%



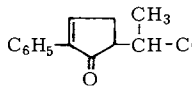
(17), 6%



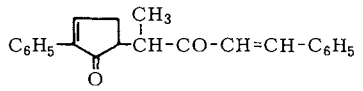
(20), 34%

Yield of *(13)* is calculated with respect to carbonylated allyl chloride. *(13a)* and *(14a)* are produced together in 13% yield.

(15a), *(17)*, and *(18)* [*(14a)*, m.p. 180–181 °C; *(15a)*, m.p. 127–128 °C; *(17)*, m.p. 38–40 °C]. The compounds *(19)* and *(20)* were isolated in the analogous reaction with crotyl chloride [*(19)*, m.p. 130–131 °C; *(20)*, m.p. 95–96 °C].

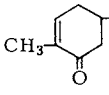


(19), 20%

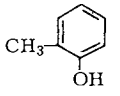


(20), 71%

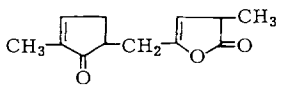
With allyl chloride, the use of propyne instead of phenylacetylene leads to the compounds *(21)–(24)*.



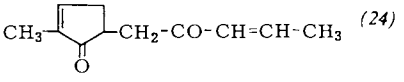
(21)



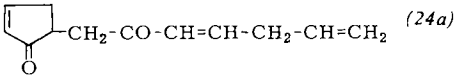
(22)



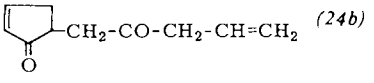
(23)



(24)

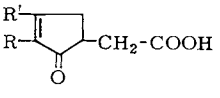


(24a)

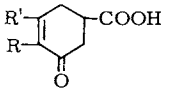


(24b)

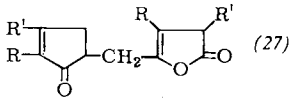
With alkylacetylenes (R,R′ = alkyl or H; RR′ = alkylene), the principal products are *(25)–(27)*.



(25)

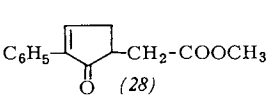


(26); *(26a)*, R = R′ = H

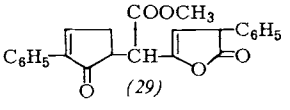


(27)

Even allyl derivatives with electron-attracting substituents react in inert solvents such as acetone. Under such conditions, the reaction of methyl 4-bromocrotonate, phenylacetylene, carbon monoxide, and tetracarbonylnickel yields *(28)* and *(29)*.



(28)



(29)

$HOOC-CH=CH-CH_2-CH=CH-COOCH_3$ *(29a)*

$H_2C=CH-CH_2-COOCH_3$ *(29b)*

The stoichiometry of the reactions leading to the compounds *(3)–(29)* is rather complex. Tetracarbonylnickel acts catalytically in the formation of acids or esters or of phenols [eq. (g) and (h)], but stoichiometrically in the other reactions [equations (i), (j), and (k)].

Though equation (h) is formulated as a catalytic process, the nickel consumption at room temperature is closer to that of a stoichiometric reaction. This is due to the formation of a nickel complex with H and Cl, which,

[16a] *L. Cassar, G. P. Chiusoli*, and *M. Foà*, Tetrahedron Letters, in press.

[16b] *L. Cassar* and *G. P. Chiusoli*, Chim. e Ind. (Milano) *48*, 323 (1966).

[17] *G. P. Chiusoli, G. Bottaccio*, and *C. Venturello*, Tetrahedron Letters *1965*, 2875; Chim. e Ind. (Milano) *48*, 107 (1966).

$$CH_2{=}CH{-}CH_2Cl + CH_3{-}C{\equiv}CH + 2\ CO + H_2O \xrightarrow{Ni(CO)_4} (21) + HCl \quad (g)$$

$$CH_2{=}CH{-}CH_2Cl + CH_3{-}C{\equiv}CH + CO \xrightarrow{Ni(CO)_4} (22) + HCl \quad (h)$$

$$BrCH_2{-}CH{=}CH{-}COOCH_3 + C_6H_5{-}C{\equiv}CH + Ni(CO)_4 + H_2O \longrightarrow (28) + NiOHBr + 3\ CO \quad (i)$$

$$CH_2{=}CH{-}CH_2Cl + 2\ HC{\equiv}CH + Ni(CO)_4 + H_2O \longrightarrow (3) + NiOHCl + CO \quad (j)$$

$$2\ CH_2{=}CH{-}CH_2Cl + 2\ HC{\equiv}CH + Ni(CO)_4 \longrightarrow (24a) + NiCl_2 + 2\ CO \quad (k)$$

instead of being liberated as HCl, hydrogenate other substances present, as is shown by the formation of cyclohexenones.

The products discussed here are listed in Tables 3, 4 and 5.

Table 3 Carbonylation products obtained from the reaction of allyl bromide with acetylene or phenylacetylene, carbon monoxide, and tetracarbonylnickel at 20 °C in various solvents.

Solvent	Products with HC≡CH
Acetone (0.1 % H_2O)	*(7)*; little *(8)*, *(4)*, *(3)*, phenol, 2,5-Hexadienoic acid and *(26a)*
Acetone (0.5 % H_2O)	*(3)*; little *(7)*, *(4)*, phenol, 2,5-Hexadienoic acid and *(26a)*
Ethylether (0.1 % H_2O)	*(24a)* and *(4)*; little *(24b)*, *(3)* and *(26a)*
Ethylacetate (0.1 % H_2O)	*(3)* and *(24a)*; little *(24b)* and *(4)*
	Products with C_6H_5—C≡CH
Acetone/H_2O (20 % H_2O)	*(15)* and *(13)*, little *(14)* and *(16)*

Table 4 Carbonylation products obtained from the reaction of allyl compounds with acetylene, carbon monoxide, and tetracarbonylnickel at 20 °C in relation to the structure of the allyl compounds.

Allyl compound	Products with HC≡CH in acetone (0.1 % H_2O)	Products with C_6H_5—C≡CH in acetone/H_2O (20 % H_2O)
$CH_2{=}CH{-}CH_2Cl$	*(7)*; little *(8)*, *(4)*, *(3)*, phenol, 2,5-hexadienoic acid and *(26a)*	*(15)* and *(13)*; little *(14)* and *(16)*
$CH_3{-}CH{=}CH{-}CH_2Cl$	*(7a)*; little *(5)*, *(6)* and 2,5-heptadienoic acid	*(20)* and *(19)*
$CH_2{=}C(CH_3){-}CH_2Cl$	*m*-cresol; little *(10)*, *(11)*, *(12)* and 5-methyl-2,5-hexadienoic acid	*(15a)*, *(18)* and *(13a)*; little *(14a)* and *(17)*
$H_3COCO{-}CH{=}CH{-}CH_2Br$	*(29a)* and methyl ester of *(4)*; little methyl ester of *(26a)*	*(28)*; little *(29)*

Table 5 Carbonylation, dimerization, and hydrogenation products obtained from the reaction of methyl 4-bromocrotonate with acetylene, carbon monoxide, and tetracarbonylnickel at 20 °C in various solvents.

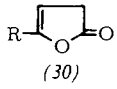
Solvent (0.1 % H_2O)	Products
Acetone	*(29a)* and methyl ester of *(4)*; little *(29b)*, *(2)*, and methyl ester of *(26a)*
Ethyl ether	*(2)*; little *(29b)* and *(29a)*
Ethyl acetate	*(29a)*, *(2)* and methyl ester of *(4)*; little *(29b)* and methyl ester of *(26a)*
Acetonitrile	*(2)*, little *(29b)* and *(29a)*

6. Carbonylation of Acyl Halides to form Lactones and Cyclopentenone Derivatives

Acyl halides react with acetylene and carbon monoxide under the same conditions as allyl halides to form lactones *(30)* [17a]. Ketones are used as solvents, esters being less suitable.

[17a] *L. Cassar* and *G. P. Chiusoli*, Tetrahedron Letters *1966*, 2805.

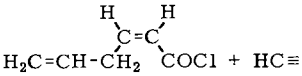
$$RCOCl + HC{\equiv}CH + Ni(CO)_4 + H_2O \longrightarrow$$



$$+ NiOHCl + 3\ CO$$

(30)

The behavior of 2,5-hexadienoyl chloride (and bromide) is rather interesting. The *cis* isomer cyclizes in acetone at 20 °C to give *(3)* [16a, 17a], while the *trans* isomer reacts "normally" to form *(30)* with R = *trans*-$CH_2{=}CH{-}CH_2{-}CH{=}CH$.



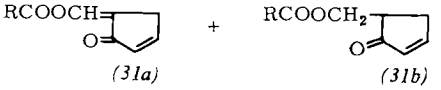
$$+ NiOHCl + 2\ CO$$

(3)

2-*cis*-5-Hexadienoyl chloride and its nickel complex are formed directly from allyl chloride, acetylene, and tetracarbonylnickel. This has been shown spectroscopically (in ether) by *Heck* [35], and is further substantiated by the fact that hexadienoic acid is obtained in part on hydrolysis of the reaction mixture. The compound 2-*cis*-5-hexadienoyl chloride cyclizes readily (the main product being *(3)*) and can be isolated only in traces.

When a halide of an organic acid reacts with carbon monoxide, acetylene, and tetracarbonylnickel in the presence of an α,β-unsaturated aldehyde, the products obtained are esters of oxocyclopentenylidenemethanol or of oxocyclopentenylmethanol, depending on whether hydrogen is given off or taken up. For example, acrolein gives *(31a)* and *(31b)* [17a].

$$RCOCl + CH_2{=}CH{-}CHO + HC{\equiv}CH + Ni(CO)_4 \longrightarrow$$



(31a) *(31b)*

7. Reactions with Activated Olefins

We have seen that an addition induced by the allyl group can terminate with the uptake or loss of hydrogen. This is generally observed when the carbon atoms of the allyl group carry an electron-attracting substituent.

The same phenomenon is found in the addition of such allyl compounds to activated olefins such as acrylonitrile or methyl acrylate [eq. (l)].

$$CH_2{=}CH{-}CH_2X + CH_2{=}CHZ + H_2O + Ni \longrightarrow CH_2{=}CH{-}CH_2{-}CH_2{-}CH_2Z + NiOHX \quad (l)$$

This reaction proceeds in ethanol at about 40 °C [18]. In solvents such as benzene and with tetracarbonylnickel as the catalyst [19], the reaction yields a mixture of compounds formed by uptake or loss of hydrogen, which can be isolated by distillation of the crude products without the addition of water.

For example, methyl 5-hexenoate and methyl 2-*trans*-5-hexadienoate are obtained from allyl bromide and methyl acrylate. (The product obtained from acetylene according to eq. (b) is in the *cis* form.) The fact that the two products are formed in varying ratios indicates that they are formed independently of each other.

Acrylonitrile reacts with allyl halide and tetracarbonylnickel to form a nickel complex [19a], which yields 5-hexenonitrile on treatment with water or acids. Pyrolysis of the complex, on the other hand, gives a mixture containing 2-*trans*-5-hexadienonitrile together with 5-hexenonitrile and other linear isomers of hexadienonitrile.

8. Carbonylation of Other Organic Halogen Compounds

a) Reactions of Aromatic Iodine Derivatives

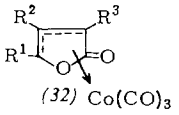
Other aliphatic halides, and even benzyl chloride, do not react under the very mild conditions used for reactions with tetracarbonylnickel. However, at temperatures above 100 °C, iodobenzene and other aromatic iodine derivatives react with tetracarbonylnickel and acetylene to form γ-keto acids or their esters [20], which may be

$$C_6H_5I + HC{\equiv}CH + Ni(CO)_4 + 2\,H_2O \longrightarrow C_6H_5{-}CO{-}CH_2{-}CH_2{-}COOH + NiOHI + 2\,CO$$

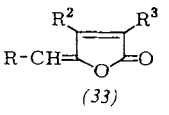
regarded as hydrolysis products of β,γ-unsaturated γ-lactones or as hydrogenation products of α,β-unsaturated γ-keto acids or esters. The α,β-unsaturated γ-keto acids or esters are hydrolysed under the conditions of the reaction, but owing to the presence of electron-attracting substituents, they do not take up CO.

b) Related Reactions with Other Catalysts

Even saturated halogen compounds react with carbon monoxide when the carbonylcobalt anion is used as the catalyst [22]. *Heck* has synthesized unsaturated lactone complexes such as *(32)* in systems consisting of acylcarbonylcobalt complexes and alkynes in an inert solvent.



(32) $Co(CO)_3$



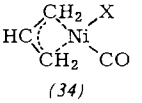
(33)

If R^1 contains an activated CH_2 group, addition of a base leads to the loss of a proton, followed by catalytic formation of a diene *(33)*. We have also carried out a stoichiometric synthesis of γ-keto acids with the carbonylcobalt anion in solvent/water mixtures, *e. g.* acetone/water [21]. Allyl halides react with carbon monoxide in the presence of palladium chloride [23–28] or a platinum complex [29] as a catalyst. A review of allylnickel complexes has been published by *Wilke* [29a]; for other reviews see [29b–29e].

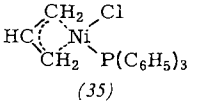
9. Investigations on the Course of the Reaction

a) Nature and Formation of the Catalytically Active Intermediate

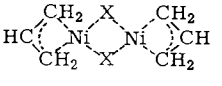
We at first formulated the reaction (for $CH_2{=}CH{-}CH_2X$) as proceeding *via* a complex $[C_3H_5{-}CO{-}Ni(CO)_3]^{\oplus}X^{\ominus}$ [2a, 30]. After the isolation of allyl complexes of other transition metals [54, 55], we suggested the structure *(34)* for the complex (X = halogen), by analogy with π-allylcobalt and π-allylcarbonylmanganesecomplexes. The isolation of the complex *(35)* led *Heck*, *Chien*, and



(34)



(35)



(36)

[18] *G. P. Chiusoli*, Chim. e Ind. (Milano) *43*, 365 (1963).

[19] *M. Dubini, F. Montino*, and *G. P. Chiusoli*, Chim. e Ind. (Milano) *47*, 839 (1965).

[19a] *M. Dubini* and *F. Montino*, J. organometallic Chem. *6*, 188 (1966).

[20] *N. L. Bauld*, Tetrahedron Letters *1963*, 1841.

[21] *G. P. Chiusoli, S. Merzoni*, and *G. Mondelli*, Tetrahedron Letters *1964*, 2777.

[22] *R. F. Heck* and *S. D. Breslow*, J. Amer. chem. Soc. *85*, 2779 (1963).

[23] *J. Tsuji, J. Kiji*, and *M. Morikawa*, Tetrahedron Letters *1963*, 1063, 1811.

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[27] *W. T. Dent, R. Long*, and *G. H. Whitfield*, J. chem. Soc. (London) *1964*, 1588.

[28] *R. Long* and *G. H. Whitfield*, J. chem. Soc. (London) *1964*, 1852.

[29] *G. W. Parshall*, Z. Naturforsch. *18b*, 772 (1963).

[29a] *G. Wilke et al.*, Angew. Chem. *78*, 157 (1966); Angew. Chem. internat. Edit. *5*, 151 (1966).

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[29c] *M. L. H. Green* and *P. L. I. Nagy*, Advances organometallic Chem. *2*, 325 (1964).

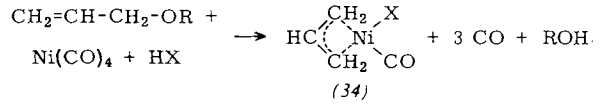
[29d] *R. F. Heck*, Advances Chem. Ser. *49*, 181 (1965).

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[30] *G. P. Chiusoli*, Gazz. chim. ital. *89*, 1332 (1959).

Breslow [31] to the same theoretical conclusions. *Fischer* and *Bürger*, who had isolated dimers *(36)* [32] (X = halogen), considered such compounds to act as catalysts [33].

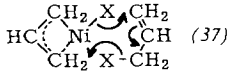
The existence of intermediates such as those with the structures *(34)* and *(35)* would explain the formation of methyl 3-butenoate by carbonylation of allyl chloride in methanol [34] and of 3-butenoyl chloride in ether, as well as the formation of 2,5-hexadienoic acid derivatives in the presence of acetylene [35]. The intermediate *(34)* could be formed from alcohols, allyl ethers, or allyl esters and hydrogen chloride as follows [2g]:



(34)

The catalytic systems iron/nickel halide/thiourea and nickel powder/thiourea may give a similar complex in the presence of the allyl halide. Thiourea favors the reduction of the nickel halide and permits the formation of a π-allyl complex.

It was not known at first whether the allyl group reacts under the usual conditions, in the π-form or in the σ-form. The results of our investigations with ^{14}C-labeled allyl bromide ($1-^{14}C]CH_2=CH-CH_2Br$) show that the allyl group always undergoes an allyl rearrangement in the reaction with tetracarbonylnickel. However, this rearrangement is not due to fast equilibration of the σ-forms before the reaction (for example, in the reaction of allyl acetate with acetylene and carbon monoxide in methanol, allyl acetate with only 10% of [3-^{14}C] could be recovered). It may therefore be concluded that the reaction proceeds *via* a π-allyl complex. Allyl halides can be isomerized by monohalogenonickel complexes *via* an independent reaction as in *(37)* [3a]. The isolation of nickel acetate and methyl hexadienoate in the $Ni(CO)_4$-catalysed reaction of allyl acetate with acetylene and carbon monoxide shows that the nickel cleaves the $-CH_2-O-$ bond, as was also found by *Bauld* in the dimerization of allyl esters with tetracarbonylnickel [36].

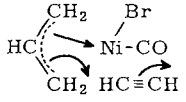


(37)

b) Reaction of Allyl Compounds with Acetylene and Carbon Monoxide and with Other Compounds

Acetylene is polymerized by (^{14}C-labeled) π-allylnickel bromide dissolved in benzene; we were unable to isolate any product formed from one mole of allyl bromide and one mole of acetylene. Although the polymer contained labeled allyl groups, it was not possible to decide whether the first step involved the addition of the allyl group to acetylene or the dimerization of two allyl groups to give 1,5-hexadiene, which then reacted with acetylene. (Labeled allyl groups have also been detected in the copolymer of acetylene with 1,5-hexadiene [19]). If carbon monoxide is present, treatment with water yields 2,5-hexadienoic acid.

This behavior suggests that CO and acetylene first add to the π-allylnickel bromide; the coordinately bound components then react as indicated in *(34a)*.



(34a)

The addition of halogens and CO to olefinic ligands in the presence of palladium chloride [23] is thought to proceed in the same manner [37]. Instead of CO and C_2H_2, activated olefins, such as methyl acrylate and acrylonitrile, can react with π-allylnickel bromide [19]. The selective formation of the dimerization products may also be explained by the reaction of the π-allylnickel bromide with one molecule of allyl halide [13].

c) Formation of Acids and Esters

The acyl nickel compound, which is formed by the addition of the allyl group to the carbonyl group attached to nickel (with or without the introduction of acetylene), is cleaved by water or alcohols into hydrogen halide and acid or ester.

The reaction may proceed in two stages, *i.e.* addition of halogen to form the acyl halide, followed by hydrolysis or alcoholysis. We have demonstrated the formation of the acyl chloride in benzene by isolating this product [2a].

Heck detected 3-butenoyl chloride and 2,5-hexadienoyl chloride by IR spectrometry of π-allylnickel halide in ether solution in the presence of carbon monoxide and of carbon monoxide and acetylene [35]. However, it was not known whether acyl halides are formed also as the initial products in water or alcohol. We have investigated the *Reppe* synthesis [5a] of acrylic compounds from alkynes and carbon monoxide, in which an acyl compound of this type is split off. Such syntheses proceed smoothly with acetic acid [38] instead of hydrogen chloride; it was therefore to be expected that an acid anhydride would be formed, and would be detectable, even in alcoholic solution, by virtue of its greater stability.

When a mixture of 1-octyne, tetracarbonylnickel, and acetic acid was heated in methanol for a few minutes at 60 °C, the mixed anhydride of acetic and α-hexylacrylic acid could be detected by IR spectroscopy and by chemical methods (as acetanilide and α-hexylacrylanilide) [39].

This suggests that acyl halides also occur as intermediates when the reaction is carried out with hydrogen halide in alcohol.

It seems that halide ions compete with alcohol to cleave the acyl nickel halide.

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[32] *E. O. Fischer* and *G. Bürger,* Z. Naturforsch. *16b*, 77 (1961); Chem. Ber. *94*, 2409 (1961).

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[35] *R. F. Heck,* J. Amer. chem. Soc. *85*, 2013 (1963).

[36] *N. L. Bauld,* Tetrahedron Letters *1962*, 859.

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[38] *E. R. H. Jones, T. O. Shen,* and *M. C. Whiting,* J. chem. Soc. (London) *1950*, 280; *1951*, 48, 763, 766.

[39] *G. P. Chiusoli* and *A. Cameroni,* Chim. e Ind. (Milano) *46* 1063 (1964).

d) Cyclization to Form Derivatives of Ketones and Phenols

The cleavage of the 2,5-dienoic acids from nickel complexes such as *(34a)* can be prevented by the use of inert solvents such as ketones, esters, and ethers (see Section 5). In solvents containing hydroxyl groups, the liberation of the 2,5-dienoic acids is also suppressed by the use of higher alkynes which form much more stable nickel complexes.

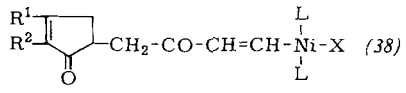
Ketones have a stronger stabilizing action than the other solvents. This action is particularly evident in the formation of the unsaturated lactone in the reaction of allyl compounds, or acyl halides, with acetylene, and tetracarbonylnickel. The tendency of the ketones or aldehydes to stabilize acyl groups by attack on the oxygen has been observed in the formation of enol esters from acyl halides and ketones [20] and of complexes from acylcarbonylcobalt complexes and aldehydes [53]. The stabilizing action on the acyl group is even more evident in the case of compounds having electron-attracting substituents on the allyl group; these compounds form dienoic acids more readily in ketonic than in "inert" solvents such as ether, ethyl acetate, or acetonitrile. Exceptions are observed with substituents which (like the CN group) tend to interact with the metal and favor the formation of products such as 1,6-dicyano-1,5-hexadiene and small quantities of dienoic acids.

After its formation on the nickel complex, the hexadienoyl group forms a cyclic, ketonic ligand containing five or six carbon atoms. A cyclohexenone or a phenol can be split off from the ligand containing six carbon atoms. Ring closure to form alicyclic ketones has also been observed when acyl cobalt complexes, such as 5-hexenoylcarbonylcobalt, are heated [40]. The tendency toward phenol formation with loss of hydrogen is strongest in the methallyl halides. Allyl halides and their straight chain homologues give little phenol; the reaction leads mainly to the formation of a cyclopentenone ring, which adds on further carbon monoxide. Hydrolysis of the acyl nickel complex yields mainly the acid *(4)* and its homologues.

The cyclization of 2,5-hexadienoyl chloride to form phenol can take place in the absence of CO, but transition metals such as palladium must be present. The intermediate is probably similar to that formed in the Rosenmund reaction [12,41]. The reaction proceeds catalytically and in almost quantitative yield. When the cyclization is carried out with tetracarbonylnickel at room temperature, the products contain very little phenol and a large quantity of (4).

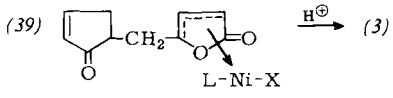
e) Other Reactions with Acetylene and Carbon Monoxide

The initially formed cyclopentenone and cyclohexenone complexes tend to react further with acetylene and carbon monoxide, probably to form complexes such as *(38)* and *(39)* (L = *e.g.* CO). *(39)* is similar to the complex *(34)*. The products isolated also require the formation of *(38)* and *(39)*.

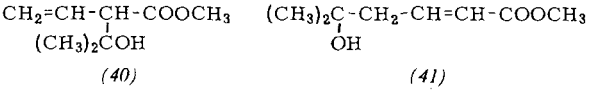


(38)

In the reaction of allyl chloride with carbon monoxide and phenylacetylene, we isolated the diketone *(15)* as the main product. Propyne reacts to give the analogous product *(24)*. When the reaction was carried out in ether, we also obtained *(24a)*, which is presumably formed by the reaction of allyl halide with *(38)*. In the reaction with acetylene, in slightly moist (< 0.5% water) ketones, a second carbonyl group can be readily introduced to form unsaturated β,γ-lactone derivatives such as *(3)* [42]. *(3)* is less stable than the α,β tautomer *(9)*.



The π-allyl intermediate *(39)* was assumed to react with ketones in a Reformatsky-type reaction. To check the validity of this supposition, methyl 4-bromocrotonate and acetone were made to react in the presence of tetracarbonylnickel (instead of zinc as used by *Reformatsky*) [16]. The esters *(40)* and *(41)* were obtained in the ratio 88:12.



(40) *(41)*

Unsaturated γ-lactone structures and cyclic structures with five or six carbon atoms are generally obtained in reactions with acetylene or other alkynes and carbon monoxide. (See [43–49] for reactions with iron, cobalt, and nickel complexes).

f) Stability of the Acyl Carbonyls

We have shown that in the reaction of allyl halides with tetracarbonylnickel and acetylene, the allyl group adds on to acetylene, while the other groups, such as 2-oxo-3-cyclopentenylmethyl or -phenyl (in the reactions of

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[41] *J. Tsuji* and *K. Ohno*, Tetrahedron Letters *1965*, 3969.

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[45] *G. Albanese* and *M. Tovaglieri*, Chim. e Ind. (Milano) *41*, 189 (1959); *46*, 1169 (1964).

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[49] *P. J. Ashworth, G. H. Witham*, and *M. C. Whiting*, J. chem. Soc. (London) *1957*, 4633.

the aromatic iodine derivatives) react with carbon monoxide. This is due to the instability of the 1-oxo-3-butenyl group formed from the allyl group. For example, the reaction of 3-butenoyl chloride with tetracarbonylnickel in tetrahydrofuran yields 1,5-hexadiene, with liberation of carbon monoxide.

$$2\ CH_2{=}CH{-}CH_2{-}COCl + Ni(CO_4) \longrightarrow CH_2{=}CH{-}CH_2{-}CH_2{-}CH{=}CH_2 + NiCl_2 + 6\ CO$$

Most acyl carbonyls are too stable to split off carbon monoxide; they add on acetylene and carbon monoxide to form lactones *(30)*.

We are grateful to Prof. A. Quilico for the interest which he has shown in our work.

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Translated by Express Translation Service, London

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[52] *A. S. Hay*, Belg. Pat. 630862 (1963); Chem. Abstr. *60*, 13192 (1964).

[53] *R. F. Heck*, J. Amer. chem. Soc. *87*, 4727 (1965).

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Chemical Effects of Nuclear Transformations in Solids

BY HORST MÜLLER [*]

Nuclear reactions and radioactive transformations offer the possibility of investigating the chemical reactions of "bare" nuclei. The interest in such chemical processes following nuclear transformations has already led to two international symposia [1, 2]. In solids, the chemical reactions of recoil nuclei having energies lower than 1 keV proceed not via molten states, but via regions of little disorder.

I. Introduction

Nuclides produced in nuclear reactions or resulting from radioactive decay can escape from their parent molecule and enter into chemical reactions by virtue of their kinetic energy and charge. The study of such reactions, *i.e.* of the behavior of an atom from the time of the nuclear transformation to the instant at which it finally forms a new chemical bond, is possible if the new nucleus is radioactive and therefore can be distinguished from the large numbers of atoms which remain unchanged.

In 1934, *Szilard* and *Chalmers* [3] found that the ^{128}I formed by the nuclear reaction $^{127}I(n,\gamma)^{128}I$ in the neutron activation of ethyl iodide can be separated from the far greater amount of unchanged organically bound iodine by extraction into aqueous media. A similar "Szilard-Chalmers process" was frequently used to obtain radioactive nuclides of high specific activity – ideally in the carrier-free state. The separation of active from inactive isotopes is possible only with elements that occur in at least two oxidation states (*e.g.* BrO_3^-/Br^-) or types of bonding (*e.g.* covalently bound iodine/I^-); moreover, there must be no exchange between these two forms.

The chemical reactions following isomeric transitions, *e.g.* $^{80m}Br \rightarrow {}^{80}Br$, are very similar to the Szilard-Chalmers process. These subsequent reactions offer the only method known at present for the separation of nuclear isomers.

The greatest success has been achieved so far in the study of gases, especially of tritium atoms from the nuclear processes $^3He(n,p)^3T$ and $^6Li(n,\alpha)^3T$ and ^{11}C atoms from $^{12}C(\gamma,n)^{11}C$ and other nuclear reactions [4–8]. Investigations on liquids, mainly organic halogen compounds, have been less successful [9]. Least of all is known about the chemical effects of nuclear transformations [**] in solids [10–14].

[*] Priv.-Doz. Dr. Horst Müller
Chemisches Laboratorium der Universität
Albertstr. 21
78 Freiburg (Germany)

[1] Chemical Effects of Nuclear Transformations. Proceedings Symposium, in Prague October 24th to 27th 1960. Internat. Atomic Energy Agency, Vienna 1961; cf. Angew. Chem. *73*, 34 (1961).

[2] Chemical Effects Associated with Nuclear Reactions and Radioactive Transformations. Proceedings Symposium, inVienna December 7th to 11th, 1964. Internat. Atomic Energy Agency, Vienna 1965; cf. Angew. Chem. *77*, 384 (1965); Angew. Chem. internat. Edit. *4*, 362 (1965).

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[**] Other terms used for "chemical effects of nuclear transformations" are "recoil chemistry" and "hot atom chemistry". However, these terms should be avoided, since they overemphasize one aspect of the primary process.

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[13] *A. N. Murin, R. V. Bogdanov*, and *S. M. Tomilov*, Russian chem. Review (English translation of Usp. Chim.) *33*, 295 (1964).

[14] *G. Harbottle*, Annu. Rev. nuclear Sci. *15*, 89 (1965).

II. Nuclear Recoil [15]

The energy of the compound nucleus formed by the capture of a thermal neutron is 6 to 8 MeV higher than that of the nucleus in the ground state. Most of the excess energy is emitted as γ radiation. A γ-quantum of energy E_γ has a momentum

$$p = E_\gamma/c \qquad (1)$$

(c = velocity of light).

Owing to the conservation of momentum, the product nucleus receives an equal and opposite momentum. The kinetic (recoil) energy E_R of a nucleus having mass M and velocity v is found to be

$$E_R = Mv^2/2 = p^2/2\,M = E_\gamma^2/2Mc^2 \qquad (2)$$

The kinetic energy of (n,γ)–recoil nuclei is therefore between 100 and 1000 eV.

However, most compound nuclei emit not one, but on average three γ quanta, and proceed by various routes to the ground state *via* intermediate states; these intermediate states accumulate close to the ground state. The total momentum and hence also the recoil energy become smaller as a result of the splitting, and for two γ quanta having energies $E_{\gamma 1}$ and $E_{\gamma 2}$, for example,

$$E_R = (Mc^2/2)\,(E_{\gamma 1}^2 + E_{\gamma 2}^2 + 2\,E_{\gamma 1}\,E_{\gamma 2}\cos\Theta) \qquad (3)$$

(Θ is the angle enclosed by γ_1 and γ_2).

If the various γ cascades and their frequencies are known, the distribution of the recoil energies can be calculated by stochastic methods, under the (not strictly valid) assumption that the distribution of the γ quanta is isotropic. The most accurate calculation so far has shown that for $^{35}Cl(n,\gamma)^{36}Cl$, the average recoil energy is about 75 % of the maximum possible value found from equation (2), and that low recoil energies are very rare [16]. The various γ quanta are not emitted simultaneously, since the intermediate states have lifetimes of between 10^{-16} and 10^{-12} sec or longer. Consequently, a recoil atom may already have lost the kinetic energy resulting from the first γ emission before it is set in motion again by a second emission. From equation (1), the velocity v after a γ emission is

$$v = E_\gamma/Mc \qquad (4)$$

After a 2 MeV γ emission, a recoil atom of mass number 100 would travel 12.5 Å in 2×10^{-13} sec. This distance is greater than the mean free path in a solid. The loss of energy of recoil atoms as a result of collisions has been detected in nuclear resonance experiments [17]. Owing to the non-uniform distribution of the intermediate states, most of the kinetic energy is derived from the first step of the γ cascade. For nuclear isomers decaying to the ground state by γ emission, the recoil calculated from equation (2) is small since the γ energy of such transitions is only of the order of 100 keV; for a nucleus of mass number 100, E_R = 0.054 eV.

Nuclear isomers can decay, not only by γ emission, but also by internal conversion. Instead of a γ quantum, a shell electron is emitted with an energy E_β equal to the difference of the energy of the isomeric state and the binding energy of the electron emitted from the K, L, ... shell. The ratio of the number of electrons emitted to the number of γ quanta emitted is known as the conversion factor α. The recoil energy of the nucleus is

$$E_R = \frac{m_0 + m_e}{2\,M}\,E_\beta \qquad (5)$$

where m_0 and m_e are the rest mass and the relativistic mass of the electron, respectively.

For a mass number of 100 and E_β = 80 keV (binding energy of the K electron about 20 keV), it is found that E_R = 0.47 eV.

In β^- decay, the recoil energy is given by vectorial addition of the contributions of the emitted electron [eq. (5)] and of the neutrino. The resulting recoil energy has a distribution between 0 and E_R(max); the maximum value is found by insertion of the maximum β energy in equation (5); for medium-heavy atoms and E_β = 1 MeV values around or below 10 eV are obtained. The average recoil energy is about half of the maximum.

For nuclear reactions involving particles with energies greater than those of thermal neutrons, the recoil energies are always greater than a few tens of keV; recoil energies of between 50 and 100 MeV are obtained for fragments produced by nuclear fission. A particularly interesting class of nuclear reactions consists of those involving fast neutrons, n_f *i.e.* (n_f, 2n) and (n_f, γ), as well as the (γ,n) reaction, which, like the (n,γ) reaction, give isotopic nuclei and permit the study of the influence of the recoil energy.

The recoil energy is distributed between the translational energy and the internal energy of the molecule; in diatomic molecules, the increase in internal energy corresponds to the fraction $m/(M+m)$ of the recoil energy (M = mass of the recoil atom, m = mass of the second atom [18]; in polyatomic molecules, the mass of the rest of the molecule may be used, to a rough approximation, for m). The recoil atom can be liberated only if the vibrational component of the internal energy (the rotational component in polyatomic molecules is small) is greater than the energy (about 2–3 eV) of the bond between the recoil atom and the rest of the molecule [19, 20]. These observations are strictly valid for gases; corrections are to be expected in solids, owing to the hindrance of translation and the fact that the rest of the molecule is bonded to other atoms in the lattice, so that the error involved in an estimate based on the total recoil energy should be small.

It follows that only about 1 % of the recoil atoms keep their bonds intact in the (n,γ) process. In isomeric transitions without internal conversion, on the other hand, practically all the molecules concerned "survive". In β^- decays, the maximum recoil energy is often of the same order of magnitude as, or smaller than, the bond energy, so that a considerable fraction of the bonds may remain intact.

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III. Influence of Charge[15]

In β^- decay, the nuclear charge increases by +1, so that the product nucleus is in the form of a singly charged positive ion. Fast rearrangement of the electron cloud sometimes also leads to excitation and to a loss of electrons, particularly from the outer shells, which is known as "shake-off". In the case of heavy atoms, ionization also occurs as a result of collision of the β^- particle with electrons in the inner shells. As a result, 10–20 % of the product nuclides have a charge of +2, higher charges rapidly becoming less common. In β^+ decay, the primary products are singly negatively charged ions which can give neutral (sometimes excited) atoms and positive ions by electron loss.

A molecule in which one of the atoms undergoes β decay may survive this change if the recoil is too weak to break the bond and if the new chemical compound resulting from the change in the atomic number of the atom in question is stable. The reaction sequence

$$-{}^{14}CH_3 \xrightarrow{\beta^-} -{}^{14}NH_3^+ \xrightarrow{-H^+} -{}^{14}NH_2$$

for labeled ethane, toluene, or ethylbenzene yields 47 % of methylamine, 98 % of aniline, or 82 % of benzylamine respectively[21,22]. Similar reactions take place in solids:

Reaction	Yield (%)	Ref.
$Cs^{51}MnO_4 \xrightarrow{\beta^+} \square^+Cs^{51}CrO_4$[*]	99.6	[23]
$^{99}Mo(C_6H_6)_2 \xrightarrow{\beta^-} {}^{99m}Tc(C_6H_6)_2^+$	80—90	[24]
$M_2^{125}SnCl_6 \xrightarrow{\beta^-} M^{125}SbCl_6 + M^+ (M = K, NH_4)$	76—78	[25]
$^{144}Ce(acac)_3 \xrightarrow{\beta^-} {}^{144}Pr(acac)_3^+ + e^-?$ $\longrightarrow {}^{144}Pr(acac)_3$	100	[26]
$K^{131}IO_4 \xrightarrow{\beta^-} {}^{131m}XeO_4\,(?) + K^+$	40	[27]
$K^{131}IO_3 \xrightarrow{\beta^-} {}^{131m}XeO_3\,(?) + K^+$	>40	[27]
$^{105}Ru(C_5H_5)_2 \xrightarrow{\beta^-} {}^{105}Rh(C_5H_5)_2^+ + e^-?$ $\longrightarrow {}^{105}Rh(C_5H_5)_2$	*ca.* 10	[28]
$^{239}U(C_5H_5)_3X \xrightarrow{\beta^-} {}^{239}Np(C_5H_5)_3X^+ + e^-?$ $\longrightarrow {}^{239}Np(C_5H_5)_3X$ (X = F, Cl)	$\geqslant$ 90	[29]
$C_5H_5{}^{99}Mo(CO)_3 \xrightarrow{\beta^-} C_5H_5{}^{99m}Tc(CO)_3^+ + e^-?$ $\longrightarrow C_5H_5{}^{99m}Tc(CO)_3$		[30]

[*] $\square^+$ = Cation vacancy.

The high yields obtained in most cases indicate retention of the bond. The β^--active sandwich compounds were prepared directly by neutron activation of the inactive substances. The methods indicated were the first known syntheses of the benzenetechnetium(I) cation and of rhodocene.

Similar processes have been suggested for the preparation of rare gas compounds that are not yet known[31,32]:

$$KTF_2 \xrightarrow{\beta^-} K^+ + {}^3HeF_2$$

$$^{22}NaF \xrightarrow{\beta^+} {}^{22}NeF^- \xrightarrow{-e^-?} {}^{22}NeF$$

$$^{131}IX_n \xrightarrow{\beta^-} {}^{131m}XeX_n^+ \xrightarrow{+e^-?} {}^{131m}XeX_n$$

X = Halogen

However, anomalous charge states cannot be produced in association with nuclear transformations. For example the reaction

$$^{51}MnCO_3 \xrightarrow{\beta^+} {}^{51}Cr^+ + CO_3^{2-}$$

does not take place; instead, 70 % of Cr^{3+} and 30 % of CrO_4^{2-} are obtained[23].

The vacancy formed, generally in the K or L shell, as a result of the internal transition of nuclear isomers may be filled by electrons from higher shells with emission of X-ray quanta. However, the excess energy may also be used to emit another shell electron. This process may be repeated several times, progressing in an outward direction, and finally yielding an atom with a multiple positive charge. In the mass spectrometer, a maximum of the charge distribution is found between +5 and +10. This process is known as the Auger process (or vacancy cascade), and is completed in 10^{-15} sec. It can also be studied for non-radioactive atoms if vacancies in inner electron shells are produced by X-ray or electron radiation[33]. A molecule containing such an Auger atom decomposes as a result of the loss of bonding electrons and Coulombic repulsion following distribution of the positive charge to other atoms of the molecule. The fragments of the molecule can easily have kinetic energies of between 10 and 100 eV, *i.e.* much greater than the recoil energy resulting from the emission of shell electrons as given by eq. (5).

In isomeric transitions without internal conversion the atom gains no charge, and according to eq. (2), there is only a very slight recoil, so that the molecules remain intact; in this case the isomers cannot be separated. Well known examples are $^{69m}Zn(C_2H_5)_2$, $^{127m}Te(C_2H_5)_2$, and $^{129m}Te(C_2H_5)_2$. With conversion coefficients of 0.06, ~ 100, and ~ 100, 95 %, 0 %, and 0 %, respectively, of the starting substance remains unchanged[34,35].

The positive charge of atoms after internal conversion is not reflected in the charge state that is finally found, despite the unambiguous mass spectrometric results. Thus on decay in an

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electric field, the final products are mainly found at the anode[36,37]. ^{80}Br formed from ^{80m}Br does not react as an electrophile[38].

Low-energy intermediates of the (n,γ) process decay, not only by γ emission, but also by internal conversion followed by the Auger effect, so that the recoil atoms also carry considerable positive charges. Since γ transitions and internal conversion proceed differently for each nuclide, even nuclei having the same atomic number behave differently, so that an isotope effect may be observed.

The following proportions of positively charged recoil atoms were found on neutron irradiation of gaseous ethyl bromide and ethyl iodide: 12 % of ^{80m}Br, 18 % of ^{80}Br, and 25 % of ^{82}Br, and 50 % of ^{128}I[39]. About 50 % of the recoil atoms ejected from the surfaces of indium, gold and manganese or from compounds of these metals are positively charged[40,41]. Of the products formed in the reaction of recoil ^{128}I atoms with methane, 25 % are formed *via* I^+ (spectroscopic state: $^1D_2$)[42]. Since the lifetimes of the lower states of the compound nucleus are greater (about 10^{-10} sec) than those of the higher, the charge arises only after the recoil atom has already acquired most of its kinetic energy and is no longer associated with its neighbors. If the recoil and the charging took place simultaneously, the recoil atoms ejected from metals would necessarily be neutral.

Thus while a considerable proportion of the (n,γ) recoil atoms are positively charged, a large part of the positively charged atoms resulting from internal conversion possess kinetic energy due to Coulombic repulsion. These facts explain why such nuclides generally exhibit a qualitatively similar behavior.

In solids, however, the (n,γ) process accompanied by internal conversion does not generally lead to a transition into a higher valence state, as was found for compounds of Sb^{3+}, As^{3+}, Ce^{3+}, Cr^{3+}, and Tl^{1+}[43]. An electron exchange probably takes place. Similarly the high initial positive charges of the high-energy fragments formed by nuclear fission have only a small influence on their ultimate chemical fate.

Of the iodine isotopes formed by the nuclear fission of uranium in neutron-irradiated uranyl iodate, 14 % of the ^{131}I and 18 % of the ^{133}I are found in the reduced form (I^-, I_2, IO^-), and the remainder as iodate; on the other hand, ^{135}I is reduced to the extent of 67 %. Consideration of the properties of the iodine atom and its environment offers a ready explanation of these observations. Since iodine has a relatively high ionization potential, it should be found mainly in the reduced form, as is the case with the primary fission product ^{135}I. ^{131}I and ^{133}I are formed as secondary products in a β^- decay chain involving Sn, Sb, and Te as precursors. These elements, particularly Sn, have low ionization energies, and in the bulk of the uranyl iodate they will therefore be preferentially converted into an oxidized form, which may be retained in the subsequent β^- decays[44].

The general conclusion is that the chemical fate of the recoil atom is determined only after it has lost most of its kinetic and electronic energy. The chemical consequences of (n,γ), (γ,n), and (n_f,2n) nuclear processes are therefore generally very similar. Even the unexpected results concerning the charge state in the internally converted isomeric transition and in the (n,γ) process accompanied by internal conversion can be explained in this way. The chemistry of the system is more important than the primary effects.

IV. Fundamental Observations

The proportion of radioactive atoms present in a new chemical form after irradiation of a suitable compound with thermal neutrons and subsequent dissolution is the *yield*. The proportion of the radioactive atoms that remain chemically unchanged in the starting material is the *retention*. The definition of the retention should be rigidly adhered to, so that even species that are closely related to the starting compound should be included in the yield. If no secondary radiolytic changes take place, the yield fraction is free from carrier, and only the retention fraction is mixed with the mass of the unactivated starting substance. Some examples are shown in Table 1.

Since it is not known *a priori* what compounds are present, no assumptions should be made in the chemical separation of the irradiated substances, *i.e.* no carriers should be added. Methods such as chromatography, gas chromatography, ion exchange, and ionophoresis have proved suitable, whereas precipitation, solvent extraction, and distillation are generally inadequate.

Fig. 1 represents schematically the Szilard-Chalmers process for bromates. A number of recoil atoms return to the initial potential and remain as bromates, while others are trapped in higher potential troughs. Dissolution of the solid leads to the liberation of such atoms, which then undergo further reaction, possibly with the solvent, to give the form having the lowest energy, *i.e.* bromide. If the irradiated material is heated before

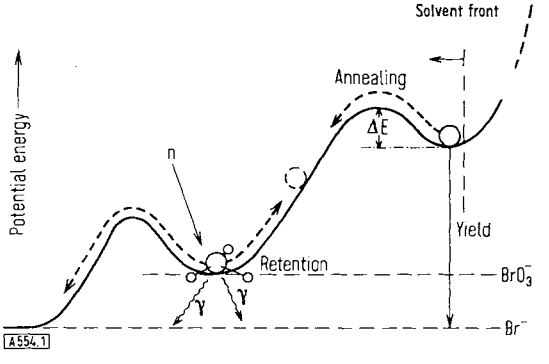


Fig. 1. Simplified scheme of the Szilard-Chalmers process in bromates.

being dissolved, atoms from the higher potential troughs return to the potential of the bromate. Thus this "annealing" decreases yields and increases retentions. This phenomenon refutes the otherwise tempting assumption that the recoil atoms that are not in the

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Table 1. Some Szilard-Chalmers systems and the products found as the yield.

Irradiated substance	Present in yield fraction	Ref.
Perchlorates	ClO_3^-, Cl^-	[45,46]
Chlorates	Cl^-	[45–47]
Bromates	Br^- (Br_2)	[48]
Hexabromoosmates, -iridates, -rhenates	Br^-	[49]
Periodates	IO_3^-, I^-	[50]
Iodates	I^-	[51]
Sulfates	S_8, SO_3^-	[52–54]
Phosphates *etc.*	10–15 products	[55]
Arsenates, arsenites, arsenic oxides	AsO_3^{3-}, AsO_4^{3-}	[56]
Cobaltchelate complexes	Co^{2+}	[57]
Cobaltammine complexes	Co^{2+}, cobaltammine complexes	[58–63]
Hexachloroosmates	various unidentified Os compounds	[64,65]
Hexachloroiridates	*ca.* 15 Ir compounds	[66,67]
Hexahalogenorhenates	ReO_4^-	[68–70]
Permanganates	Mn^{2+} (MnO_2)	[71]
Chromates, dichromates	Cr^{3+}	[72–74]
Xenon tetrafluoride	XeF_2, Xe	[75,76]
Potassium bromide	Br^0	[77]
Porphins, phthalocyanines	free metal ions	[78–80]
Sandwich compounds, carbonyls	free metal ions	[81–83]
Hexabromoethane	$Br_2(C_2Br_4)$	[84]

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retention form are immediately converted into the yield form. There are also systems in which this is impossible on chemical grounds; thus hexahalogenorhenates(IV) K_2ReX_6 give ReO_4^- as the yield fraction, the oxygen clearly coming from the solvent. If the yield form is particularly stable, it may also be formed directly, as indicated by the arrow over the left-hand potential barrier; this fraction, *e.g.* the $^{13}N^{14}N$ from the nuclear reaction $^{14}N(n_f,2n)^{13}N$ of NaN_3, would not be susceptible to annealing [85].

In systems that give several yield forms, it is generally not clear which of these are formed in the solid state and which are formed only on dissolution. Apart from the Mössbauer effect (see Section XII), however, there is no method that permits the investigation of the state of the atoms in the solid phase itself.

Important problems are:

1. How is the kinetic and electronic energy of the recoil atom lost? How far does the recoil atom travel, what reactions does it undergo, and what changes does it bring about in its environment?

2. What is the chemical, electronic, spatial, and energetic structure of the disturbed regions containing the recoil atom after it has come to rest?

3. What types of reactions take place during the annealing?

4. When end products are not formed in the crystal itself, how are they formed on dissolution out of the defect centers?

5. How are questions 1. to 4. affected by the compound under investigation?

V. The Retention

The retention consists of the primary retention and the secondary or reaction retention. The primary retention includes molecules that have not been disrupted in spite of excitation by the nuclear process. Reaction retention results from the reaction of temporarily free recoil atoms with their surroundings.

In the Szilard-Chalmers process in gases, *e.g.* organic halides, the primary retention is generally less than 1 %. The addition of a large excess of free-radical scavengers (*e.g.* NO + I_2, Br_2) inhibits recombination of recoil atoms to form the starting substance [86]. In

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solids, recombination of the fragments of a disrupted molecule may be facilitated by a cage effect. Thus disruption is no longer decided solely by the strength of a chemical bond, but also depends on the energy required to move an atom from one lattice site to another (roughly 25 eV, cf. Section VII.3). Nevertheless, it may be assumed that even in solids, the primary retention (including the cage effect) is very small, since systems are known to exist in which the total retention is very small (cf. Table 2).

Table 2. Systems with low retention [45–47, 50, 87].

Irradiated substance	Retention (%)
$LiMnO_4 \cdot 3H_2O$	3
KIO_4	4
$NaClO_3$	1.5–5
$KClO_3$	4
$LiClO_3$, $NaClO_4$, $KClO_4$	0

To determine the primary retention in K_2CrO_4, mixed crystals of this substance with K_2BeF_4 were studied [88]. The retention decreases from about 70 % for pure K_2CrO_4 to 25 % (which is still a very high value) at high dilutions. Tris(acetylacetonato)cobalt(III) has a retention of 19.8 %, which falls to 2.8 % on dilution with tris(acetylacetonato)aluminum(III) [89]. This value may correspond to the primary retention, but it is not clear why the cobalt recoil atoms do not also react with fragments from the similar aluminum compound.

There is seldom a clear relationship between the retention and the properties of the substance under investigation. Thus no simple relationship could be recognized on variation of the cation and the content of water of crystallization in permanganates [87], arsenates [90], and chromates (cf. Table 3), or of the central atom in phthalocyanines and porphins [78, 80]. The same is true of the influence of the anion in cobaltammine complexes [59]. Dipseudocumene-, di-

Table 3. Retention in chromates [73, 91, 92].

Irradiated substance	Retention (%)	Irradiated substance	Retention (%)
Li_2CrO_4	66.0	$K_2Cr_2O_7$ mcl.	82.4
Na_2CrO_4	73.6	$K_2Cr_2O_7$ tricl.	89.5
$Na_2CrO_4 \cdot 2H_2O$	72.7	$(NH_4)_2CrO_4$	17.5
$Na_2CrO_4 \cdot 4H_2O$	87.8	$^{24}MgCrO_4$	56.7
K_2CrO_4	60.8	$^{26}MgCrO_4$	52.7
		$ZnCrO_4$	34.6

mesitylene-, dibenzene-, benzenetricarbonyl-, and hexacarbonyl-chromium showed no relationship between retention and the number of ligands, heat of formation, aggregation state, bond strength, and mass of the ligands [81]. The decrease in retention in ammonium salts and salts containing water of crystallization is explained by the reducing properties of H_2O and NH_4 [93]. No decrease in retention is observed in acid salts and ammine complexes. In complexes such as cobalt phthalocyanine, where the screening of the cobalt atom by the organic ligands is not the same on all sides, the Co retention is lower than in *e.g.* the fully shielded tris(acetylacetonato)cobalt(III) [57].

For some oxo anions, there is a relationship between the retention and the oxidation potential (cf. Fig. 2) [72]. This comparison is open to the objection that the processes considered take place in the solid whereas redox potentials are measured in solution. The relationship is not valid for phosphates and solid solutions such as K_2CrO_4/K_2SO_4, $KMnO_4/KClO_4$, and KH_2PO_4/KH_2AsO_4.

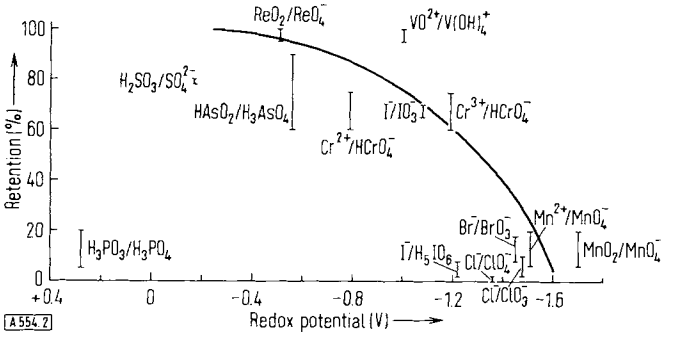


Fig. 2. Relationship between retention and redox potential.

In complicated organic compounds containing P, S, Co, or Se, the retention is usually extremely small. Thus ^{60}Co-labeled vitamin B_{12} [94], ^{32}P-labeled DNA and ATP [95, 96], and ^{35}S-labeled cysteine [97] cannot be prepared by direct activation. High retention values [98–103] are probably due to radioactive impurities.

Annealing can take place even below room temperature, and also can be induced by ionizing radiation. In order to prevent annealing and so to avoid changes in the retention, it is necessary not only to carry out the activation at the lowest possible temperature (−196 °C) and with the smallest possible dose, but also to carry out the dissolution at a low temperature. Temperatures down to −95 °C have been attained with organic solvents, and down to −55 °C with a eutectic $LiCl/H_2O$ mixture. The retention for $KMnO_4$ then falls from 20 % to 5 %, and that for $Na_2CrO_4 \cdot H_2O$ from 89 % to 39 % [104].

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These experiments show that it is not possible to speak of an intrinsic retention value, since it may be assumed that substances irradiated and dissolved slightly above 0 °K would have extremely low retentions.

VI. Older Models of Recoil Chemistry

1. The Billiard-Ball Model

According to *Libby*[105], retention is due to displacement of an unactivated atom by an activated atom of the same element. This mechanism proceeds even when the collision is not central, provided that the residual energy is not sufficient to disrupt the newly formed molecule. The maximum energy ΔE that can be transferred in a central collision is

$$\Delta E = 4\, E_R\, M_1 M_2/(M_1 + M_2)^2 \qquad (6)$$

(M_1, M_2 = masses of the colliding species).

On average, half of this energy is transferred on collision. The recoil atom also loses considerable energy in collisions with atoms of different masses; thus for a mass ratio $M_1/M_2 = 0.5$, $\Delta E/E_R = 0.89$, whereas for $M_1 = M_2$, $\Delta E/E_R = 1.00$.

There are many observations that cannot be explained by the billiard-ball model. For example, the retention for some compounds is very low; higher retentions in other compounds appear to be due to annealing. It is also not clear how recoil atoms in complexes can reach other central atoms without disturbing the ligands. Secondly, a billiard-ball collision can occur only if the range of the recoil atom is at least equal to the distance to the nearest atoms of the same type, and appreciable retention values would be possible only if the range were many times this distance, since the nearest neighbors occupy only a fraction of the space angle 4π. However, the range of (n,γ)-recoil atoms is only of the order of 10 Å (Section VII, 7 and 8). The billiard-ball model is also contradicted by the results of experiments with mixed crystals K_2CrO_4/K_2SO_4[72,73,88], $KMnO_4/KClO_4$[106], and KH_2PO_4/KH_2AsO_4[107](Szilard-Chalmers component named first). In all these cases, the retention should be lower than in the pure compound since the recoil atom still retains some energy, even on central collision; however, the retention increases.

2. The Ligand-Loss Model

The ligand-loss model, which is also due to *Libby*[108], is based on the hypothesis that central atoms of complex ions that undergo an (n,γ) process lose some of their ligands. Though the model has often been used, the mechanism of this ligand loss has not been discussed.

According to *Libby*, ligand-*ions* are split off from the complex ions of metals. Irradiation of $KMnO_4$, for example, leads to the following forms:

$$Mn^{VII}O_4^- \xrightarrow{-O^{2-}} Mn^{VII}O_3^+ \xrightarrow{-O^{2-}} Mn^{VII}O_2^{3+} \xrightarrow{-O^{2-}} Mn^{VII}O^{5+} \xrightarrow{-O^{2-}} Mn^{7+}$$

On dissolution in water, these forms are either reduced (giving yield) *e.g.*

$$4\, MnO_3^+ + 2\, H_2O \longrightarrow 4\, MnO_2 + 3\, O_2 + 4\, H^+ \qquad (a)$$

or hydrated (giving retention) *e.g.*

$$MnO_3^+ + H_2O \longrightarrow MnO_4^- + 2\, H^+ \qquad (b)$$

In complex anions of nonmetallic elements, the nuclear process is assumed to lead to the removal of ligand-*atoms*, *e.g.* for bromate

$$Br^{V}O_3^- \xrightarrow{-O} Br^{III}O_2^- \xrightarrow{-O} Br^{I}O^- \xrightarrow{-O} Br^-$$

The ligand-loss model fails to explain the results of a large number of experiments. The pH-dependence of the retention is only approximately compatible with equations (a) and (b); furthermore, these two reactions must have the same activation energy, since the retention is not affected by a temperature rise of 40 °C[87]. The retention is also unchanged by the use of acetone as the solvent, though hydration in accordance with eq. (b) is then impossible[108,109]. It was recently shown that the yield fraction consists mainly of Mn^{2+}, which is adsorbed on added manganese dioxide, but can be separated in strongly acidic solution[71]. With bromates, Br^0 is found as well as Br^-, but no BrO^- or BrO_2^-[48].

The species required by the ligand-loss model have never yet been detected in the crystal itself. The solution reactions that relate these species to the end products are hypothetical.

VII. High-Energy Atoms in Solids

Formerly, the chemical phenomena accompanying nuclear reactions in solids were considered from a purely chemical viewpoint whereas more consideration now is given to the physical changes.

The changes brought about by high-energy atoms in solids are known as radiation damage[110–113]. Metamict minerals exhibit such damage and, although of crystalline appearance, they are internally largely isotropic. This is due to the high-energy recoil atoms (*ca.* 100 keV) resulting from the α decay of the uranium or thorium present in the mineral. Extensive study of radiation damage became possible only after the construction of accelerators and reactors. However, such investigations immediately assumed great importance in nuclear technology since radiation-resistant materials are necessary in the construction of power reactors.

1. Production of Primary Atoms

Atoms with kinetic energy are produced in solids by collision of high-energy particles such as protons, deuterons, helium nuclei, fast neutrons, electrons, or

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[113] *L. T. Chadderton*: Radiation Damage in Crystals. Methuen and Co., Ltd., London 1965.

fragments from nuclear fission, or even as a direct result of nuclear processes. If the energy transferred is greater than a limiting value E_d (about 25 eV), known as the displacement energy, the lattice atom concerned is displaced. This displacement energy was estimated by *Seitz* [114] as early as 1949, *i.e.* before measurements had been carried out. It is approximately four times the sublimation energy; one factor of 2 is due to the fact that, unlike surface atoms, the lattice atoms are bonded on all sides, and the second factor of 2 results from the irreversibility of the collision process. The displaced lattice atom is known as a primary atom. If its energy is sufficiently high, it can displace further lattice atoms, so that secondary and tertiary atoms give rise to a cascade of lattice defects.

2. Nature of the Lattice Defects

A displaced lattice atom leaves a vacancy and generally comes to rest as an interstitial atom, as shown schematically in Fig. 6. A vacancy and an interstitial atom together form a Frenkel pair. Another form of interstitial atom is the static crowdion, in which a lattice row that is normally occupied by n atoms contains $n+1$ atoms.

Defects are present even at thermal equilibrium. In copper, the energy of formation of a vacancy is 1 eV, and that of an interstitial atom is 4 eV. At 1000 °C, the vacancy concentration is 0.01 %. Such defects lead macroscopically to changes in the specific heat, density, lattice parameters, optical properties, and electric conductivity.

3. Displacement Energy

The displacement energy E_d is best determined by collision experiments with electrons ($E_e \sim 0.5$ MeV). The maximum energy $E_p(\max)$ that can be transferred to a lattice atom of mass M is

$$E_p(\max) = 2\,(E_e + 2\,m_0\,c^2)\,E_e/M\,c^2 \qquad (7)$$

(E_e = energy of the electron, m_0 = rest mass of the electron).

The electron energy E_e that just causes a measurable change, *e.g.* in conductivity, is measured; $E_p(\max)$ in eq. (7) corresponds to the desired energy E_d. In Table 4, the expected value $E_d \sim 25$ eV is confirmed, except in the case of semiconductors and the ordered alloy phase.

Table 4. Displacement energies found experimentally from equation (7) [111, 115, 116].

Substance	E_d (eV)
Graphite	25
Si	13
Al	32
Ag	28
Cu	22
Fe	24
Ni	24
Cu_3Au (ordered)	≈ 10 [a]
GaAs	9.1 (Ga); 9.5 (As)

[a] Migration energy, not displacement energy (see Section VII.5).

4. Number of Displacements

The calculation of the number of displacements $\nu(E_p)$ produced by a primary atom of energy E_p is roughly as follows: A primary atom of energy $E_p < E_d$ does not produce any change. Primary atoms having an energy $E_d < E_p < 2E_d$ displace an atom after the transfer of at least E_d; however, their remaining energy is then less than E_d, and the atom remains at the point of collision, so that effectively no new vacancy is formed. Only primary atoms with $E_p > 2E_d$ can transfer the energy E_d to an atom with which they collide and still retain the energy E_d, so that a new vacancy is produced. This reasoning leads to the expression

$$\nu(E_p) = E_p/2\,E_d \qquad (8)$$

The same result was obtained by *Kinchin* and *Pease* [117] by a mathematically more formal method. The energy stored in the vacancies is about 5 eV per Frenkel pair in metals, and so amounts to only 10 % of the energy required for their formation.

5. Replacement

In the calculation of the number of displacements, though primary atoms with $E_d < E_p < 2E_d$ cause the displacement of a new atom, they themselves remain trapped at the collision site. This process is known as replacement. *Kinchin* and *Pease* [118] consider such replacements possible even at energies as low as 0.1 E_d.

Whereas replacement reactions in metals and disorded alloys cause no observable changes, in ordered alloy phases such as $MnNi_3$ or Cu_3Au they lead to a more statistical arrangement of the atoms even at energies below E_d (cf. Table 4).

6. Thermal Spikes

Instead of describing individual defects, *Seitz* and *Koehler* [119] considered the damage process collectively in their thermal-spike model. In a displacement, only a small part of the energy is stored in defects, the remainder being liberated as heat. If a quantity of heat Q is liberated at a lattice point in a collision at time $t = 0$, then the temperature T at a distance r from this point at time t is

$$T(r,t) = \frac{Q}{8\,\pi^{3/2}\,c_p d} \cdot \frac{1}{(Dt)^{3/2}} \cdot \exp\,(-r^2/4\,Dt) \qquad (9)$$

where the heat diffusion coefficient D is given by $D = C/c_p d$

(C = thermal conductivity, c_p = specific heat, d = density).

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Fig. 3 shows such a temperature distribution at various times.

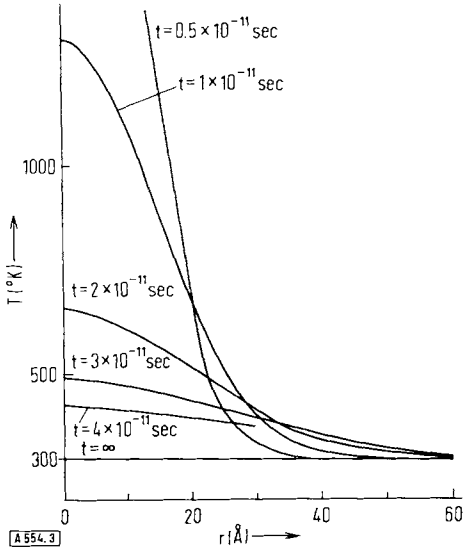


Fig. 3. Local temperature distribution in a thermal spike in Cu (D = 0.001 cm²/sec; Q = 1000 eV). According to G. H. Vineyard (personal communication), Q = 300 eV in the original is a misprint [110].

For an event with Q = 300 eV, which approximately corresponds to the recoil energy in (n,γ) processes, a region of about 10 atomic diameters (about 1000 atoms) is heated for 10^{-11} sec to about 1000 °K, *i.e.* approximately to the melting point. However, the diffusion of heat in atomic regions is probably faster than would be expected from eq. (9) and the time and the size of the thermal spike so calculated are therefore too large. Differences of opinion exist as to whether the hot region can be regarded as a true melt or simply as a superheated solid without appreciable mixing of the atoms. According to *Seitz* and *Koehler*, at least the central part of the spike is in thermal equilibrium, and so can be treated as a macroscopic melt.

The problems of interpretation should have no bearing on processes that can be thermally activated in the excited region, such as the conversion of ordered alloy phases into disordered phases, the transition from low-temperature to high-temperature phases, segregation, thermal production of Frenkel pairs, *etc.*. However, attempts to detect such thermal processes, *e.g.* the transition from gray to white tin[120] or the transition from metastable tetragonal ZrO_2 into the monoclinic form[121] on irradiation with fast neutrons, have been largely unsuccessful. The transition from ordered into disordered alloy phases is better explained by the replacement model. However, spikes were detected at higher energies, for example with the fragments from nuclear fission. When monoclinic ZrO_2 is bombarded with fission fragments in the presence of stabilizing foreign atoms such as V, Cr, or Ta, it is converted into the cubic high-temperature modification[122,123]. Near the surface in *e.g.* uranium and plutonium, evaporation takes place at a rate of the order of 1000 atoms per fission fragment[124]. The rate of evaporation is reduced if the surface is coated with oxide.

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7. Energy Loss and Range of Primary Atoms

Bohr[125] proposed the expression (10) for the interaction potential between primary and lattice atoms.

$$V(r) = (Z_1 Z_2 e^2/r) \exp(-r/a) \qquad (10)$$

(Z_1, Z_2 = nuclear charges of the two particles concerned, r = distance between the particles, a = the screening parameter). $a = a_H/(Z_1^{2/3} + Z_2^{2/3})^{1/2}$

(a_H = 0.529 Å, radius of the Bohr hydrogen atom in the ground state).

For primary atoms having Ep (eV) $< 30\,Z^{7/3}$, the electron clouds scarcely penetrate each other, and the scattering is given by a hard-sphere model. Above this energy limit, the Rutherford scattering model (which will not be described here) is valid[111]. For energies above E_i (eV) $=10^3\,M$, energy is lost mainly by ionization of the surroundings.

To summarize, it may be said that most primary atoms lose their energy by hard-sphere scattering, while fission fragments and accelerated particles lose their energy mainly by ionization. Whereas the ionization causes no permanent changes in metals, electronic defects are produced in semiconductors and nonconductors.

The path length of a primary atom is found by summation of the various free paths. For elements ($Z_1 = Z_2 = Z$), *Holmes* and *Leibfried*[126] equated the Bohr potential of equation (10) to the energy of the primary atom:

$$2\,V(R) = E_p = \frac{2Z^2e^2}{R} \exp(-R/a) = E_B \frac{a}{R} \exp(-R/a) \qquad (11)$$

$E_B = 2Z^2e^2/a$, R is the interaction distance in such a collision, *i.e.* the "diameter of the sphere". It can be seen that R increases as E_p decreases.

According to the kinetic gas theory, the collision cross-section is

$$\sigma_p = \pi R^2 \qquad (12)$$

and the mean free path L_p of a primary atom is

$$L_p = 1/N_A \pi R^2 \qquad (13)$$

(N_A = number of atoms in the unit volume). Fig. 4 shows the relationship between L_p and E_p for Cu primary atoms in copper. Summation of the individual free paths L_p, assuming that the energy of the primary particle is halved at each collision, shows that the mean total path $\bar{L}$ is given by

$$\bar{L} = L_p\,(3/2 + R/a), \qquad (14)$$

and the mean maximum range by

$$\overline{(R^2_{max})}^{1/2} = L_p\,(7/2 + 2\,R/a)^{1/2} \qquad (15)$$

The maximum range is the greatest distance from the starting point that is ever reached by the primary atom, while the

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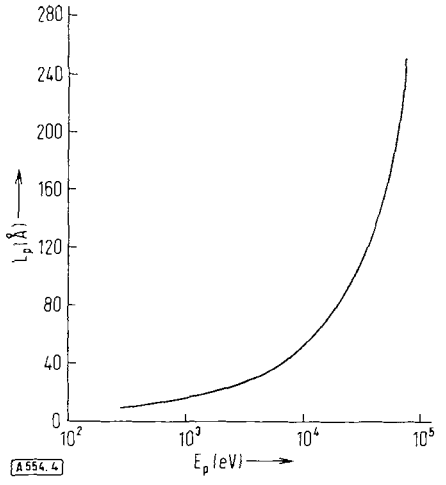


Fig. 4. Relationship between the mean free path L_p and the energy E_p of a primary atom in copper [111].

vector range is the distance between the atom after it has come to rest and the starting point. The penetration depth is the projection of the vector range in the original direction.

The Bohr potential gives only a moderately good description of the interaction. The agreement between theory and experiment is generally not very satisfactory.

8. Experimental Determination of Ranges

The range of the high-energy fragments from nuclear fission ($\sim$ 2–12 mg/cm^2 $\sim$ 0.007–0.045 mm in Al) is determined by allowing the fragments produced in a very thin layer to penetrate a series of thin foils which are then analysed individually to find their content of radioactive fission fragments. In nuclear reactions producing atoms of lower primary energies and correspondingly smaller ranges, layers of target material and of catcher material are pressed together alternately. The range R in the target material is then (for $d \gg R$)

$$R = 2\,df. \qquad (16)$$

d = thickness of target layer, f = proportion of the radioactive atoms penetrating the catcher foils [127].

The maximum range is found if the atomic number of the atoms of the catcher material is significantly lower than that of the target material, since atoms that have left the target layer cannot return to this layer by backscattering. Instead of the foils, powdered target material may be mixed with solid catcher materials or suspended in liquids (cf. Table 5).

Table 5. Recoil ranges of target nuclei in the target material, after *Pauly* and *Süe* [128–131].

Target	Nuclear reaction	Catcher	Recoil energy (MeV)	Range (Å)	Range (μg/cm²)
P_{red}	$^{31}P(\gamma,n)^{30}P$	Tetralin	0.16	800	19
P_{red}	$^{31}P(\gamma,n)^{30}P$	Tetralin	0.40	2300	54
$CuSO_4 \cdot 5H_2O$	$^{63}Cu(\gamma,n)^{62}Cu$	$CaCO_3$	0.20	2600	59
Cu	$^{63}Cu(\gamma,n)^{62}Cu$	NaCl,$BaCl_2 \cdot 2H_2O$	0.20	600	53
NaCl	$^{35}Cl(n,\alpha)^{32}P$	Naphthalene, paraffin	0.59	5000	105
NH_4Cl	$^{35}Cl(n,\alpha)^{32}P$	SiO_2	0.59	7000	107
NaCl	$^{35}Cl(n,p)^{35}S$	Naphthalene, paraffin	0.12	500	10
NH_4Cl	$^{35}Cl(n,p)^{35}S$	SiO_2	0.12	700	11
S_8	$^{32}S(n,p)^{32}P$	H_2O	0.6	6500	135
NaCl	$^{37}Cl(d,p)^{38}Cl$	$CaCO_3$	0.48	3200	66
NaCl	$^{23}Na(d,p)^{24}Na$	$CaCO_3$	0.82	3700	76

A few years ago, another method of range determination became prominent. In this method radioactive ions (*e.g.* ^{24}Na, ^{86}Rb, ^{133}Xe, ^{222}Rn), which have acquired a definite energy by passage through an electric field, are used to bombard the catcher material (generally aluminum). The penetration and distribution are then determined by successive dissolution of thin layers of the catcher. Fig. 5 shows the penetration probability for ^{85}Kr in aluminum at energies between 2 and 600 keV [136].

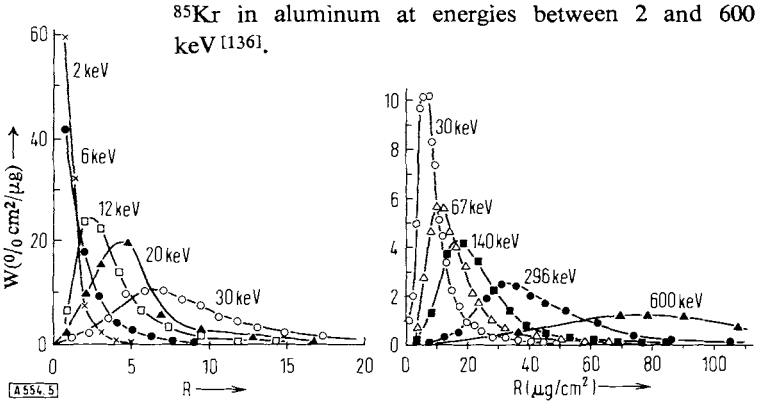


Fig. 5. Relationship between penetration probability W and the penetration R of ^{85}Kr in aluminum for energies between 2 and 600 keV [136].

(W = percentage of ^{85}Kr atoms which come to rest in layers of thickness 1 μg/cm² at a distance R from the surface).

Aluminum is anodically oxidized and the oxide film is dissolved by hot phosphoric acid/chromic acid solution. The thickness of the oxide film is proportional to the formation voltage; it is possible to dissolve away layers as thin as 1 μg/cm² $\triangleq$ 37 Å [132]. The process can also be used with

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[132] *J. A. Davies, J. Friesen,* and *J. D. McIntyre,* Canad. J. Chem. *38,* 1526 (1960).

tungsten and with silicon [133,134]. Reproducible removal of thin layers can also be achieved by cathode sputtering [135].

The range of (n,γ) recoil atoms is extremely small. In the case of indium and gold foils, only those recoil atoms that are produced in the outermost monoatomic layer emerge; thus the range is approximately one lattice layer [40]. On neutron irradiation of a slurry of sulfur particles of radius 0.8 μ in water, 0.26% of the ^{35}S atoms were found in the water; this corresponds to a range of 40 Å for the recoil atoms [128,137]. The ranges of the ^{28}Al produced in aluminum and in Al_2O_3 by the reaction $^{27}Al(n,\gamma)$ were 11 and 4.4 Å respectively, and the range of the ^{56}Mn resulting from the $^{55}Mn(n,\gamma)$ reaction in iron containing Mn was 35 Å [138,139].

9. Focusons, Dynamic Crowdions

So far we have not considered the fact that the atoms at rest have a strict geometrical arrangement. The real crystals were replaced by a random distribution of atoms, *i.e.* were regarded as amorphous. Consideration of the lattice structure leads to some entirely new aspects of the behavior of atoms travelling through solids.

Close-packed atoms along a lattice row can behave as a row of billiard balls in contact with one another. A collision directed along this line leaves all the balls in their original position except the last, which moves away. This is the case in the crystal lattice when the lattice row is interrupted *e.g.* by a small or light foreign atom, a vacancy, or a grain boundary, and the ejected atom enters an interstitial site. If the lattice row is not interrupted, the collision process stops after about 100 interatomic distances owing to loss of energy.

The angle between the collision direction and the lattice direction becomes smaller with each collision. Thus the energy transport becomes focused along lattice lines without any transport of material [140,141]. This phenomenon is referred to as focusing collisions (cf. Fig. 6).

There is an upper energy limit E_F for focusons, since the atomic diameter becomes steadily "smaller" as the energy increases [cf. eq. (11)], until the lattice rows are apparently no longer close-packed. This limit for copper in the ⟨110⟩ direction is about 50 eV.

If the energy of a primary atom is greater than the focusing energy E_F, or if the lattice rows are less closely packed, each atom in the collision chain moves into the position of its nearest neighbor, leaving a vacancy at the origin of the collision chain. Focusing mainly occurs because the moving atoms are held in the direction of the line by adjacent lattice rows. This process is known as a dynamic crowdion (cf. Fig. 6). Thus, such a crowdion transports both energy and material, whereas a focuson transports only energy. The crowdions in ordered lattices replace the Kinchin-Pease replacement reactions. A crowdion can change into a focuson when its energy falls below E_F.

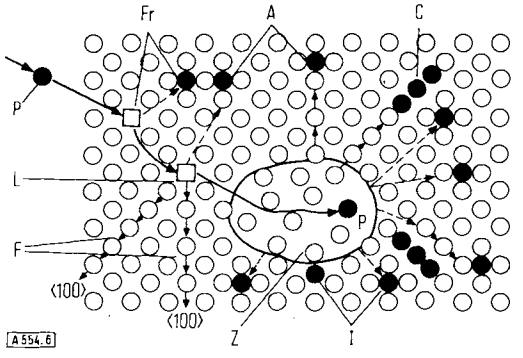


Fig. 6. Scheme of a depleted zone after *Seeger* [142].
P = primary atom (originating in a lattice region that is not shown); L = vacancy; F = focusons; Z = depleted zone; I = interstitial atoms; C = crowdion; A = replacement collisions; Fr = Frenkel pair.

Crowdions and focusons lose, to the lattice, small amounts of energy, which is no longer available for the production of radiation damage. Owing to the fast transport of energy from the point of collision, the formation of thermal spikes becomes less likely, and interstitial atoms can be expected at greater distances from the starting point.

10. Depleted Zones

For lattice structures, *Seeger* [142] has developed a defect model that is more probable than the thermal-spike model. An essential feature of the Seeger model is the occurrence of dynamic crowdions which transport the energy and material away from the surroundings of the primary atom coming to rest. At a certain distance this gives rise to defects, *e.g.* a static crowdion resulting from the "freezing-in" of the dynamic crowdion, or an interstitial atom resulting from the ejection of the excess atom. A depleted zone is formed around the rest position of the primary atom. Frenkel pairs and focusons (cf. Fig. 6) are also formed directly. The maximum diameter of the depleted zone is 20 Å.

11. Kinematics of High-Energy Atoms in Solids

In order to be able to follow the behavior of primary atoms in detail, *Vineyard* [143] used a computer in a study of the changes occurring when a single copper atom in a Cu lattice moves with a certain energy in a definite starting direction (*e.g.* see Fig. 7).

[133] *J. A. Davies, J. D. McIntyre,* and *G. Sims,* Canad. J. Chem. *40,* 1605 (1962).

[134] *M. McCargo, J. A. Davies,* and *F. Brown,* Canad. J. Physics *41,* 1231 (1963).

[135] *H. Lutz* and *R.Sizmann,* Z. Naturforsch. *19a,* 1079 (1964).

[136] *J. A. Davies, B. Domeij,* and *J. Uhler,* Ark. Fysik *24,* 377 (1963).

[137] *J. Pauly* and *P. Süe,* J. Physique Radium *18,* 22 (1957).

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[143] *J.B.Gibson, A.N.Goland, M.Milgram,* and *G.H.Vineyard,* Physic. Rev. *120,* 1229 (1960).

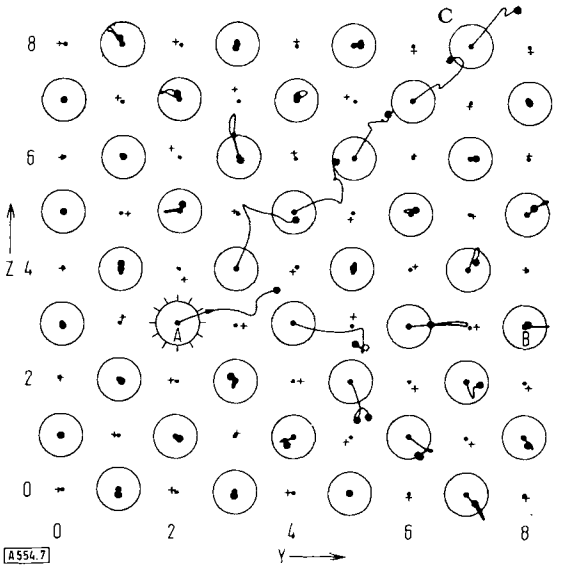


Fig. 7. Changes in the (100) plane of a copper lattice 3.24×10^{-13} sec after the transfer of an energy of 40 eV to the atom A (energy vector at an angle of 22.5° to the y axis). Large circles with medium-bold centers denote the starting positions of the atoms, and bold dots indicate the final positions. The routes travelled by the atoms are shown. Small dots show the starting positions of the atoms of the next-lower plane, and crosses indicate their final position. The event leads to the transient formation of three vacancies and two interstitial atoms in the neighborhood of A, resulting in one stable vacancy. A dynamic crowdion in the direction AC, after four changes of position, leads to the formation of an interstitial atom in the neighborhood of C. A focuson is observed in the direction AB [143].

The threshold energy E_d for the formation of a Frenkel pair is clearly dependent on direction and is 25 eV for the ⟨100⟩ direction, 25 to 30 eV for ⟨110⟩, and about 85 eV for ⟨111⟩. Thus the electron collision experiments give not an average value, but the minimum value of E_d. For a 400 eV event, the vacancies are found in the neighborhood of the point of origin, in agreement with Seeger's depleted-zone model, but the interstitial atoms are farther away.

Vineyard[144] used the kinetic energies obtained by computer calculations to calculate temperatures. He found no gradually spreading region of relatively uniform temperature, but temperature maxima in the vicinity of the collision chains. In a 100 eV event, the temperature maxima fell to below the melting point in only 10^{-12} sec, and after 1.65×10^{-12} sec the temperature was substantially that of the surroundings. Though there are similarities to the thermal-spike model, the initial fall in temperature is much faster.

12. Radiation Damage in Heteropolar Compounds

Processes such as those described above probably also occur in non-metallic solids. However they are less important than electronic processes, which already belong to the field of radiation chemistry. The essential measurable changes are the rupture of chemical bonds and the formation of color centers.

When irradiated inorganic substances are dissolved, it is possible to detect decomposition products, *e.g.*

a) $NO_3^- < NO_2^- + 1/2\ O_2$

b) $ClO_3^- < Cl^- + 3/2\ O_2$

c) $BrO_3^- < BrO_n^- + (3-n)/2\ O_2 \quad 2 \geqslant n \geqslant 0$

d) $IO_3^- < I^- + 3/2\ O_2$

e) $SO_4^{2-} < SO_3^{2-} + 1/2\ O_2$

f) $NaN_3 < Na + 3/2\ N_2$

Annealing can take place at least in cases a), b), and c).

VIII. New Models

1. Hot-Spot Model

Yankwich[145] and *Harbottle*[146] have discussed the chemical effects of nuclear transformations in solids on the basis of the thermal spike model. The recoil atom produces a hot spot (or a displacement spike) with displaced atoms. Thermodynamic considerations show that reactions with activation energies of about 1 eV can proceed in good yield in this hot spot. Exchange reactions lead to retention; other reactions lead to yield forms, generally with high chemical stability. The theory allows at least a qualitative understanding of annealing. Defects remain in the rapidly cooling hot spot, and these react further only when the temperature is raised. However, it is not clear why annealing nearly always leads to an increase in retention.

2. Disorder Model[70,147]

The disorder model is based on *Vineyard*'s computer calculations[143] the result of which is also regarded as an adequate model of the chemical effects of nuclear transformations. According to this model, an (n,γ) recoil atom having an energy of about 100 eV loses its kinetic energy very quickly and comes to rest only a few interatomic distances away from its starting point. Retention of the original molecular group or complex ion would be possible *e.g.* if a focuson were formed (primary retention). The general damage to the lattice is small, *i.e.* only a few atoms change places with neighboring atoms or become interstitial atoms. The process does not involve an intermediate liquid-like state.

The changes taking place, including those of a purely electronic nature, cannot be described in detail. Simulation by computer calculations has not so far been possible.

After having lost its energy, the recoil atom is in a new environment. From the chemical point of view, this state may have the character of a compound, which may remain intact on dissolution or may enter into a purely chemical reaction with the solvent. Other atoms are in metastable states, and with their surroundings they constitute the disorder center; these give yield forms,

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[145] *P. E. Yankwich*, Canad. J. Chem. *34*, 301 (1956).

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[147] *H. Müller* in [2], *2*, 359 (1965).

or may be annealed to give retention (cf. Fig. 1) [68]. The defects in this model formally resemble the intermediate forms of the ligand-loss model (cf. Section VI, 2). Since the disorder center is formed only when the recoil atom is nearly at rest, it is not determined by the initial energy of the recoil atom. Melting processes can occur only at recoil energies greater than 10 keV.

Even for substances with a retention of 100 %, for which no Szilard-Chalmers process is observed, some of the recoil atoms may well be found in defects. The difference in the arrangement of the surrounding atoms can lead to a change in the angular correlation of coincident γ quanta of the decaying nucleus. This effect was first observed for ^{188}Re from the nuclear reaction $^{187}Re(n,\gamma)^{188}Re$, in which $K^{188}ReO_4$ with all the ^{188}Re in crystallographically known sites was compared with neutron-activated $KReO_4$ [148].

The disorder model differs from the hot-spot model in that the reaction region is smaller and less disturbed, thus resulting in no appreciable mixing of the contents, and that the temperature rise is smaller and of shorter duration.

IX. Annealing [93, 149]

Annealing is the disappearance of defects (*e.g.* Frenkel pairs or dislocations) in solids. The defect centers produced in chemical compounds by nuclear reactions can be annealed, not only by the action of heat and ionizing radiations, (electrons, γ quanta), but also by pressure [150], UV irradiation [68, 151], or ultrasonics [152]. Fig. 8 shows the course of thermal annealing in calcium bromate at various temperatures [153]. This type of curve,

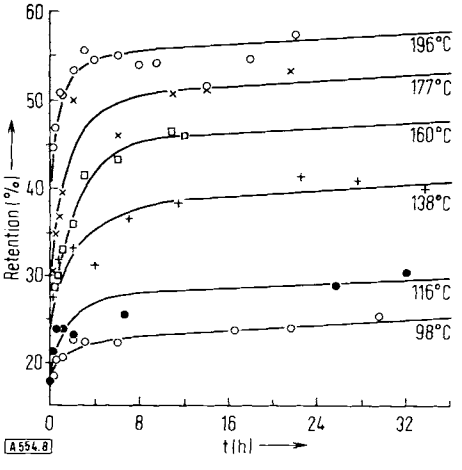


Fig. 8. Thermal annealing of calcium bromate [153].

which rises rapidly to a temperature-dependent pseudo-plateau, is quite common, though curves containing maxima [154], and/or minima [155] are also found as well as families of curves with the same pseudo-plateau for a range of temperatures [84]. The annealing curves become very complicated when different processes are combined. The curves should reflect the properties of the defect and thus be of use in its characterization.

The Maddock defect theory [156] applied to K_2CrO_4 explains annealing as an interaction of the Szilard-Chalmers center with a lattice defect, *e.g.* a vacancy. The fast annealing (steep part of the curve) corresponds to annealing of centers situated close to such a defect; the extent of the annealing increases with temperature and the process is of the first order. The pseudo-plateau region corresponds to annealing by the diffusion of a defect towards the center; since the number of defects is large in comparison with the number of Szilard-Chalmers centers, this recovery process is of the zeroth order. If new defects are produced at this stage, some of these will be situated very close to Szilard-Chalmers centers, so that a new phase of fast annealing can occur. The initial retention is also influenced by defects, such as can be produced by doping with foreign atoms or even by quenching or crushing [157]. The defect theory explains the frequently observed dependence of the Szilard-Chalmers phenomena on the properties of the starting material.

According to the defect theory, radiation annealing is due to the action of an exciton (electron hole + electron) on the Szilard-Chalmers center; electron holes or electrons, however, can also be active. The radiation annealing tends towards saturation, since the irradiation itself produces defects, which compete with the Szilard-Chalmers centers for the excitons. However these defects can be thermally eliminated even at temperatures at which the Szilard-Chalmers centers are not affected.

A theory related to that of Maddock was developed for C_2Br_6 [84]. Here the recoil atom is again regarded solely as an indicator for the changes in the defect center.

The action of electronic effects becomes clearest in experiments on KCl, in which the phosphorus produced by the reaction $^{35}Cl(n,\alpha)^{32}P$ is found mainly in the reduced form (not P^{5+}), but is converted into $^{32}P^{5+}$ on annealing [158]. No annealing occurs when the neutrons are produced by the D–T reaction and not in a reactor. Such neutrons are free from γ-radiation, which produces the electronic defects.

If $Ca(IO_3)_2$ doped with $^{131}I^-$ or K_2CrO_4 doped with $^{51}Cr^{3+}$ is heated, the charge transfers $^{131}I^- \rightarrow {}^{131}IO_3^-$ and $^{51}Cr^{3+} \rightarrow {}^{51}CrO_4^{2-}$ exhibit strong resemblance to the annealing curves of neutron-activated $Ca(IO_3)_2$ and

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[156] *A. G. Maddock, F. E. Treloar,* and *J. I. Vargas,* Trans. Faraday Soc. *59*, 924 (1963).

[157] *T. Andersen* and *A. G. Maddock,* Trans. Faraday Soc. *59*, 2362 (1963).

[158] *J. S. Butterworth* and *I. G. Campbell,* Nature (London) *196*, 982 (1962).

K_2CrO_4 respectively [159–161]. The same is true of the system $KBrO_3/^*Br^-$ [162]. The obvious interpretation is that annealing is due to simple chemical transfer reactions in these cases.

The interpretation of this annealing mechanism according to the disorder model is that the defect property (*e.g.* abnormal charge, abnormal coordination of neighboring atoms) is not associated permanently with the primary defect atom, but can be passed on to other atoms in the manner of a transfer. The greater the number of atoms (only one of which is radioactive) involved in this exchange, the greater is the retention, which may in the extreme case be as high as 100 %. Conversely, the number n of atoms involved in the transfer can be calculated from the maximum retention at temperature T, *i.e.* $R_\infty(T)$, using the expression $n = 1/(1-R_\infty(T))$.

A possible example of this process is given by *Schmidt*'s experiments [163] on the chemical effects of the isomer transition $^{80m}Br \rightarrow {}^{80}Br$ in the complexes $[Rh(NH_3)_5{}^{80m}Br]X_2$ and $[Ir(NH_3)_5{}^{80m}Br]X_2$ (X = Cl, Br). In these experiments the retention decreased from an initial value of between 45 and 55 % to 34 % on annealing above 200 °C. This behavior can be most easily explained as an activated transfer, in which ^{80}Br occupies one of a total of three halogen sites with equal probability. Normal annealing curves with increasing retention, however, were found for the nitrates (X = NO_3). Thus halide and nitrate cannot undergo transfer, probably on steric grounds.

In activated NH_4Cl (nuclear reaction $^{14}N(n,p)^{14}C$), 10 % of the ^{14}C is in the form of HCOOH, HCHO, and CH_3OH, even after sublimation of the material. Thus the precursors of these substances do not anneal, even on complete reformation of the lattice [164].

The annealing in $[Co(NH_3)_6]Cl_3$ is attributed to a purely chemical reaction [165]:

$$[^{60}CoCl(NH_3)_5]Cl_2 \xrightarrow{NH_3} [^{60}Co(NH_3)_6]Cl_3$$

X. Experimental Support for the Disorder Model

The neutron irradiation of anhydrous Na_2HPO_4 gave 10 % retention together with 11 % each of triphosphate and diphosphate, 26 % of isohypophosphate, 3 % of hypophosphate, and 9 % each of diphosphite, phosphite, and hypophosphite. In view of the absence of large quantities of polyphosphate, the hot-spot model may be ruled out. Isohypophosphate is not labeled randomly, but as $P^5-O-{}^{32}P^3$. These experiments were taken as the first evidence that the disorder is only slight [55]. It is assumed that triphosphate, isohypophosphate, and hypophosphate [166] are formed in the crystal, and not on dissolution. The fact that 80 % of the triphosphate is in the form $P-O-{}^{32}P-O-P$, *i.e.* is labelled in the center, indicates a high steric specificity of the reaction; thus the triphosphate is formed by the insertion of a ^{32}P recoil atom between two PO_4^{3-} tetrahedra. Accordingly, the triphosphate yield decreases on neutron irradiation of hydrated orthophosphates, since the distance between the PO_4 groups is greater in this case. Triphosphate obtained from diphosphates is labeled mainly in the terminal position [167].

On irradiation of rhombic sulfur, the active sulfur from the reaction $^{34}S(n,\gamma)^{35}S$ (maximum recoil energy *ca.* 750 eV) remains in the rhombic sulfur, whereas the phosphorus atoms from the reactions $^{32}S(n,p)^{32}P$ and $^{32}S(n,p)^{33}P$ (recoil energies 45 and 15 keV respectively) are found in the S_μ fraction [168]. However, this enrichment is due to adsorption of phosphorus-oxygen compounds, and so does not support the hot-spot theory even for the high energies mentioned [169].

On neutron activation of white phosphorus, 66 % of the ^{32}P is found in the red phosphorus, which amounts to only about 1 % of the total. However, this transmutation is brought about, not only by heat, but also by the rupture of the bonds in the P_4 molecule as a result of the recoil. When the irradiated product is heated, the annealing reaction $^{32}P_{red} \rightarrow {}^{32}P_{white}$ is masked by the polymorphous transition $P_{white} \rightarrow P_{red}$ [170]. These results also favor the disorder model.

Following the nuclear reaction $^{80}Se(n,\gamma)^{81m}Se$ in red selenium, only 2 % of the recoil atoms are found in the gray and vitreous selenium; the hot-spot model predicts a higher proportion [171].

Annealing reactions can follow a very specific course. After the nuclear reaction $^{59}Co(n,\gamma)^{60}Co$, the initial retention of (+)-$[Co(en)_3](NO_3)_3 \cdot 3H_2O$ is 4.5 %, while that of the (−)-form amounts to 0.4 %. On prolonged annealing at 80 °C, these values increased to 69.2 and 3.1 % respectively, *i.e.* on annealing the original optical isomer is reformed [58]. Similar behavior is found for *cis-trans* isomers of $[Co(en)_2Cl_2]NO_3$ and $[Co(en)_2Br_2]NO_3$ [172–174].

The hot-spot theory explains this phenomenon as being due to recrystallization of the molten region during which the matrix that has remained unchanged impresses its own structure on the recrystallized material. However, there is no parallel for such a process in inorganic chemistry. According to the disorder model, only very slight changes occur, so that the starting material can be readily reformed. At higher recoil energies, however, greater damage is expected; the formation of an isomer that was not originally present indicates rearrangement.

[159] *S. Kaucic* and *M. Vlatkovic*, Croat. chem. Acta *35*, 305 (1963).

[160] *D. J. Apers, K. E. Collins, C. H. Collins, Y. F. Ghoos*, and *P. C. Capron*, Radiochim. Acta *3*, 18 (1964).

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[162] *G. E. Boyd*, cited in [160].

[163] *G. B. Schmidt* and *W. Herr*, Z. Naturforsch. *18a*, 505 (1963).

[164] *P. E. Yankwich* and *P. J. Marteney* in [2], *2*, 81 (1965).

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[168] *G. Nilsson*, Acta chem. scand. *10*, 94 (1956).

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[171] *J. Cifka*, Radiochim. Acta *5*, 140 (1966).

[172] *H. E. Rauscher, N. Sutin*, and *J. M. Miller*, J. inorg. nuclear Chem. *12*, 378 (1960).

[173] *H. E. Rauscher, N. Sutin*, and *J. M. Miller*, J. inorg. nuclear Chem. *17*, 31 (1961).

[174] *P. Dimotakis* and *A. G. Maddock* in [1], *1*, 365 (1961).

This was in fact found for 100 keV ^{58}Co recoil atoms from the nuclear reaction $^{59}Co(n_f,2n)$ in *cis*- and *trans*-$[Co(en_2)Cl_2]NO_3$ [175]. Migration of the recoil atom back to its original place is unlikely. For *cis-trans* complexes containing only monodentate ligands such as $Co(NH_3)_4(NO_2)_2^+$ and $Co(NH_3)_2(NO_2)_4^-$, the stereospecificity of the annealing process is low even at low recoil energies, *i.e.* rearrangements can take place more readily [61,63].

Many elements give two or more active nuclides on (n,γ) activation. The chemical secondary reactions of such isotopes may differ quantitatively. This is referred to as an isotope effect, and can result from: 1. differences in the recoil energy, 2. differences in the charge as a result of the Auger effect, 3. differences in the masses of the recoil atoms.

It is not generally possible to attribute an isotope effect definitely to any one of these factors. However, an exception is found in zinc phthalocyanine [79]. The retention was 28.9 % for ^{65}Zn and 41.6 % for ^{68m}Zn; the values for the dipyridine complex Zn(phthalocyanine)(pyridine)$_2$ are 4.7 % and 14.3 % respectively. Thermal annealing is observed only for ^{69m}Zn. From the γ spectra of the compound nuclei, it can be estimated that the recoil experienced by ^{65}Zn is approximately twice as strong as that experienced by ^{69m}Zn, so that the former travels farther. Thus recombination of the organic residue with ^{65}Zn becomes less likely; the retention decreases and annealing by recombination does not take place. The lower retention values for the dipyridine complex are explained by hindrance of recombination by the pyridine or its fragments.

A wealth of information was obtained in the study of the nuclear reaction $^{185}Re(n,\gamma)^{186}Re$ in homogeneous mixed crystals K_2ReBr_6/K_2SnCl_6 and K_2ReBr_6/K_2OsCl_6 containing 1 to 28 and 6 to 20 mole-% of K_2ReBr_6 respectively [70,147]. In mixed crystals containing little K_2ReBr_6, primary retention would give $^{186}ReBr_6^{2-}$; retention *via* a billiard-ball collision would yield $^{186}ReCl_6^{2-}$, since the recoil atom would probably displace Sn or Os. According to the hot-spot and disorder models, however, mixed bromochlororhenates should also be expected.

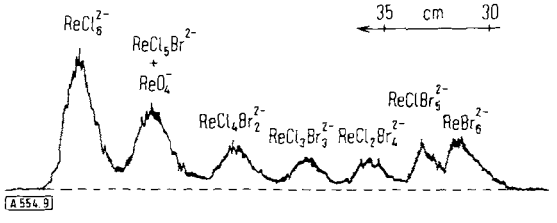


Fig. 9. ^{186}Re activity after ionophoretic separation of neutron-irradiated K_2ReBr_6/K_2SnCl_6 mixed crystals (see also Table 6) [70].

The various species were separated by ionophoresis; an example of an activity distribution is shown in Fig. 9; numerical values are given in Table 6. Normal ligand exchange occurs neither during the preparation of the mixed crystals nor during the ionophoretic separation [176,177]. Most of the recoil atoms are in the form of mixed bromochlororhenates, which must therefore

Table 6. Products of the nuclear process $^{185}Re(n,\gamma)^{186}Re$ in mixed crystals. The figures are expressed as percentages of the total ^{186}Re content.

Ion found	K_2ReBr_6 in K_2SnCl_6 (molar prop. 1:>100)	K_2ReBr_6 in K_2OsCl_6 (molar prop. 1:>100)
$^{186}ReBr_6^{2-}$	13	13
$^{186}ReBr_5Cl^{2-}$	7	5
$^{186}ReBr_4Cl_2^{2-}$	6	8
$^{186}ReBr_3Cl_3^{2-}$	8	12
$^{186}ReBr_2Cl_4^{2-}$	11	13
$^{186}ReBrCl_5^{2-}$	13	11
$^{186}ReCl_6^{2-}$	32	3
$^{186}ReO_4^-$	10	35

have been formed according to either the hot-spot or the disorder model (the forms $^{186}ReCl_6^{2-}$ and $^{186}ReBr_6^{2-}$ can also be formed in this way). The billiard-ball mechanism can be abandoned as a general model, since only 3 % of $^{186}ReCl_6^{2-}$ was found in the system K_2ReBr_6/K_2OsCl_6. Similarly, $^{186}ReBr_6^{2-}$ is thought to result from annealing, and not to represent the primary retention.

Even when very dilute solid solutions are used (up to 1 and 6 %, respectively, of K_2ReBr_6), bromide accumulates in the ligands around the recoil nuclei to concentrations of 34 % in K_2ReBr_6/K_2SnCl_6 and 53 % in K_2ReBr_6/K_2OsCl_6, based on the total number of ligands. This is not due to any preference of the recoil atom for bromine, since in the mixed crystal K_2ReCl_6(2 mole-%)/K_2SnBr_6, 48 % of the ligands in the recoil products are chloride. The only explanation for the enrichment is that a small reaction zone, in consequence of a small recoil range, is situated around the locality of the nuclear event so that the six original ligands form a considerable proportion of all the halogen atoms available for recombination with the recoil atom. From the number of Br ligands in excess of the statistical probability, it is calculated that 18 halogen atoms are involved for K_2ReBr_6/K_2OsCl_6. The unit cell of the matrix substance, which has a volume of about 1000 Å^3, contains 24 halogen atoms; thus the reaction zone of the Szilard-Chalmers process is calculated to have a volume of 500 to 700 Å^3 and an average radius of about 5 Å. This value is also a measure of the recoil range, and agrees with the figures given in Section VII.8.

The size of the reaction zone is about one order of magnitude smaller than predicted by the hot-spot model, but is approximately as expected from the computer calculations [143]. This supports the disorder model. The idea of a "melt" is also opposed by the fact that the distribution of all possible bromochlororhenates is not statistical, relative to the halogen atoms in the reaction zone; it reflects instead the special position of the recoil atom after the loss of its energy and the smallness of the changes in the arrangement of the other atoms. The fact that only 3 % of $^{186}ReCl_6^{2-}$ is found for K_2ReBr_6/K_2OsCl_6, as compared with 32 % for K_2ReBr_6/K_2SnCl_6, shows that the recoil range in the former system is just small enough to prevent the recoil atom passing into the pure chloride environment of the K_2OsCl_6 matrix, probably because of the greater mass of osmium and the stronger bonding between the osmium and its ligands. This difference cannot be explained by the hot-spot model. All the changes described take place in the crystal before dissolution.

A reaction zone of only one or two molecular diameters was also found in experiments on the chemical effects of the isomeric transition $^{80m}Br \rightarrow {}^{80}Br$ in solid alkyl bromides [178].

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XI. Other Experimental Results

The $^{59}Co(n,\gamma)^{60}Co$ reaction in $[Co(NH_3)_6][Co(CN)_6]$ and in $[Co(NH_3)_6][Fe(CN)_6]$ leads to all of the seven possible complexes $[^{60}Co(CN)_n(NH_3)_{6-n}]^{3-n}$ $(0 \leq n \leq 6)$, but this result cannot be interpreted in the same manner as for the hexahalogenometalate mixed crystals (see Section X) [179].

In the complex salts $[CoX_n(NH_3)_{6-n}]Y_{3-n}$ ($X = NO_2$; $Y = NO_2$, NO_3; $n = 1,2,3$), $K[Co(NO_2)_4(NH_3)_2]$, and $NH_4[Co(NO_2)_4(NH_3)_2]$, further nitro groups, but no NH_3 groups, enter the coordination sphere [60]. In cobalthexammine salts, the entry of a free ion into the coordination sphere is observed: $[Co(NH_3)_6]X_3 \rightarrow [^{60}CoX(NH_3)_5]X_2$ ($X = Cl$, Br) (as well as after the isomeric transition $^{80m}Br \rightarrow {}^{80}Br$) [62, 165, 180]; the tetrammine complexes $[^{60}CoX_2(NH_3)_4]^+$ are no longer stable. On annealing, the pentamminehalogeno complexes disappear in favor of the starting substance. The same is true of nitroammine complexes $[Co(NO_2)_n(NH_3)_{6-n}]^{3-n}$ ($n = 2, 3, 4$) [63]. In these cases, therefore, the chemical difference of the ligands does not allow the simple requirements of the disorder model to become effective. In activated K_2ReBr_6/K_2ReCl_6 mixed crystals, on the other hand, annealing leads to the formation of all the mixed bromochlororhenates (IV) [147].

Entry of ions into the ligand sphere also takes place in the bromine activation $^{79}Br(n,\gamma)^{80m}Br$ of $[CoX(NH_3)_5]Br_{2\text{ or }3}$ and $[CoX_2(en)_2]Br_{1\text{ or }3}$ ($X = NH_3$, NCS, NO_2, H_2O, ONO, ONO_2, F, Cl, Br, I); the products are $[Co^*Br(NH_3)_5]^{2+}$ and $[CoX^*Br(en)_2]^{1+\text{or}2+}$ [181, 182]. In the neutron irradiation of sparingly soluble hydroxo salts such as $4Co(OH)_2 \cdot Mn(OH)Cl$ or $4Zn(OH)_2 \cdot Ni(OH)Br$ with disordered intermediate layers of basic hydroxides, some of the ^{60}Co and ^{65}Zn recoil atoms accumulate in the disordered layers, and can be removed by ion exchange [183].

The nuclear reaction $^{35}Cl(n,p)^{35}S$ in alkali metal chlorides sublimed under vacuum or drawn from the melt leads to more than 50 % of a precursor that can be obtained as sulfide on dissolution in aqueous sulfide solution. This precursor is probably in the form of neutral atomic sulfur (possibly also of S^+ or S^-). The life of the fragment in question in the solution must be at least 10^{-6} sec, since owing to the low sulfide carrier concentration, the protective transfer reaction, can

$$^{35}S^0 + S^{2-} \longrightarrow {}^{35}S^{2-} + S^0$$

occur on average only after 10^{-6} sec. Sulfur can be extracted from the irradiated crystals; on annealing, it appears to accumulate on the crystal surface. The sulfide yield is increased by the incorporation of cation vacancies, by electron irradiation before activation, and by the use of alkali metal chloride containing F centers. On dissolution in sulfide-free water, or if analytically pure alkali metal chloride is used without pretreatment, the main product is sulfate, together with a little sulfite [53, 184–186].

When a mixture of a uranium compound with a catcher substance is irradiated with neutrons, fission fragments can be used for syntheses [28, 187–189]. The following reactions have been carried out (the yields are given in brackets; the uranium compound is not indicated:)

$$Cr(CO)_6 \longrightarrow {}^{99}Mo(CO)_6\ (60\,\%),\ {}^{99m}Tc(CO)_6$$
$$Fe(C_5H_5)_2 \longrightarrow {}^{103}Ru(C_5H_5)_2\ (60\,\%),\ C_5H_5FeC_5H_4{}^{131}I$$
$$C_6H_6 \longrightarrow C_6H_5{}^{131}I\ (60\,\%)$$
$$C_6H_5X \longrightarrow C_6H_5{}^{131}I,\ C_6H_4X{}^{131}I$$
$$\beta\text{-}C_{10}H_7Br \longrightarrow \beta\text{-}C_{10}H_7{}^{131}I\ (40\,\%)$$
$$CH_3COONH_4 \longrightarrow CH_3{}^{131}I$$
$$LiF \longrightarrow Xe\text{–}F\ \text{compounds.}$$

The first reaction permitted the rapid separation of the previously unknown nuclides ^{103}Mo, ^{104}Mo, and ^{105}Mo [190–192]. The decisive synthetic step in the labeling with fission fragments is the β^- decay of the precursor [193]. Syntheses induced by β decay are also known for liquids [194–196].

XII. Mössbauer Effect

Probably the greatest obstacle to an understanding of the chemical effects of nuclear transformations in solids is ignorance of the state of the recoil atom when it has come to rest. All the usual methods fail because of the low concentration of the defect centers.

However, it has now been found that the position and structure of the Mössbauer resonance lines depend on chemical bonding, *i.e.* on the charge and environment of the Mössbauer nucleus [197]. It is therefore possible to study the structure of individual atomic defects in the solid [198, 199]. In

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contrast to the usual Mössbauer investigations, the compound to be investigated must be used as the Mössbauer radiation source, and not as the absorber.

^{57}Co decays ($\tau_{1/2}$ = 267 days) with electron capture to give an excited (14.4 keV) ^{57}Fe state. About one third of the new nuclides have the same charge as the ^{57}Co used and the rest have a higher positive charge, owing to the Auger effect. The excited ^{57}Fe state decays to the ground state with an average life of about 10^{-7} sec. Investigation of this transition by means of the Mössbauer effect provides information about the chemical state, *i.e.* the charge, of an iron atom 10^{-7} sec after its formation from ^{57}Co. The atomic environment of the 14.4 keV ^{57}Fe is the same as that of the original ^{57}Co, since the recoil after the decay of the latter is too small to cause displacements.

^{57}Co-doped CoO, ZnF_2, and NaF[200,201], as well as $^{57}CoCl_2$ that has separated out in NaCl[202], contain only Fe^{2+}, while isolated $^{57}Co^{2+}$ cations in NaCl give some Fe^{+}[203]. Both Fe^{2+} and Fe^{3+} are found in $^{57}Co^{III}(acac)_3$[204], $[^{57}Co^{III}(C_5H_5)_2]B(C_6H_5)_4$[205], (Fe, $^{57}Co)(NH_4)_2(SO_4)_2 \cdot 6H_2O$[201], $^{57}CoCl_2 \cdot 6H_2O$, $^{57}CoSO_4 \cdot 7H_2O$, $^{57}Co(NH_4)_2(SO_4)_2 \cdot 6H_2O$, and $^{57}CoSiF_6 \cdot 6H_2O$[206]. Small quantities of Fe^{4+} are also found in $^{57}Co(NH_4)_2(SO_4)_2 \cdot 6H_2O$ and $CoSiF_6 \cdot 6H_2O$.

^{129}I decays with β^- emission ($\tau_{1/2} = 1.6 \times 10^7$ years), to give an excited (40 keV) state of ^{129}Xe, which goes to the ground state with an average lifetime of 10^{-9} sec. The chemical state of the xenon depends on the starting compound[207].

$$^{129}I_2 \longrightarrow {}^{129}Xe^0?$$

$$Na^{129}I \longrightarrow {}^{129}Xe^0$$

$$Na^{129}IO_3 \longrightarrow {}^{129}XeO_3$$

$$K^{129}IO_4 \longrightarrow {}^{129}XeO_4$$

$$Na_3H_2{}^{129}IO_6 \longrightarrow \text{6 O octahedrally arranged around } {}^{129}Xe$$

$$K^{129}ICl_4 \cdot H_2O \longrightarrow {}^{129}XeCl_4 \ (\geqslant 75\,\%)$$

$$K^{129}ICl_2 \cdot H_2O \longrightarrow {}^{129}XeCl_2$$

(Nothing can be said about the stability of the $XeCl_4$ at a later time; $XeCl_2$ has recently been synthesized[208]).

The chemical effects of nuclear transformations would be directly comparable only with the results of Mössbauer investigations on nuclei produced by a nuclear process in the substance under investigation. However, all that is known is that the ^{56}Mn nuclei formed from $KMnO_4$ in (n,γ) reactions are in the form of Mn^{7+}, Mn^{4+}, and $Mn^{<4+}$, while ^{119m}Sn from both SnO_2 and SnO is entirely in the form of Sn^{4+}[209].

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New Methods of Preparative Organic Chemistry V[1]

Organic Syntheses with Imides of Sulfur Dioxide

BY G. KRESZE AND W. WUCHERPFENNIG [*]

Cycloadditions and other reactions of compounds containing the groups N=SO and N=S=N are reviewed.

Two series of imides are derived from sulfur dioxide, *i.e.* the *N*-sulfinyl compounds R–N=SO and the sulfodiimides[1] R–N=S=N–R'. In the organic derivatives, R and R' may be alkyl or aryl groups, or organic groups attached to the N atom *via* heteroatoms.

The first compound of this class to be identified as such by *Michaelis* and *Herz*[2] was *N*-sulfinylaniline ("thionylaniline") *(1a)*, which was obtained by the reaction of aniline with $SOCl_2$:

$$C_6H_5{-}NH_2 + SOCl_2 \longrightarrow C_6H_5{-}NSO + 2\,HCl \qquad (1a)$$

This compound had been described even earlier by *Böttinger*[3], but its constitution had not been given.

In recent years the properties and behavior of such compounds have been reinvestigated by several research groups. It was found that these compounds, and particularly the extremely reactive *N*-sulfinylsulfonamides[4,5], can undergo

[*] Prof. Dr. G. Kresze and Dr. W. Wucherpfennig
Organisch-Chemisches Institut der Technischen Hochschule
Arcisstr. 21
8 München 2 (Germany)

[1] The papers in the preceding series have been published in four volumes by Verlag Chemie, Weinheim/Bergstr.; English edition: Academic Press New York-London. Volume V will appear shortly.

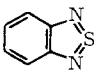
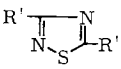
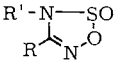
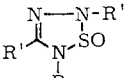
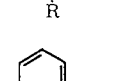
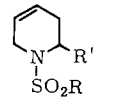
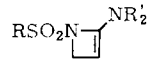
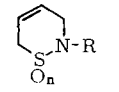
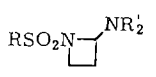
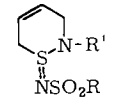
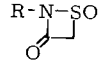
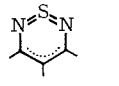
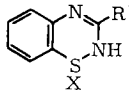
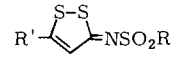
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Table 1. Classes of compounds that can be prepared by reactions with *N*-sulfinyl compounds and sulfodiimides.

Classe of compound	Section	Class of compound	Section
a) By introduction of new functional groups			
$RR'C{=}CR'R$	1.2.4.4.		1.2.4.3., 2.2.3.
$RSO_2N{=}CR'R''$	1.2.3.1., 1.2.3.2.		1.2.3.4.
$RSO_2N{=}CR'NR_2''$	1.2.2.2., 1.2 3.2., 1.2.3.4.		1.2.2.2.
$RN{=}C{=}NR'$	1.2.2.2., 2.2.2.		1.2.2.2.
$Ar{-}C{\equiv}N$	1.2.3.2.		1.2.3.1.
$Ar{-}N{\equiv}N^{\oplus}X^{\ominus}$	1.2.6.		
$RSO_2N{=}SR'R''$	1.2.3.3.		
$RSO_2N{=}PR'R''R'''$	1.2.3.3., 1.2.6.		
$RNHS(O){-}R'$	1.2.6.		
$RNHS(O){-}SR'$	1.2.4.2		
$Ar{-}SSS{-}R$	1.2.4.2.		
$RSO_2NH{-}CHR'{-}CHR''{-}CH{=}CHR'''$	1.2.2.1.		
b) By ring closure to form heterocycles			
	1.2.4.4		1.2.3.1.
	1.2.3.1.	 (n = 0, 1, 2)	1.2.2.1.
	1.2.3.1.		2.2.1.
	1.2.2.3.		1.2.4.3.
	1.2.2.1.		1.2.4.3.
	1.2.3.4.	(X = O, O_2, NSO_2R, $(O)NSO_2R$)	

a wide variety of reactions and can be used for many syntheses. This use of the *N*-sulfinyl compounds is discussed below. Reviews dealing with the reactivity of the compounds, their physical properties, and their molecular structure have already been published [4,6]. These questions are not discussed here, nor is the chemistry of unsubstituted thionylimide HNSO [7]. Experimental details of the methods of preparation and reactions of *N*-sulfinyl compounds, which are only summarily referred to here, have been given in the first review article [4].

The first sulfodiimides were prepared in 1956 [8]. Benzo-2,1,3-thiadiazole (piazthiole) [9] could be formally regarded as a sulfodiimide, but the properties of this highly aromatic system are quite different from those of the "open-chain" sulfodiimides. In particular, piazthiole does not give the reactions of the N=S linkage that are characteristic of the other N=S=N compounds.

The classes of compounds that can be synthesized by reactions with imides of sulfur dioxide are listed in Table 1.

1. *N*-Sulfinyl Compounds

N-Sulfinyl compounds known so far are derived from aliphatic or aromatic amines, hydrazines [10,11,12], *O*-substituted hydroxylamines [13], acid hydrazides [12, 14,15], thiosemicarbazide [14], hydroxamide *O*-ethers $R{-}C(NOR')NH_2$ [16], sulfenamides [4], sulfonamides [4, 5], and dialkyl phosphoramidates $(RO)_2P(O)NH_2$ [17].

The *N*-sulfinylsulfonamides and the *N*-sulfinylamines have hitherto been most widely used for synthetic work and the preparation of these compounds will be described in detail. The *N*-sulfinyl derivatives of acid hydrazides

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and thiosemicarbazide are thermally unstable [12,14,15], while with the hydrazones of benzaldehyde and benzophenone, nitrogen is liberated even under mild conditions during the preparation of the *N*-sulfinyl compound [12,16]. The *N*-sulfinylhydrazines, which are very stable to hydrolysis, have been used as acaricides [18,23].

1.1. Preparation of *N*-Sulfinylamines and *N*-Sulfinylsulfonamides

1.1.1. *N*-Sulfinylamines

N-Sulfinylamines are generally prepared from the amines with thionyl chloride in ether or benzene.

Treatment of aromatic amino acids [20], or their Pb or Ag salts [21], with $SOCl_2$ yields *N*-sulfinylaminoacyl chlorides.

The *N*-sulfinyl derivatives of sensitive amines can be advantageously prepared by "transsulfinylation", which is based on the equilibrium

$$R{-}NH_2 + R'{-}NSO \rightleftharpoons R{-}NSO + R'{-}NH_2.$$

The lower the basicity of the amino compound $R'{-}NH_2$ and the higher the basicity of $R{-}NH_2$, the farther is this equilibrium displaced to the right. Consequently, *N*-sulfinylsulfonamides $R{-}SO_2{-}NSO$ *(2)* are excellent sulfinylating agents (cf. also Section 1.2.4.3.).

1.1.2. *N*-Sulfinylsulfonamides

Sulfonamides *(3)* can also react with thionyl chloride [4],

$$\underset{(3)}{R{-}SO_2{-}NH_2} + SOCl_2 \longrightarrow \underset{(2)}{R{-}SO_2{-}NSO} + 2\,HCl.$$

The reaction proceeds smoothly when the sulfonamide is heated with an excess of thionyl chloride in the absence of solvents; in benzene it proceeds much slower than the reaction of amines, but gives good yields if the reaction mixture is heated under reflux for several days. The sulfinylation is complete when the sulfonamide has dissolved and (except in the case of the *p*-nitrobenzene derivative) is not reprecipitated even after the reaction solution has cooled.

Instead of the sulfonamides *(3)*, the Na salts of the *N*-chlorosulfonamides

$$R{-}SO_2{-}NClNa + SOCl_2 \longrightarrow \underset{(2)}{R{-}SO_2NSO} + NaCl + Cl_2,$$

or the *N,N*-dichlorosulfonamides may be treated with $SOCl_2$ to obtain *N*-sulfinylsulfonamides *(2)* [5].

$$R{-}SO_2{-}NCl_2 + SOCl_2 \longrightarrow \underset{(2)}{R{-}SO_2{-}NSO} + 2\,Cl_2$$

Table 2. Examples of *N*-sulfinylsulfonamides $R{-}SO_2{-}NSO$ *(2)*.

R	M.p. (°C)	Yield (%)	Method
CH_3	[a]	86	B
C_6H_5	70	80	B
p-$CH_3{-}C_6H_4$	53	80	A
p-$CH_3O{-}C_6H_4$	30	75	A
p-$F{-}C_6H_4$	59.5	69	A
p-$Cl{-}C_6H_4$	58–60	88	B
p-$Br{-}C_6H_4$	60–61	83	B
o-$NO_2{-}C_6H_4$	112–113	99	C
m-$NO_2{-}C_6H_4$	79–80	73	C
p-$NO_2{-}C_6H_4$	115–117	96	C

[a] B.p. = 80–81 °C/10^{-4} mm.

Procedures

N-Sulfinyl-p-toluenesulfonamide (2a) (method A)

100 g of *p*-toluenesulfonamide *(3a)* is refluxed for 8 h with 180 ml of $SOCl_2$. The excess of thionyl chloride is removed by distillation and the residue is then distilled at about 0.1 mm Hg. M.p. 53 °C, yield 75–80%.

N-Sulfinyl-p-chlorobenzenesulfonamide [4] (method B)

31 g of *p*-chlorobenzenesulfonamide and 13.5 ml of $SOCl_2$ are refluxed in 50 ml of dry benzene in the absence of moisture. After three days the sulfonamide has completely dissolved and is not reprecipitated on cooling. The solvent is removed at about 10 mm Hg and the brown, liquid residue is distilled in a high vacuum. 34 g (88%) of a yellow oil distils over and solidifies on cooling. B.p. 122–125 °C/10^{-4} mm, m.p. 52–53 °C.

N-Sulfinylarylsulfonamides (2) from Na Salts of N-Chloroarylsulfonamides [5] (method C)

0.15 mole of $SOCl_2$ is added dropwise to a suspension of 0.1 mole of the dry Na salt of *N*-chloroarylsulfonamide in benzene or CCl_4. The reaction mixture slowly becomes warm. After a time the precipitate of NaCl is removed by filtration and the solvent and excess of $SOCl_2$ are removed from the filtrate by distillation at reduced pressure. The oily residue of *N*-sulfinylarylsulfonamide crystallizes on cooling. Some examples of *N*-sulfinylsulfonamides prepared by methods A–C are given in Table 2.

N-Sulfinylarylsulfonamides (2) from N,N-Dichloroarylsulfonamides [5] (method D)

A mixture of 0.1 mole of *N,N*-dichloroarylsulfonamide and 0.15 mole of $SOCl_2$ is heated at 80–100 °C until the liberation of chlorine stops (2–4 h). The excess of $SOCl_2$ is distilled off under vacuum. The oily residue of *N*-sulfinylarylsulfonamide crystallizes on cooling. The yields are almost quantitative.

[18] *R. Wegler* and *G. Unterstenhöfer*, DAS 1059706 (April 17th 1957) Farbenfabriken Bayer; Chem. Zbl. *1960*, 2326.

[19] *D. Klamann, Chr. Sass,* and *M. Zelenka*, Chem. Ber. *92*, 1910 (1959).

[20] *R. Graf* and *W. Langer*, J. prakt. Chem. *148*, 161 (1937).

[21] *L. Anschütz* and *H. Boedeker*, Ber. dtsch. chem. Ges. *62*, 826 (1929); *L. Anschütz* and *Z. M. Delijski*, Liebigs Ann. Chem. *493*, 241 (1932).

[22] *A. Michaelis* and *A. Buntrock*, Liebigs Ann. Chem. *274*, 262 (1893).

[23] *R. Wegler, G. Unterstenhöfer, E. Kühle,* and *E. Enders*, DAS 1143669 (May 6th 1961) Farbenfabriken Bayer; Chem. Zbl. *1963*, 18999.

[24] *E. S. Levtschenko* and *A. V. Kirsanov*, Ž. obšč. Chim. *32*, 161 (1962).

1.2. Reactions with *N*-Sulfinylamines and *N*-Sulfinylsulfonamides

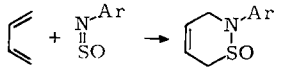
1.2.1. General

The physical properties of the *N*-sulfinylaniline derivatives show that the S=N bond of the *N*-sulfinyl compounds is to be regarded as a four-electron bond, and can enter into conjugative interaction with adjacent π-electron systems [4]. The bond is also polar, with the S atom as the positive end and the N atom as the negative end of the dipole. These structural considerations offer an explanation of the reactions of the *N*-sulfinyl compounds. Thus the substances enter into many cycloadditions with formation of six-membered, five-membered, or four-membered rings; they can add on reagents of the form HX and their analogues by a polar mechanism; and they can react with electrophilic or nucleophilic reagents in general. These reactions are discussed in the following section. In preparative work it should be noted that the primary addition products are often unstable and are readily converted into other compounds.

1.2.2. Cycloadditions

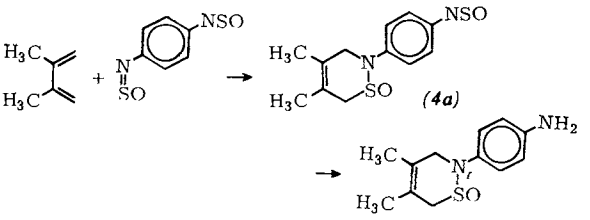
1.2.2.1. Preparation of 3,6-Dihydro-1,2-thiazine Derivatives, δ-Sultams, *N*-Alk-3-enylsulfonamides and *N*-Arylpyrroles

The diene synthesis with *N*-sulfinylarylamines as dienophiles was described by *Wichterle* and *Roček* in 1953 [25–27].



(1) *(4)*

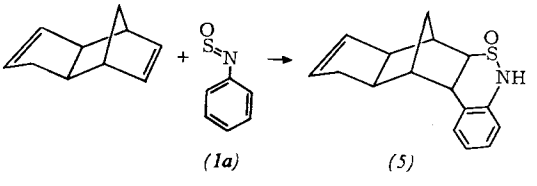
This addition takes place with all aromatic *N*-sulfinylamines *(1)*; aliphatic *N*-sulfinylamines do not react. The reactants are heated in the absence of a solvent, since the reaction is very slow in solution. An excess of diene is generally beneficial. The product often darkens when heated and vigorous decomposition sometimes occurs at higher temperatures. Polar (and probably also steric) effects of substituents on the benzene nucleus of the *N*-sulfinylarylamines have no apparent influence on the reaction. Though the *N*-sulfinylnitroarylamines react somewhat faster than N-sulfinylaniline *(1a)*, adducts are formed even by derivatives having donor substituents (such as *N*-sulfinyl-*p*-anisidine). The bis-*N*-sulfinyl derivative of *p*-phenylenediamine forms only a monoadduct *(4a)*, which reacts with water to give the amino compound.



(4a)

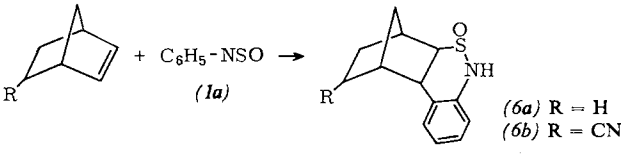
On the other hand, the steric hindrance due to substituents in positions 1 and 4 of the diene component greatly affects the rate of reaction, as do polar effects. Thus butadiene and 2-substituted and 2,3-disubstituted derivatives react normally, while butadienes with substituents at the ends of the diene system react only with difficulty, if at all. Though adducts of 1-methyl- and 1-*p*-nitrophenylbutadiene are known [28], no Diels-Alder adducts have so far been isolated with 1-acetoxybutadiene, sorbic acid (2,4-hexadienoic acid), ethyl sorbate, sorbic alcohol (2,4-hexadien-1-ol), or cyclohexadiene.

According to *Collins* [29], the 2:1 adduct obtained by the reaction of dicyclopentadiene with *N*-sulfinylaniline *(1a)* [28] has the structure *(5)*.



(1a) *(5)*

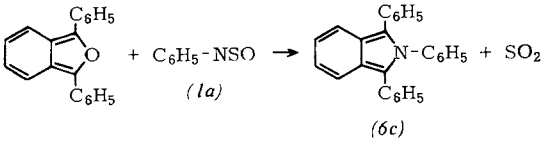
Norbornene and its 5-cyano derivative react analogously to give *(6a)* and *(6b)* respectively.



(1a) *(6a)* R = H *(6b)* R = CN

In these cases the *N*-sulfinylaniline acts not as a dienophile, but as a diene.

The reaction of *N*-sulfinylaniline *(1a)* with 1,3-diphenylisobenzofuran is anomalous [30]. The reaction without a solvent yields 46% of 1,2,3-triphenylisoindole *(6c)*. The same compound is formed in a higher yield when the reactants are heated for 13 hours in benzene in the presence of $BF_3 \cdot O(C_2H_5)_2$.



(1a) *(6c)*

The adducts *(4)* can be converted into *N*-aryl-δ-sultams *(7)*, while reduction with $LiAlH_4$ leads to 3,6-dihydro-1,2-thiazines *(8)*.

[25] *O. Wichterle* and *J. Roček*, Chem. Listy *47*, 1768 (1953).

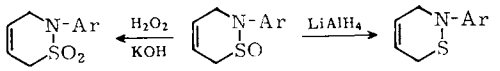
[26] *O. Wichterle* and *J. Roček*, Coll. czechoslov. chem. Commun. *19*, 282 (1954), Chem. Abstr. *49*, 10531 (1955).

[27] *J. Roček* and *O. Wichterle*, Czech. Pat. 83770 (Jan. 3rd, 1955); Chem. Abstr. *50*, 7152g (1956).

[28] *E. G. Katayev and V. V. Plemenkov*, Ž. obšč. Chim. *32*, 3817 (1962).

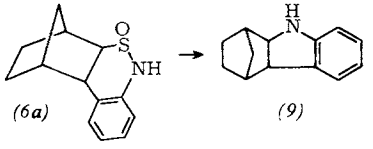
[29] *G. R. Collins*, J. org. Chemistry *29*, 1688 (1964).

[30] *M. P. Cava* and *R. H. Schlessinger*, J. org. Chemistry *28*, 2464 (1963).



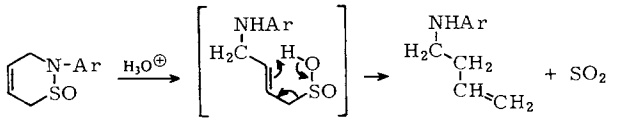
(7) (4) (8)

Desulfuration of the adduct *(6a)* with Raney nickel in ethanol yields the hexahydrocarbazole derivative *(9)* (70% yield).



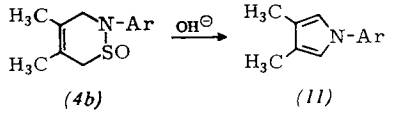
(6a) (9)

On acid hydrolysis, the *N*-aryl-3,6-dihydro-1,2-thiazine 1-oxides *(4)* lose SO_2 and the double bond migrates to give *N*-alk-3-enylarylamines *(10)*, the formation of which has been explained by *Wichterle* [25,26] as follows:



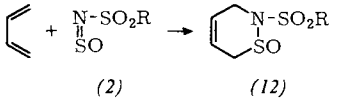
(4) (10)

The alkaline hydrolysis of the adducts *(4)* also follows an anomalous course. When the adducts are heated with alcoholic KOH, the pyrrole derivatives *(11)* are obtained, the yield being practically quantitative in the case of the 2,3-dimethylbutadiene adducts *(4b)* [25,26,31].



(4b) (11)

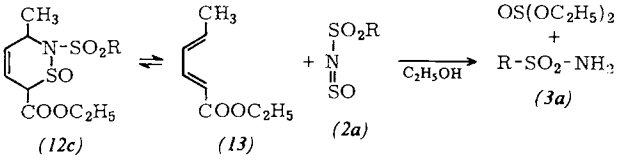
The reactivity of the NSO group in cycloadditions is generally increased by strongly electron-attracting substituents on the N atom, and is sometimes even qualitatively changed [4]. This is observed in particular in the diene synthesis with *N*-sulfinylsulfonamides *(2)* [4,24,32]. In nearly every case, these add readily and in excellent yield. The reaction is generally exothermic, and when carried out without a solvent can lead to an explosion. It is therefore recommended that an inert solvent such as benzene should be used, and that the reaction mixture should be cooled initially. The reaction is allowed to proceed to completion by prolonged standing at room temperature or by heating, and in many cases the adducts *(12)* crystallize out.



(2) (12)

All the *N*-sulfinylsulfonamides *(2)* studied so far are very reactive in the diene synthesis. However, the structure of the diene has the same influence as in the Diels-Alder reaction with *N*-sulfinylamines *(1)*. Thus butadiene, isoprene, 2,3-dimethylbutadiene, 2-chlorobutadiene, and cyclohexadiene react rapidly at room temperature, 2,3-dichlorobutadiene and 1-*p*-nitrophenylbutadiene react at a moderate rate, and ethyl sorbate reacts very slowly. 2-Chlorocyclohexa-1,3-diene reacts only on standing for several months. No adducts are obtained with hexachlorocyclopentadiene, either at room temperature or on heating.

The Diels-Alder reaction is reversible in some cases. Thus the adduct *(12c)* of ethyl sorbate *(13)* and *N*-sulfinyl-*p*-toluenesulfonamide *(2a)* is converted back into the starting materials when heated in alcoholic solution, *p*-toluenesulfonamide *(3a)* and diethyl sulfite being formed by a secondary reaction.



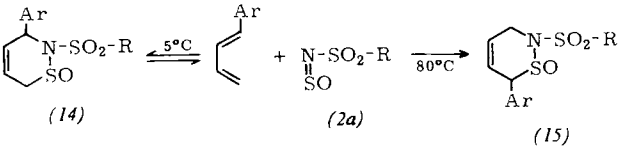
(12c) (13) (2a) (3a)

R = p–CH_3–C_6H_4

The adduct of cyclopentadiene and *N*-sulfinylbenzenesulfonamide can be isolated at low temperatures, but decomposes into its components at room temperature. *Hamer* [33] found the following data for this equilibrium in CH_2Cl_2:

25 °C	$K = 11.21$	$\Delta H° = -13.9$ kcal/mole
20 °C	$K = 18.81$	$\Delta G°_{25} = -1.4$ kcal/mole
15 °C	$K = 23.78$	$\Delta S°_{25} = -41.9$ e.u.
10 °C	$K = 35.87$	

This reversibility can also be seen in the mutual orientation assumed by the components in the Diels-Alder reaction. Thus 1-arylbutadienes react in benzene with *N*-sulfinyl-*p*-toluenesulfonamide in the cold to give 3-aryldihydrothiatine derivatives *(14)*, whereas the reaction under reflux leads to 6-aryldihydrothiazines *(15)*. The isomers *(15)*, which can be obtained from *(14)* by heating in benzene, are the thermodynamically more stable products, probably because of mutual hindrance of the aryl- and toluenesulfonyl groups in *(14)* [34].



(14) (2a) (15)

R = p–CH_3–C_6H_4

The 3-aryldihydrothiazine derivatives *(14)* and the adducts of the *N*-sulfinylsulfonamides *(2)* with 2-substituted butadienes (2-methyl-, 2-chloro-, and 2-phenylbutadiene) obey the empirical rule for orientation in the Diels-Alder reaction, which had been established in the analogous cycloadditions of nitrosobenzenes [35]. According to this rule, the orientation corresponds to that of a diene synthesis with a vinyl compound CH_2=CHX if the C^1 of the vinyl compound is replaced by the N atom of the *N*-sulfinylsulfonamide and C^2 by the S atom.

Like the *N*-aryldihydrothiazines *(4)*, the *N*-arylsulfonyldihydrothiazines *(12)* give sultams *(16)* on oxidation, preferably with H_2O_2 in acid media.

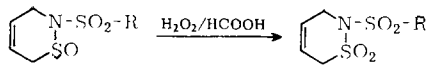
[31] *J. Roček*, Chem. Listy *47*, 1781 (1953); Coll. czechoslov. chem. Commun. *19*, 275 (1954), Chem. Abstr. *49*, 1055b (1955).

[32] *E. S. Levtschenko, Ja. G. Bal'on*, and *A. V. Kirsanov*, Ž. obšč. Chim. *33*, 1579 (1963).

[33] *J. Hamer* and *A. Macaluso*, J. org. Chemistry *31*, 3049 (1966).

[34] *G. Kresze, U. Wagner*, and *W. Wucherpfennig*, unveröffentlicht.

[35] *G. Kresze* and *J. Firl*, Tetrahedron Letters *1965*, 1163.



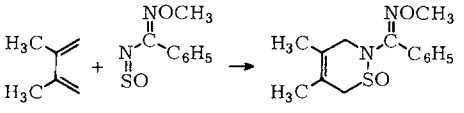
(12) (16)

However, reduction of *(12)* to the 3,6-dihydro-1,2-thiazines has not so far been observed. *(4)* and *(12)* also differ in their behavior on hydrolysis. Both acidic and alkaline hydrolysis of *(12)* lead to the same products, *N*-alk-3-enylsulfonamides *(17)* [cf. the formation of *(10)* or *(11)* from *(4)*].



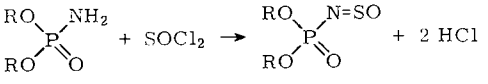
(12) (17)

N-Sulfinylbenzhydroxamide-*O*-methyl ether *(18)* can also react as a dienophile; with 2,3-dimethylbutadiene it forms the adduct *(19)* [16].



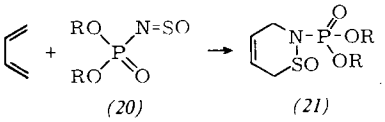
(18) (19)

The activation is not so pronounced in the case of the dialkyl *N*-sulfinylphosphoramidates *(20)* which result from the reaction of the esters *(20a)* with $SOCl_2$ [17].



(20a) (20)

The diethyl compound does not react with dienes at room temperature, but gives a Diels-Alder adduct *(21)* when butadiene is passed through a boiling solution in benzene.



(20) (21)

Procedures [*]

4,5-Dimethyl-2-phenyl-3,6-dihydro-1,2-thiazine [25, 26]

2.2 g of 4,5-dimethyl-2-phenyl-3,6-dihydro-1,2-thiazine 1-oxide is extracted for 45 min in an extraction apparatus with a boiling solution of 0.2 g of $LiAlH_4$ in 50 ml of anhydrous ether. 3 ml of water are added to the cooled reaction mixture to destroy the unreacted $LiAlH_4$. Removal of the ether by evaporation leaves 1.94 g of a yellowish oil which slowly crystallizes. Repeated recrystallization from methanol yields large rhombic plates having m.p. 93–94 °C.

1-o-Tolyl-3,4-dimethylpyrrole ((11), Ar = o-Tolyl) [31]

2.35 g of 2-*o*-tolyl-4,5-dimethyl-3,6-dihydro-1,2-thiazine 1-oxide is heated for 1.5 hours with 2 g of KOH in 25 ml of ethanol. The reaction mixture is poured into water and extracted with ether; the ether phase is then dried and evaporated to dryness. Yield 96%, m.p. 52–53 °C (coarse needles from methanol/water).

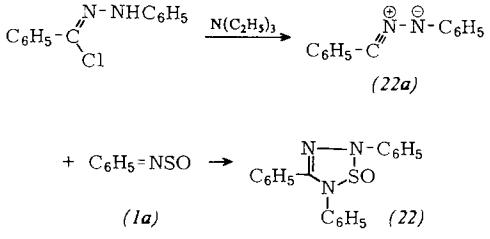
[*] The procedures given here are supplementary to those which appeared in the previous review [4]

1.2.2.2. Preparation of 2,5-Dihydro-1,2,3,5-thiatriazoles, 1,2,3,5-Oxathiadiazoles, *N*-Arylsulfonylformamidines, and Carbodiimides

Both *N*-sulfinylamines and *N*-sulfinylsulfonamides undergo 1,3-dipolar additions readily and give good yields. If the initially formed five-membered heterocyclic compound loses SO_2, the products of thermolysis rearrange.

The following components have been used so far:

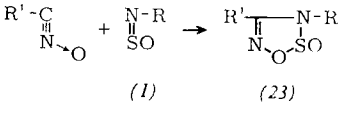
a) The nitrilimine *(22a)* (prepared *in situ* from benzoyl chloride phenylhydrazone and triethylamine) combines with *(1a)* to form 2,4,5-triphenyl-2,5-dihydro-1,2,3,5-thiatriazole 1-oxide *(22)* in 87% yield [36].



(22a)

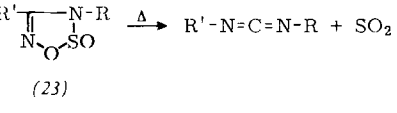
(1a) (22)

b) Nitrile oxides react exothermically with *N*-sulfinyl compounds to form 3*H*-1,2,3,5-oxathiadiazole 2-oxides *(23)*, in some cases quantitatively [37, 38].



(1) (23)

The 1,3-dipole component may be prepared *in situ*, aromatic components being prepared from the hydroxamyl chlorides and triethylamine, and the aliphatic components from the corresponding nitro compounds and isocyanates [38]. Pyrolysis of the oxathiadiazoles *(23)* leads almost quantitatively to carbodiimides, which can generally be synthesized by this route.



(23)

c) The primary adducts formed in the reaction of nitrones with *N*-sulfinylsulfonamides *(2)* are so unstable that, owing to the strongly exothermic nature of the reaction, only the secondary products, arylsulfonylformamidines *(24)*, can be isolated even at low temperatures [39, 40].

[36] *R. Huisgen, R. Grashey, M. Seidel, H. Knupfer,* and *R. Schmidt,* Liebigs Ann. Chem. *658*, 169 (1962).

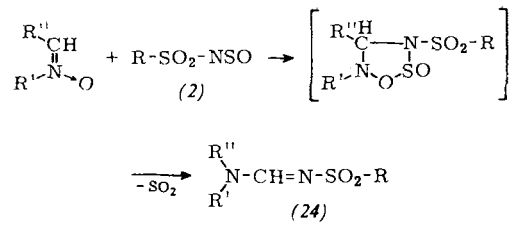
[37a] *P. Rajagopalan* and *H. U. Daeniker,* Angew. Chem. *75*, 91 (1963); Angew. Chem. internat. Edit. *2*, 46 (1963).

[37b] *P. Rajagopalan* and *B. G. Advani,* J. org. Chemistry *30*, 3369 (1965).

[38] *F. Eloy* and *R. Lenaers,* Bull. Soc. chim. belges *74*, 129 (1965).

[39] *B. P. Stark* and *M. H. G. Ratcliffe,* J. chem. Soc. (London) *1964*, 2640.

[40] *R. Albrecht* and *G. Kresze,* Chem. Ber. *98*, 1205 (1965).



(2)

(24)

Procedures

4-(p-Chlorophenyl)-3-(p-toluenesulfonyl)-1,2,3,5-oxathiadiazole 2-Oxide ((23), R' = p-Cl-C_6H_4, R = p-CH_3-C_6H_4-SO_2) [37b]

5.1 g of anhydrous triethylamine is added rapidly, with vigorous stirring, to an ice-cooled solution of 9.5 g of *p*-chlorobenzhydroxamyl chloride in 250 ml of anhydrous ether. After a few minutes the trimethylammonium chloride is filtered off and washed with a little anhydrous ether. 10.9 g of *N*-sulfinyl-*p*-toluenesulfonamide *(2a)* is added to the combined filtrates. The mixture is allowed to stand at room temperature for two hours and is then filtered, the filtrate is evaporated to dryness under vacuum, and the residue is recrystallized from n-hexane. Yield 8.5 g, m.p. 89–90 °C.

Carbodiimides [37b]

1,2,3,5-Oxathiadiazole 2-oxide in a small flask is heated at, or slightly above, its melting point in an oil bath. Moisture is excluded and a slow current of nitrogen is passed through the tube until the evolution of SO_2 stops. The flask is allowed to cool and the carbodiimides are recrystallized from hexane or benzene/hexane; liquid carbodiimides are isolated by distillation.

2,4,5-Triphenyl-2,5-dihydro-1,2,3,5-thiatriazole 1-Oxide (22) [36]

1.5 ml of triethylamine is added to a solution of 0.92 g of benzoyl chloride phenylhydrazone and 1.85 g of *N*-sulfinylaniline *(1a)* in 10 ml of boiling benzene; triethylammonium chloride is precipitated. The reaction mixture is heated for 1 hour and is then kept at room temperature for 2 hours. The reaction mixture is filtered and the filtrate is evaporated to dryness under vacuum. The crystalline residue is recrystallized from ethanol; yield 87%, m.p. 122.5–123.5 °C.

N^2-Benzene sulfonyl-N^1,N^1-diphenylformamidine [40]

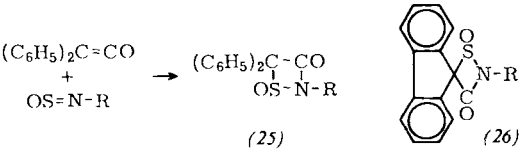
A solution of 2.5 g of *C*,*N*-diphenylnitrone in 10 ml of anhydrous benzene is added to a solution of 2.5 g of *N*-sulfinylbenzenesulfonamide in 30 ml of anhydrous benzene. The mixture becomes warm and SO_2 is evolved. After a few minutes the product begins to crystallize. Crude yield 2.5 g (59%), m.p. 187–188 °C. The substance can be recrystallized from acetone/dioxane (2:1).

1.2.2.3 Preparation of 1,2-Thiazetidin-3-one 1-Oxides

Aliphatic or aromatic *N*-sulfinylamines *(1)* and *N*-sulfinylsulfonamides *(2)* react with diphenylketene, generally at room temperature, to give *N*-substituted 4,4-diphenyl-1,2-thiazetidin-3-one 1-oxides *(25)* in good yields [4,41].

[41] *H. Beecken* and *F. Korte*, Tetrahedron *18*, 1527 (1962).

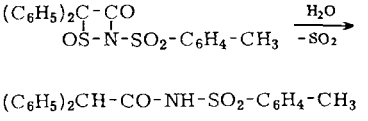
Biphenyleneketene (9-carbonylfluorene) reacts in the same way with *N*-sulfinylamine to give the spiro compounds *(26)* [41].



(25)

(26)

The diphenylketene adduct of *N*-sulfinyl-*p*-toluenesulfonamide *(2a)* can be readily hydrolysed to form *N*-(diphenylacetyl)-*p*-toluenesulfonamide *(26a)* [4].

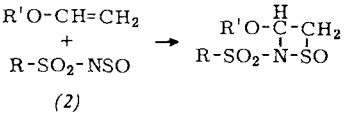


(26a)

N-Substituted diphenylacetamides are obtained from the sulfinylamine adducts by treatment with concentrated hydriodic acid or with methanolic KSH [41].

No ketene adducts of sulfinylaniline or sulfinylcyclohexylamine have so far been isolated; in the second case, sublimation in a high vacuum gave *N*-cyclohexylacetamide and *N*,*N*-dicyclohexyloxamide as secondary products.

The addition of *N*-sulfinylsulfonamides *(2)* to enol ethers is exothermic and takes place under mild conditions. In contrast to the *N*-(arylsulfonyl)isocyanate/enol ether adducts, which are readily converted into β-alkoxyacrylamides [42], the 3-alkoxy-1,2-thiazetidine 1-oxide derivatives are stable [43].



(2)

1.2.3. Reactions with Carbonyl and Sulfinyl Compounds and their Analogues

The reactions of *N*-sulfinylsulfonamides *(2)* with the groups >C=O, >C=N–, >C=S, >S=O, or >P=O vary according to the other substituents on the reactants. In many cases the reaction consists in the replacement of the *N*-aryl-(or alkyl)-sulfonylimino group by the O or S atom or by the NR group of the other reactant. On the basis of the reaction products and the feasibility of the intermediate formation of a four-membered ring, these reactions have been referred to as "quasi-Wittig reactions" [44–46]. The mechanism of the reactions is

[42] *F. Effenberger* and *R. Gleiter*, Chem. Ber. *97*, 1576 (1964).

[43] *F. Effenberger* and *R. Gleiter*, Angew. Chem. *75*, 1117(1963); Angew. Chem. internat. Edit. *3*, 142 (1964); Chem. Ber. *99*, 3963 (1966).

[44] *G. Kresze* and *R. Albrecht*, Angew. Chem. *74*, 781 (1962); Angew. Chem. internat. Edit. *1*, 595 (1962).

[45] *G. Schulz* and *G. Kresze*, Angew. Chem. *75*, 1022 (1963); Angew. Chem. internat. Edit. *2*, 736 (1963).

[46] *A. Senning*, Acta chem. scand. *18*, 1958 (1964).

still largely uncertain. A mechanism similar to that of a Wittig reaction cannot be assumed in the reaction with thionamides[14], and the stereochemistry of the sulfoxide reaction also indicates a different course[47].

1.2.3.1. Preparation of Sulfonylimines, Tetrahydropyridines, Pyridines, and Azetidines

When *N*-sulfinylsulfonamides *(2)* are heated with aldehydes having no α-H atoms, SO_2 is eliminated and *N*-sulfonylimines *(27)* are formed in good yields[44,48].

$$R\text{-}SO_2\text{-}NSO + R\text{-}CH{=}O \longrightarrow R\text{-}SO_2\text{-}N{=}CH\text{-}R' + SO_2$$
(2) *(27)*

The reaction is often catalysed by $AlCl_3$, BF_3, HCl, or similar substances. The *N*-*p*-toluenesulfonylimine of n-butyl glyoxalate [*(27a)*, R = *p*-CH_3–C_6H_4, R′ = $COOC_4H_9$] can also be obtained by this method[49]. Aliphatic aldehydes give poorer yields of 1,1-bis(arylsulfonamido)alkanes, as does polymeric trifluoroacetaldehyde. However, the sulfonylimine can be obtained by an indirect route; the hydrate of trifluoroacetaldehyde reacts with *N*-sulfinyl-*p*-toluenesulfonamide *(2a)* to form *N*-(2,2,2-trifluoro-1-hydroxyethyl)-*p*-toluenesulfonamide, whose *O*-acetyl derivative loses acetic acid on vacuum distillation to give 2,2,2-trifluoroethylidene-*p*-toluenesulfonamide *(27b)*[50].

$$CF_3\text{-}CH(OH)_2 + R\text{-}SO_2\text{-}NSO \rightarrow CF_3\text{-}\underset{\displaystyle OH}{\underset{|}{CH}}\text{-}NH\text{-}SO_2\text{-}R$$
(2a)

$$\xrightarrow{(CH_3CO)_2O} CF_3\text{-}\underset{\displaystyle OCOCH_3}{\underset{|}{CH}}\text{-}NH\text{-}SO_2\text{-}R \rightarrow CF_3\text{-}CH{=}N\text{-}SO_2\text{-}R$$
(27b)

R = p-CH_3-C_6H_4

N-Sulfinylaniline *(1a)* reacts with benzaldehyde on heating to give benzylideneaniline. However, this reaction is slower than the analogous reaction of the *N*-sulfinylsulfonamides *(2)*; an earlier report[51] of a fast exothermic reaction with formation of crystalline products could not be confirmed[48].

The reactivity of the C=N double bond in the *N*-sulfonylimines *(27)* is higher in some cases and lower in others than in normal imines. The C=N bond of the compounds derived from aromatic aldehydes is often cleaved on addition of HX, *e.g.* in the reaction with acetic acid or water. Stable adducts are obtained with thiophenol and esters of thioglycolic acid; sodiomalonic ester can also be added as an active methylene component.

$$R\text{-}SO_2\text{-}N{=}CH\text{-}R' \xrightarrow{C_6H_5SH} R\text{-}SO_2\text{-}NH\text{-}\underset{\displaystyle SC_6H_5}{\underset{|}{CH}}\text{-}R'$$
(27)

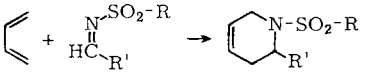
$$\downarrow CH_2(COOC_2H_5)_2 \qquad HSCH_2\text{-}COOC_2H_5 \searrow$$

$$R\text{-}SO_2\text{-}NH\text{-}\underset{\displaystyle CH(COOC_2H_5)_2}{\underset{|}{CH}}\text{-}R' \qquad R\text{-}SO_2\text{-}NH\text{-}\underset{\displaystyle SCH_2\text{-}COOC_2H_5}{\underset{|}{CH}}\text{-}R'$$

R″ = Ar

The compound derived from chloral [*(27)*, R′ = CCl_3] also gives stable adducts with water, ethanol, aniline, and *p*-toluenesulfonamide.

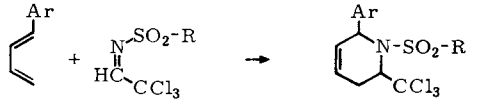
Electron-accepting substituents on a multiple bond generally increase the reactivity of this bond in Diels-Alder reactions. This effect is also observed with the *N*-sulfonylimines *(27)*. Sulfonylimines containing an aromatic group do not form adducts when heated in benzene with dienes, despite the electron-attracting action of the sulfonyl group; however, if the C atom of the CN bond also carries an electron-attracting group, as in *(27a)*, *(27b)*, and *(27c)*, adducts *(28)* are formed under the above conditions[50].



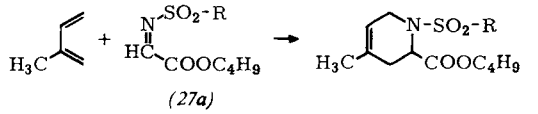
(27) *(28)*

(a) R′ = $COOC_4H_9$, R = *p*-CH_3–C_6H_4
(b) R′ = CF_3, R = *p*-CH_3–C_6H_4
(c) R′ = CCl_3, R = *p*-CH_3–C_6H_4

1-Arylbutadienes[34] and isoprene[49] form only one of the two possible isomeric adducts.



(27c)

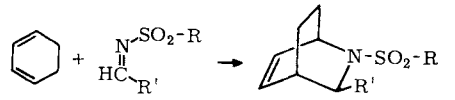


(27a)

R = p-CH_3-C_6H_4

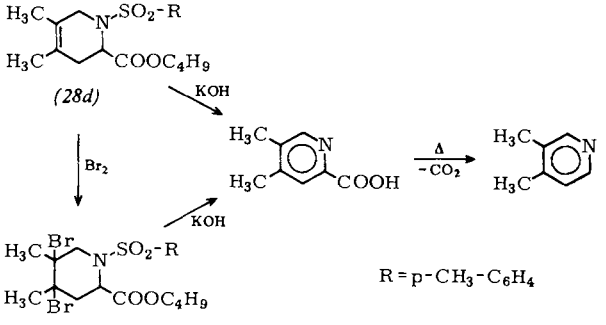
If, as is suggested by the addition reactions of the sulfonylimines, the C atom of the sulfonylimines is regarded as the positive end of the CN bond dipole and is taken to be equivalent to the β-C atom of CH_2=CHX dienophiles, the observed orientation is again in agreement with our empirical rule[35] (cf. Section 1.2.2.1).

The sulfonylimines *(27b)* and *(27a)* derived from trifluoracetaldehyde and from butyl glyoxalate react with cyclohexa-1,3-diene to form the 2-azabicyclo[2.2.2]oct-5-ene system[49, 50].



(27)

While acid hydrolysis of butyl *N*-*p*-toluenesulfonyl-1,2,3,6-tetrahydropyridine-2-carboxylate *(28a)* yields the carboxylic acid, alkaline hydrolysis also leads to elimination of *p*-toluenesulfinic acid and disproportionation; thus alkaline hydrolysis of the isoprene adduct followed by decarboxylation gives γ-picoline, while the 2,3-dimethylbutadiene adduct



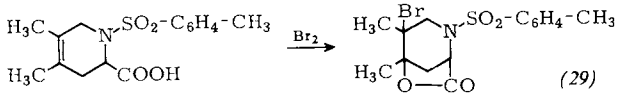
(28d)

R = p-CH_3-C_6H_4

[47] *J. Day* and *D. J. Cram*, J. Amer. chem. Soc. *87*, 4398 (1965).
[48] *R. Albrecht, G. Kresze*, and *B. Mlakar*, Chem. Ber. *97*, 483 (1964).
[49] *R. Albrecht* and *G. Kresze*, Chem. Ber. *98*, 1431 (1965).
[50] *G. Kresze* and *R. Albrecht*, Chem. Ber. *97*, 490 (1964).
[51] *M. G. Schuster*, Bull. Soc. chim. France *9*, 937 (1942).

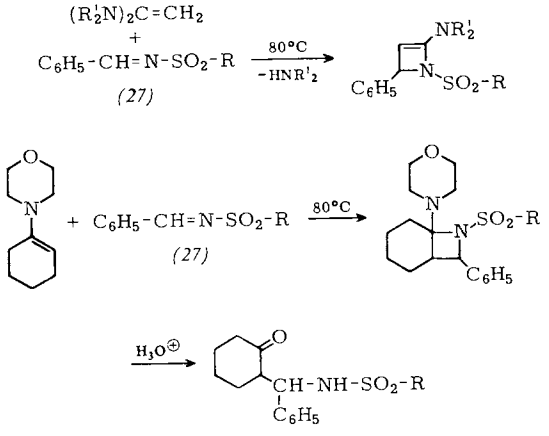
(28d) gives 4,5-dimethylpyridine-2-carboxylic acid, and hence 3,4-lutidine [49]. The yields can be improved if the adduct is first brominated and then hydrolysed with alkali; the pyridine ring system is then formed by simultaneous elimination of sulfinic acid and HBr [34].

Bromination of the free carboxylic acid corresponding to *(28d)* yields the bicyclic bromolactone *(29)* [52].



(29)

The sulfonylimines *(27)* also undergo cycloaddition with keteneaminals or enamines. 2-Aminoazetines or azetidines can be obtained in this way [53].



Procedures

N-Benzylidene-p-toluenesulfonamide ((27), R = p-CH₃–C₆H₄) [54]

A slow current of dry HCl gas is passed through a solution of 0.1 mole of benzaldehyde and 0.1 mole of *N*-sulfinyl-*p*-toluenesulfonamide *(2a)* in 50 ml of benzene, and the solution is heated to boiling and refluxed in the HCl stream for 1 hour. The benzene is removed by distillation under vacuum and the residue is recrystallized from ethanol. Yield 98%, m.p. 107 °C.

2-(p-Toluenesulfonyl)-3-trifluoromethyl-2-aza-bicyclo[2.2.2]oct-5-ene [50]

A mixture of 3.2 g of *N*-trifluoroethylidene-*p*-toluenesulfonamide *(27b)* and 1.1 g of cyclohexa-1,3-diene is refluxed for 7.5 hours in 7 ml of anhydrous benzene. The solvent is evaporated, and the residue is recrystallized from ethanol. Yield 4.0 g (95 %), m.p. 90 °C.

n-Butyl 4,5-Dimethyl-1-(p-toluenesulfonyl)-1,2,3,6-tetrahydropyridine-2-carboxylate (28d) [49,55]

A mixture of 14.0 g of *N*-(n-butoxycarbonylmethylene)-*p*-toluenesulfonamide *(27a)* and 4.1 g of dimethylbutadiene is heated for 10 hours in 25 ml of anhydrous benzene. The solvent is then evaporated under vacuum. The crude ester is obtained in a yield of 89%, and can be purified by chromatography on silica gel ($CHCl_3$).

[52] *W. Wucherpfennig*, unpublished.

[53] *F. Effenberger*, personal communication.

[54] *D. Sommerfeld*, Dissertation, Technische Hochschule München, 1966.

[55] *U. Wagner*, Diploma Thesis, Technische Hochschule München, 1965.

n-Butyl 4,5-Dibromo-4,5-dimethyl-1-(p-toluenesulfonyl)piperidine-2-cavboxylate [55]

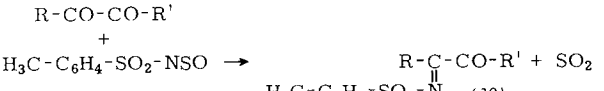
A solution of 5.7 g of bromine in 15 ml of CCl_4 is added dropwise to 13 g of n-butyl 4,5-dimethyl-1-(*p*-toluenesulfonyl)-1,2,3,6-tetrahydropyridine-2-carboxylate *(28d)* in 15 ml of CCl_4, with cooling in ice. The reaction mixture is allowed to stand overnight, the solvent is distilled off under vacuum, and the residue is extracted with 20% $Na_2S_2O_3$ solution. Yield 58.5%, m.p. 103–105 °C (from ethanol).

2-Carboxy-4,5-dimethylpyridinium Chloride Hydrate [55]

2.9 g of n-butyl 4,5-dibromo-4,5-dimethyl-1-(*p*-toluenesulfonyl)piperidine-2-carboxylate is heated for 4.5 hours with 4 g of KOH in 30 ml of absolute ethanol. Water is added and the alcohol is distilled off. The aqueous solution is extracted with ether to remove unhydrolysed material, and is then acidified with HCl and again extracted with ether. The aqueous phase is evaporated to dryness, and the residue is extracted with 50 ml of boiling ethanol. The ethanol is filtered and evaporated to dryness. The resulting residue is heated for 30 min with 10 ml of concentrated HCl, the solution is evaporated to dryness, and the residue is recrystallized from tetrahydrofuran/glacial acetic acid (1:1) with the addition of a little concentrated HCl. Yield 63%, m.p. 228 °C.

1.2.3.2. Preparation of Sulfonylimines, Sulfonylformamidines, and Nitriles

While benzophenone does not react with *N*-sulfinyl-*p*-toluenesulfonamide *(2a)*, even in the presence of $AlCl_3$, benzil reacts in the same way as benzaldehyde when heated with *(2a)* in benzene, with smooth formation of benzil mono-*p*-toluenesulfonylimine *(30a)*. Further reaction to form benzil diimine derivatives was not observed even in the presence of excess of *(2a)* [56].

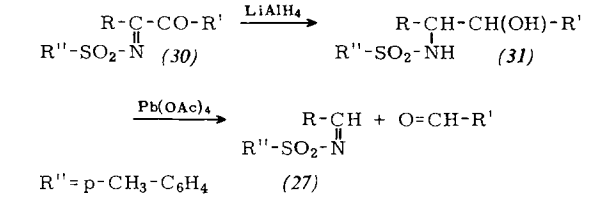


(2a) *(30)*

(a) R = R′ = C_6H_5
(b) R = *p*-Cl–C_6H_4, R′ = C_6H_5
(c) R = R′ = *p*-Cl–C_6H_4
(d) R = R′ = *p*-H_3C–C_6H_4

p-Chloro-, *p,p′*-dichloro, and *p,p′*-dimethylbenzil react in a similar manner, whereas no reaction occurs with *p*-methoxy- and *p,p′*-dimethoxybenzil, the starting materials being recovered unchanged in these cases.

Derivatives of benzil mono-*N*-toluenesulfonylimine are generally more resistant to hydrolysis than the *N*-arylsulfonylimines derived from benzaldehyde; however, the benzil derivatives are readily hydrolysed by heating with dilute sulfuric acid, to give the original benzil derivative and sulfonamide. The derivative *(30c)* of *p,p′*-dichlorobenzil is relatively stable under these conditions, and unlike *(30a)*, it cannot be reduced with $NaBH_4$. All benzil mono-*N*-sulfonylimines are reduced to the amino alcohol *(31)* by $LiAlH_4$.



(30) *(31)*

(27)

[56] *G. Kresze, D. Sommerfeld*, and *R. Albrecht*, Chem. Ber. *98*, 601 (1965).

This reduction can be used for the determination of the constitution of the product *(30b)* from *p*-chlorobenzil and *N*-sulfinyl-*p*-toluenesulfonamide *(2a)*. According to Criegee [57], *N*-toluenesulfonylamino alcohols are cleaved by lead tetraacetate with formation of *N*-toluenesulfonylimines. When treated in this way, *(30b)* gave benzaldehyde and the expected *p*-chlorobenzaldehyde *p*-toluenesulfonylimine [*(27)*, R = *p*-Cl–C_6H_4], which was also synthesized for comparison from *p*-chlorobenzaldehyde and *(2a)*.

Thus electron-acceptor groups generally favor the reaction of benzil derivatives with *N*-sulfinyl-*p*-toluenesulfonamide *(2a)*. In *p*-chlorobenzil, the reaction takes place on the carbonyl group from which the electrons are more strongly withdrawn. Strong electron donor groups, such as a methoxy group in the *p*-position, hinder the reaction.

Diacetyl also reacts with *N*-sulfinyl-*p*-toluenesulfonamide *(2a)*; analysis and the IR and NMR spectra show that the *N*-(*p*-toluenesulfonyl)-enamine *(32)*, *i.e.* the tautomeric form of the *N*-(*p*-toluenesulfonyl)-monoimine, is formed in this case.

$$H_2C=C(NH-SO_2-C_6H_4-CH_3)-COCH_3 \qquad (32)$$

Formamide reacts with *N*-sulfinyl-*p*-toluenesulfonamide *(2a)* with elimination of water and formation of hydrocyanic acid. *N,N*-Disubstituted formamides react similarly to the aromatic aldehydes, with loss of SO_2 to form N^1,N^1-disubstituted N^2-arylsulfonylformamidines *(24)* [48].

$$\underset{(2)}{R-SO_2-NSO} + O=CH-NR'_2 \longrightarrow \underset{(24)}{R-SO_2-N=CH-NR'_2} + SO_2$$

In this case the *N*-sulfinylarylsulfonamides *(2)* react similarly to *N*-arylsulfonylisocyanates [58].

The reaction of aromatic acyl chlorides with *N*-sulfinylsulfonamides *(2)* leads to *N*-sulfonylimide chlorides, which decompose under the conditions of the reaction or at higher temperatures to give a nitrile and a sulfonyl chloride [52].

$$\underset{(2)}{R-SO_2-NSO} + Ar-COCl \longrightarrow R-SO_2-N(Cl)-C-Ar + SO_2$$

$$\longrightarrow Ar-C\equiv N + R-SO_2Cl$$

Benzaldehyde azine [59] and benzylideneaniline [46] react in the same way as benzaldehyde, the reactions with *N*-sulfinylbenzenesulfonamide leading to benzylidenequenzenesulfonamide.

Procedures

Benzil Mono-N-p-toluenesulfonylimine (30a) [56]

5.5 g of dry benzil and a little $AlCl_3$ are added to 11.0 g of *N*-sulfinyl-p-toluenesulfonamide *(2a)* in 15 ml of anhydrous benzene. The mixture is heated for 1.5 hours in the absence of moisture. Small quantities of $AlCl_3$ are added at half hourly intervals. The mixture is cooled, the benzene is removed by distillation under vacuum, and the residue is extracted by boiling with 150 ml of a mixture of petroleum ether and CCl_4 (2:1 v/v). When the filtered solution is cooled, 8.4 g (68 %) of benzil mono-*N*-*p*-toluenesulfonylimine crystallizes. M.p. 132 °C (from ethanol).

N^1,N^1-Dimethyl-N^2-(p-toluenesulfonyl)-formamidine [48]

A mixture of 2.0 g of *N*-sulfinyl-*p*-toluenesulfonamide *(2a)* and 1.5 g of dimethylformamide is strongly heated for 8 min. The melt is cooled and recrystallized from ethanol. Yield 2.0 g (96 %), m.p. = 135–137 °C.

1.2.3.3. Preparation of Sulfimines and Phosphine Imides

Aliphatic sulfoxides react very readily with *N*-sulfinylsulfonamides *(2)*, in some cases exothermally, when solutions of the reactants are brought together in an inert solvent such as benzene [45].

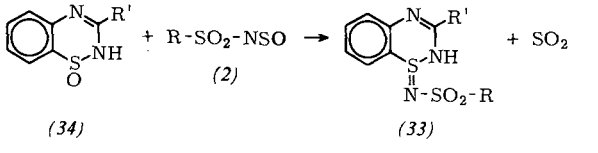
$$R'R''SO + \underset{(2)}{R-SO_2-NSO} \longrightarrow R'R''S=N-SO_2-R + SO_2$$

In some cases the resulting *N*-sulfonylsulfimides crystallize after a short time. In the case of aromatic sulfoxides the reactants must be heated for several hours at 80 to 100 °C in benzene, or in the absence of solvents; the reaction products are not so pure, and the yields are lower. *N*-Sulfinylaniline *(1a)* and its *p*-nitro derivative do not react with sulfoxides under the above conditions. When methyl sulfoxides are used, excessively vigorous reaction can lead to the formation of methane-bis(sulfonamide) derivatives as by-products.

Sulfinyl diamides react in the same way as sulfoxides [16]:

$$[(C_2H_5)_2N]_2SO + \underset{(2)}{R-SO_2-NSO} \longrightarrow [(C_2H_5)_2N]_2S=N-SO_2-R$$

Sulfinic acid derivatives also react in this way. Thus benzothiadiazineimines *(33)* are obtained from benzothiadiazine 1-oxides *(34)* by reaction with *N*-sulfinylsulfonamides *(2)* [60].



(34) *(33)*

Triphenylphosphine oxide, sulfide, *N*-phenylimide, and *O,O,O*-triethyl thiophosphate also undergo "transsulfonylimination" [61,62],

$$(C_6H_5)_3P=X + \underset{(2)}{R-SO_2-NSO} \longrightarrow (C_6H_5)_3P=N-SO_2-R + XSO$$

$$X = O, NC_6H_5, S$$

$$(C_2H_5O)_3P=S + R-SO_2-NSO \longrightarrow (C_2H_5O)_3P=N-SO_2-R + \text{"}S_2O\text{"}$$

though the yields are low in some cases.

[57] *R. Criegee* in *W. Foerst*: Neuere Methoden der präparativen organischen Chemie. Verlag Chemie, Berlin 1944, Vol. 1, p. 35.

[58] *C. King*, J. org. Chemistry *25*, 352 (1960).

[59] *A. Senning*, Recueil Trav. chim. Pays-Bas *82*, 790 (1963).

[60] *A. Trede*, Dissertation, Technische Hochschule München, 1964.

[61] *A. Senning*, Acta chem. scand. *19*, 1755 (1965).

[62] *A. Senning*, Angew. Chem. *77*, 379 (1965); Angew. Chem. internat. Edit. *4*, 357 (1965).

Procedures

Tetraethyl-S-(p-toluenesulfonylimino)-sulfinyldiamide [16]

A solution of 10.85 g of *N*-sulfinyl-*p*-toluenesulfonamide *(2a)* in 50 ml of anhydrous $CHCl_3$ is added to 9.6 g of tetraethylsulfinyldiamide in 25 ml of anhydrous $CHCl_3$. SO_2 is liberated, and the solution becomes warm and assumes a red color. The reaction mixture is allowed to stand for 15 hours at room temperature, and the chloroform is then distilled off; the residue crystallizes. Yield 93%, m.p. 56–57 °C (from water).

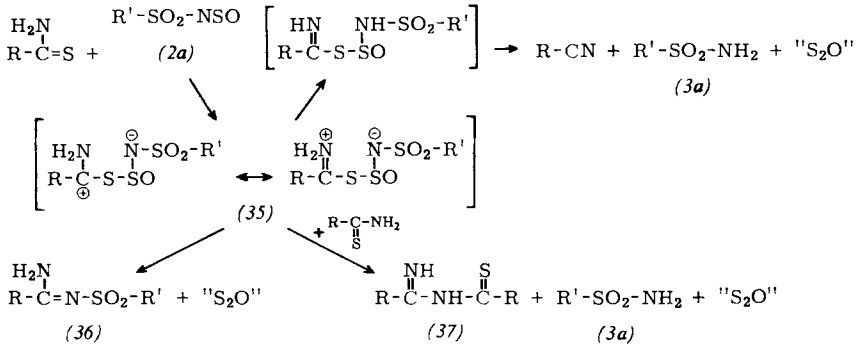
1-(p-Toluenesulfonylimino)-3-phenylbenzo-2H-1,2,4-thiadiazine ((33), R=p-CH_3–C_6H_4, R'=C_6H_5) [60]

0.7 g of 3-phenylbenzo-2*H*-1,2,4-thiadiazine 1-oxide is heated for several hours in benzene with an excess of *N*-sulfinyl-*p*-toluenesulfonamide *(2a)*. The reaction mixture is cooled and filtered, and the precipitate is extracted with ethyl acetate to remove *p*-toluenesulfonamide. Yield 0.9 g (79%), m.p. 208–208.5 °C (from dimethylsulfoxide/ethyl acetate).

1.2.3.4. Preparation of N^2-Sulfonylamidines and 1,2,4-Thiadiazoles

Thioxo compounds can undergo "transsulfonylimination" with *N*-sulfinylsulfonamides in the same way as carbonyl compounds. However, other reaction products (nitriles or 1,2,4-thiadiazole derivatives) are often obtained as by-products or even as the main products. The course followed by the reaction depends on the nature of the thioxo compound, and the ratio of the various products evidently also depends on the solvent. All three products could be formed via the intermediate *(35)* [14].

The (strongly positive) S atom of the *N*-sulfinyl compound reacts with the negative S atom of the thioxo group. Both types of polarization have been observed

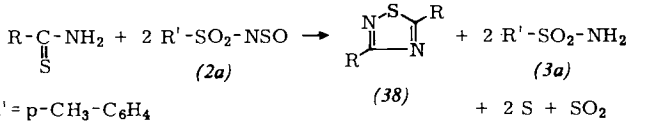


R' = p-CH_3-C_6H_4

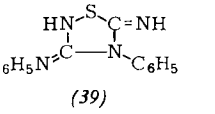
and are quite common; that of the *N*-sulfinylsulfonamides *(2)* is evident in the reaction with pyridine *N*-oxides [40], and that of the thionamides in many other reactions. The resulting dipolar product *(35)* can be stabilized in various ways:

1. by loss of S_2O to form the sulfonylamidine *(36)*,
2. by proton transfers and loss of S_2O and toluenesulfonamide to form the nitrile, and
3. by S_N reaction on the C atom with the N atom of a second molecule of thionamide. Proton transfer and subsequent loss of S_2O and toluenesulfonamide lead to the thioacylamidine *(37)*. The thioacylamidines *(37)* are readily oxidized to 3,5-disubstituted 1,2,4-thiadiazoles *(38)*.

The reaction of *N*-sulfinyl-*p*-toluenesulfonamide *(2a)* with *N*-substituted aliphatic or aromatic thionamides lead to moderate or satisfactory yields of 1,2,4-thiadiazoles *(38)*.

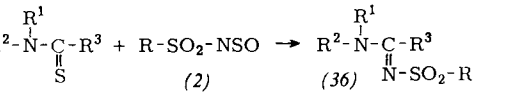


The nitriles corresponding to the thionamides are sometimes also formed as by-products. The reaction of *N*-phenylthiourea yields the "Hector base" *(39)*, which can also be obtained by oxidation with H_2O_2.

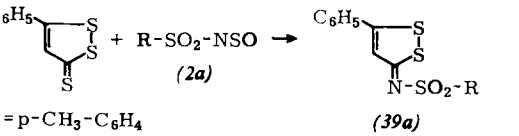


(39)

The conversion of thionamides into 3,5-diaryl-1,2,4-thiadiazoles and that of thioureas into Hector bases can be carried out with many different reagents, but this method fails with aliphatic compounds. In this case the reaction with *N*-sulfinylsulfonamides *(2)* may be useful for preparative purposes.



N^2-Sulfonylamidines *(36)* are obtained in the reaction of *N*-sulfinylsulfonamides *(2)* with thioformamide, *N*-substituted thionamides [14], and *N,N*-disubstituted thioureas [46], and as by-products in the reaction of *N*-acylthioureas [63] and of an excess of thiobenzamide with *N*-sulfinylsulfonamides *(2)*. 1,2-Dithiacyclopent-3-ene-5-thiones (trithiones) also undergo transsulfonylimination with *(2a)*.



R = p-CH_3-C_6H_4 *(39a)*

[63] *A. Horn*, Dissertation, Technische Hochschule München, 1966.

Procedure

N^1,N^1-Dimethyl-N^2-p-toluenesulfonylbenzamidine ((36), $R = p\text{-}CH_3\text{–}C_6H_4$, $R^1 = R^2 = CH_3$, $R^3 = C_6H_5$) [14,63]

A solution of 2.7 g of *N*-sulfinyl-*p*-toluenesulfonamide *(2a)* in 25 ml of chloroform is added to 2.0 g of *N*,*N*-dimethylthiobenzamide in 50 ml of anhydrous chloroform, and the mixture is heated for 16 hours. The solvent is distilled off and the residue is extracted with boiling ethanol. The product that crystallizes from the hot filtered solution can be recrystallized from ethanol and acetonitrile. Yield 2.7 g (75%), m.p. 161–162 °C.

1.2.4 Additions of Proton-Activated Compounds

Corresponding to the polarity of their S=N bond, the *N*-sulfinyl compounds react with compounds of the type HX in accordance with the scheme

$$R\text{–}NSO + HX \longrightarrow R\text{–}NH\text{–}SO\text{–}X$$

In most cases this addition product rapidly reacts further with a second mole of HX:

$$R\text{–}NH\text{–}SO\text{–}X + HX \longrightarrow R\text{–}NH_2 + X_2SO$$

The reaction leads to the transfer of a sulfinyl group. The resulting sulfinyl compound can react further in a similar manner as the primary product. This is the reason for the preparative importance of "transsulfinylation", particularly in the reactions with amidines, active methylene compounds, and thiols. The addition of HX to *N*-sulfinylsulfonamides *(2)* is generally much faster than to *N*-sulfinylamines *(1)*, and in many cases only the more reactive sulfonamide derivatives can be used.

1.2.4.1. Addition of Water, Alcohols, or Hydrogen Halides

The simplest example of the addition of HX is hydrolysis, which is evidently catalysed both by acids and by bases. *N*-Sulfinylsulfonamides *(2)* and aliphatic *N*-sulfinylamines *(1)* are more resistant to hydrolysis. *N*-Sulfinylmesidine can be steam-distilled without appreciable decomposition [64].

Alcoholysis proceeds analogously to hydrolysis and leads to the formation of sulfites $(RO)_2SO$ [65]. In this case it has been qualitatively found that the reactivity of the *N*-sulfinylamines is increased by electron-attracting substituents. The alcoholysis is assumed to lead first to esters R–NH–SOOR′, which are very unstable and immediately react further [66]. The reaction of the *N*-sulfinylamines with dry hydrogen halide is a reversal of

$$R\text{–}NSO + 2\,HCl \longrightarrow R\text{–}NH_2 + SOCl_2$$

their formation, and has been recommended for the preparation of pure thionyl chloride [67].

According to *Smith* and *King* [68], this reaction is also involved in the reaction of *N*-sulfinylamines *(1)* with carboxylic acids to form anilides, as reported by *Carré* and *Libermann* [69], since pure compounds containing no HCl or $SOCl_2$ do not react.

The *N*-sulfinylsulfonamides *(2)*, the formation of which from sulfonamides *(3)* and $SOCl_2$ is much slower than that of the *N*-sulfinylamines *(1)* (cf. Section 1.1.1.2.), are more resistant to cleavage by HCl [54].

Unlike the *N*-sulfinylamines *(1)*, however, *N*-sulfinyl-*p*-toluene-sulfonamide *(2a)* that has been distilled in a high vacuum, and which no longer contains chlorinated impurities, reacts smoothly with acetic acid to give good yields of *N*-acetyl-*p*-toluenesulfonamide [52]. It therefore seems likely that direct reaction occurs in this case:

$$\underset{(2a)}{H_3C\text{–}C_6H_4\text{–}SO_2\text{–}NSO} + CH_3COOH \longrightarrow H_3C\text{–}C_6H_4\text{–}SO_2\text{–}NHCOCH_3 + SO_2$$

It was mentioned in Section 1.2.3.1. that HCl also acts as a catalyst in the reactions of the *N*-sulfinyl compounds. Many discrepancies in the reports on the reactivities and the nature of the reactions of *N*-sulfinylamines and *N*-sulfinylsulfonamides can apparently be explained by the presence or absence of HCl or $SOCl_2$ (from the preparation of the *N*-sulfinyl compound) in the reaction mixture.

1.2.4.2. Preparation of Unsymmetrically Substituted Trisulfides

In the reaction of *N*-sulfinylamines *(1)* [70] or *N*-sulfinyl-*p*-toluenesulfonamide *(2a)* with thiols, the first step in the "transsulfinylation" can be carried out separately:

$$R\text{–}NSO + HSR' \longrightarrow \underset{(39b)}{R\text{–}NH\text{–}SO\text{–}SR'}$$

An exothermic reaction takes place with the formation of *N*-arylamidothiosulfites (thio esters of *N*-arylsulfamic acid) *(39b)*, whose N–S bonds are easily cleaved; the reaction with thiols can be used for the preparation of unsymmetrically substituted alkyl aryl trisulfides [70]:

$$R\text{–}NH\text{–}SO\text{–}SR' + 3\,R''\text{–}SH \longrightarrow R\text{–}NH_2 + R''\text{–}S\text{–}S\text{–}S\text{–}R' + R''\text{–}S\text{–}S\text{–}R'' + H_2O$$

1.2.4.3. Preparation of *N*-Sulfinyl Compounds, 2,1,3-Thiadiazoles, 2,1,3-Thiadiazines, and Benzo-1,2,4-thiadiazines

The reaction of *N*-sulfinylamines or *N*-sulfinylsulfonamides with compounds containing amino groups is useful for preparative purposes. This reaction generally leads to smooth transsulfinylation, particularly when the difference in basicity between the original and final

[64] *A. Michaelis* and *G. Junghans*, Liebigs Ann. Chem. *274*, 233 (1893).

[65] *W. T. Smith jr.*, *D. Trimnell*, and *L. D. Grinninger*, J. org. Chemistry *24*, 664 (1959); *W. T. Smith jr.* and *L. D. Grinninger*, *ibid. 26*, 2133 (1961); *L. Jannelli*, *L. Senatore*, and *C. Carpanelli*, Ann. Chimica *53*, 1150 (1963).

[66] *G. Zinner*, Chem. Ber. *91*, 966 (1958).

[67] *P. Carré* and *D. Libermann*, Bull. Soc. chim. France [5], *6*, 579 (1939).

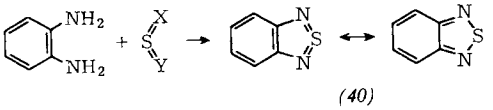
[68] *W. T. Smith jr.* and *G. G. King*, J. org. Chemistry *24*, 976 (1959).

[69] *P. Carré* and *D. Libermann*, C.R. hebd. Séances Acad. Sci. *194*, 2218 (1932).

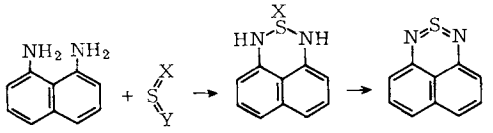
[70] *G. Kresze* and *H. P. Patzschke*, Chem. Ber. *93*, 380 (1960).

amino compounds is large[73]. The *N*-sulfinylsulfonamides *(2)* are therefore particularly suitable for the preparation of other *N*-sulfinyl compounds. Transsulfinylation with *N*-sulfinyl-*p*-toluenesulfonamide *(2a)* and its analogues can be used not only for the preparation of sensitive *N*-sulfinylamines (cf. Section 1.1.1.) but also of *N*-sulfinylhydrazides[71], *N*-sulfinylhydroxamide *O*-ethers[72], and *N*-sulfinylsulfenamides[4].

The reaction of aromatic *o*- or *peri*-diamines with compounds of the type X=S=Y yields benzo-2,1,3-thiadiazoles [piazthioles, *(40)*][9,22,74–78] or naphtho[1,8,8*a* – *c*,*d*]thiadiazines *(41)*[79,80].



(40)

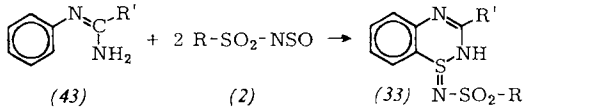


(42) *(41)*

These ring-closure reactions proceed increasingly readily with the reagents SO_2[9,76,79], $SOCl_2$[22,74], Ar–NSO[74,75,77,79,80], and $(RSO_2N)_2S$[78].

Mono-*N*-sulfinylamines[75] and the cyclic sulfinyldiamide *(42)*, X = O[79,80] have been isolated as intermediates. Numerous derivatives of *(40)* and *(41)*, some of them heterosubstituted, have been prepared in this way.

The course of the reaction of N^2-arylamidines *(43)*[81] with *N*-sulfinylsulfonamides *(2)* seems surprising. These compounds react even at room temperature in chloroform to give the 1-*N*-arylsulfonylimines *(33)* of the 2*H*-1,2,4-benzothiadiazines, often in yields of more



(43) *(2)* *(33)* N-SO_2-R

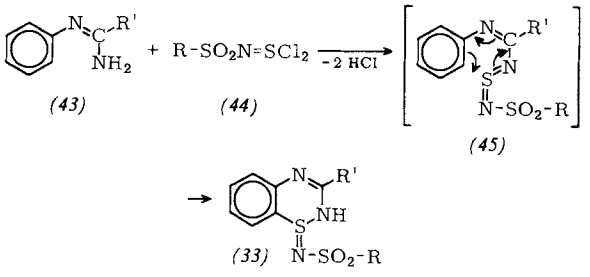
+ SO_2 + R-SO_2-NH_2

(3)

than 90%. The amidines *(43)* may also be replaced in this reaction by similar compounds such as *N*-arylguanidines (R′ = NR″$_2$), *N*-arylisoureas (R′ = OR″), and *N*-arylisothioureas (R′ = SR″).

When *(43)* and *(2)* are allowed to react in a molar ratio 1:1, the only product is again *(33)*, and half of the amidine used is recovered unchanged. The great ease with which the aromatic nucleus is attacked is particularly surprising; the reaction is not prevented even by strong electron-acceptor substituents (NO_2 in the *p*-position, SO_2–NH_2 in the *m*-position with respect to the point of attack).

The arylsulfonyliminosulfur dichlorides *(44)* react in the same way as the *N*-sulfinylsulfonamides *(2)*. In this case only 1 mole of *(44)* is required per mole of *(43)* if a base is added to remove the liberated HCl.



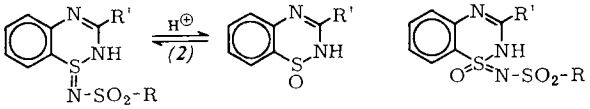
(43) *(44)* *(45)*

(33) N-SO_2-R

As in the reaction of the arylsulfonyliminosulfur dichlorides *(44)* with primary aromatic amines[78], it must again be assumed that the first step is the formation of a sulfodiimide *(45)*. However, this is evidently unstable, and undergoes valence isomerization and proton migration with formation of the stable benzothiadiazine derivative *(33)*. A similar mechanism was suggested recently[82] for the isomerization of imidoyl isothiocyanates to form quinazolinethiones. Thus the reaction may be compared to an intramolecular "polar" diene synthesis.

(45) could also occur as an intermediate in the reaction with *N*-sulfinylsulfonamides. This is supported by the fact that *N*-phenyl-*N*′-methylbenzamidine does not react to form the methyl-substituted benzothiadiazine. The formation of a sulfodiimide without scission of a C–N bond is inconceivable in this case.

Solvolysis of the 2*H*-benzothiadiazine derivatives *(33)* with glacial acetic acid, formic acid, or sulfuric acid leads to the formation of 2*H*-1,2,4-benzothiadiazine 1-oxides *(34)*.



(33) *(34)* *(46)*

The structure of the starting materials *(33)* was verified by oxidation of the sulfoxides *(34)* with H_2O_2 in glacial acetic acid to obtain the 2*H*-1,2,4-benzothiadiazine 1,1-dioxides, which are known. The reduction of *(34)* with zinc and glacial acetic acid proceeds abnormally, with the ring contraction to form benzothiazoles. Oxidation of the 1-sulfonylimino-2*H*-benzothiadiazines *(33)* with alkaline permanganate leads to the sulfoximine analogues *(46)*. The results obtained so far indicate that in the "sulfinylation" of the amidines *(43)*, the primary adduct *(47)* undergoes transsulfinylation with a second

[71] *G. Kresze, A. Horn, R. Philippson*, and *A. Trede*, Chem. Ber. *98*, 3401 (1965).

[72] *Chr. Seyfried*, Dissertation, Technische Hochschule München, 1966.

[73] *W. T. Smith jr., W. K. Plucknett*, and *T. L. Dawson*, US Dept. Commerce, Office Tech. Serv., PB Rept. 153451, Chem. Abstr. *58*, 11180h (1963).

[74] *V. G. Pessin, A. M. Chalezki*, and *Tschǐ-tschǔn Tschǐao*, Doklady Akad. Nauk. SSSR *106*, 88 (1956) and following work.

[75] *Y. F. Shealy, J. D. Clayton*, and *J. A. Montgomery*, J. org. Chemistry *27*, 2154 (1962).

[76] *W. T. Smith jr.* and *W.-Y. Chen*, J. org. Chemistry *27*, 676 (1962).

[77] *M. P. Cava* and *R. H. Schlessinger*, Tetrahedron Letters *1964*, 3815.

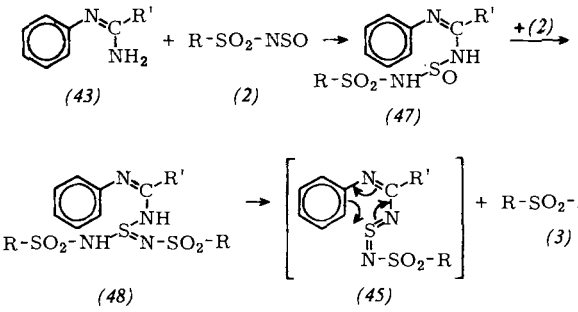
[78] *E. S. Levtschenko* and *A. V. Kirsanov*, Z. org. Chim. *1*, 300 (1965).

[79] *R. Dietz*, Chem. Commun. (London) *1964*, 57.

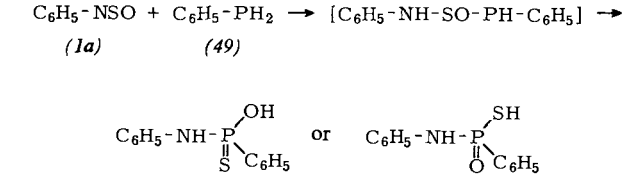
[80] *H. Behringer* and *K. Leiritz*, Chem. Ber. *98*, 3196 (1965).

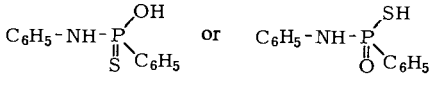
[81] *G. Kresze, Chr. Seyfried*, and *A. Trede*, Tetrahedron Letters *1965*, 3933.

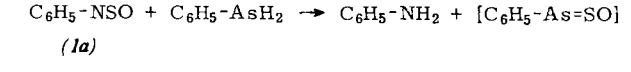
[82] *H. M. Blatter* and *H. Lukaszewski*, Tetrahedron Letters *1964*, 855.



mole of *(2)* (cf. Section 1.2.3.3.); the resulting guanidine analogue *(48)*, a sulfurous acid diamide imide, then loses sulfonamide to form the sulfodiimide intermediate *(45)*. In the reactions of *N*-sulfinylamines *(1a)* with phenylphosphine *(49)*[83] and with phenylarsine[84], the primary adducts again undergo complex secondary reactions.









Procedures

7-Amino-1,2,5-thiadiazolo[3,4-d]pyrimidine [75]

3 mmoles of *N*-sulfinylaniline *(1a)* is added to 1 mmole of 4,5,6-triaminopyrimidine in 10 ml of pyridine under nitrogen and in the absence of moisture, and the mixture is heated at 110 °C for 4¾ hours. The solvent is distilled off under vacuum, and to remove pyridine and aniline, ethanol/water is repeatedly added and evaporated. The residue is treated with aqueous alcohol and filtered off. Yield 94%, yellow crystals having m.p. 250 °C.

3-Phenyl-1-(p-toluenesulfonylimino)-benzo-2H-1,2,4-thiadiazine ((33), R = p-CH₃–C₆H₄, R′ = C₆H₅) [60,81]

9.8 g of solid *N*-phenylbenzamidine is added to a solution of 21.7 g of *N*-sulfinyl-*p*-toluenesulfonamide *(2a)* in 150 ml of $CHCl_3$. SO_2 is evolved and the reaction mixture becomes warm and turns red. The mixture is allowed to stand for 6 hours at room temperature and the precipitate that separates is removed by filtration and digested with ethyl acetate at room temperature to remove *p*-toluenesulfonamide. Yield 18.8 g (95%), m.p. 208–208.5 °C (from dimethyl sulfoxide/ethyl acetate).

3-Phenylbenzo-2H-1,2,4-thiadiazine 1-Oxide ((34), R′ = C₆H₅) [60,81]

A suspension of 25 g of 3-phenyl-1-(*p*-toluenesulfonylimino)-benzo-2*H*-1,2,4-thiadiazine in 500 ml of glacial acetic acid is prepared and is heated slowly to 120 °C with stirring. The solid dissolves to give a pale yellow solution. After cooling, the solution is added to an equal amount of water and the mixture is filtered, yield 10.0 g. A further 2.7 g can be obtained by evaporation of the filtrate to dryness under vacuum and extraction of the residue with boiling water. Total yield 12.7 g (83%), m.p. 250–252 °C (from ethanol).

3-Phenylbenzo-2H-1,2,4-thiadiazine 1,1-Dioxide [60]

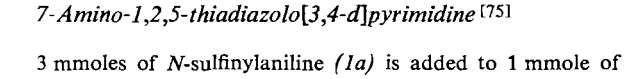
0.6 g of 3-phenylbenzo-2*H*-1,2,4-thiadiazine 1-oxide is dissolved in hot glacial acetic acid, and an excess of 30% H_2O_2 is added to the hot solution. The mixture is heated for 1 hour on a water-bath, allowed to stand for several hours at room temperature, and filtered. Yield 0.3 g (47%), m.p. 306–308 °C.

3-Phenyl-1-(p-toluenesulfonylimino)-benzo-2H-1,2,4-thiadiazine 1-Oxide (46) [60,81]

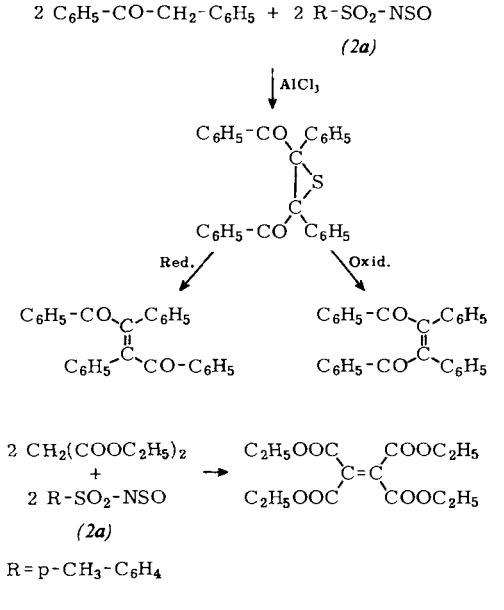
3 g of 3-phenyl-1-(*p*-toluenesulfonylimino)-benzo-2*H*-1,2,4-thiadiazine is dissolved in 60 ml of 2N NaOH. A solution of 3 g of $KMnO_4$ in 50 ml of water is added dropwise to the boiling solution with stirring. The mixture is then heated for 1 hour on a water-bath, and acidified after cooling. The MnO_2 that is precipitated is reduced with $NaHSO_3$ until the precipitate becomes colorless. It is then filtered off and washed thoroughly with water. Yield 0.9 g (29%), m.p. 248–250 °C/decomp. (from ethanol/benzyl alcohol).

1.2.4.4. Preparation of Tetrasubstituted Ethylenes

In principle, compounds containing acidic methylene groups should also undergo "transsulfinylation" with *N*-sulfinyl compounds; this reaction should lead to the formation of sulfines RR′C=SO, at least as the primary products. As was mentioned in Section 1.2.3.1., the only products found in the reaction of aliphatic aldehydes



with *N*-sulfinyl-*p*-toluenesulfonamide *(2a)* are 1,1-bis-(*p*-toluenesulfonamido)alkanes [48], while the only product isolated so far with carbonyl compounds such as cyclohexanone is *p*-toluenesulfonamide *(3a)*. However, the reactions with malonic ester and with deoxybenzoin

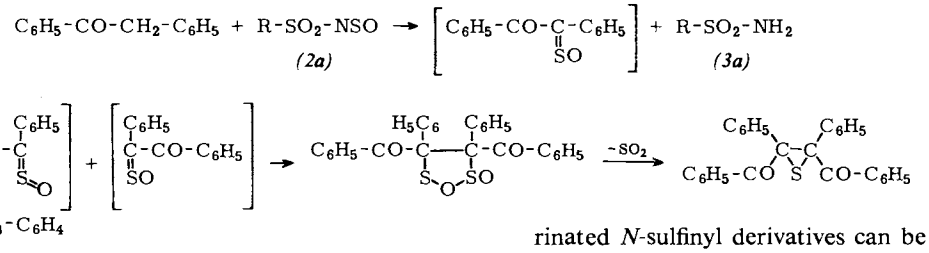


[83] *L. Anschütz* and *H. Wirth*, Naturwissenschaften *43*, 16 (1956).

[84] *L. Anschütz* and *H. Wirth*, Naturwissenschaften *43*, 59 (1956).

and its derivatives in the presence of $AlCl_3$ follow a different course; the products obtained in these cases are tetrasubstituted ethylenes, or as their precursors, thiiranes [54]:

A plausible course for this oxidative dimerization of the methylene components would be as follows: (a) "Transsulfinylation" to form the sulfine, whose C=SO system acts both as a 1,3-dipole and as a dipolarophile in the second step, (b) 1,3-dipole addition, and then (c) stabilization of the five-membered heterocycle in the usual manner (cf. Section 1.2.2.2.) by elimination of SO_2 and formation of the thiirane.



The *N*-sulfinylsulfonamides often can be replaced by thionyl chloride.

Procedures

1,2-Diphenyl-1,2-dibenzoylthiiran [54]

A solution of 0.1 mole of deoxybenzoin and 0.01 mole of $AlCl_3$ in 150 ml of ether is added dropwise with stirring to 0.1 mole of *N*-sulfinyl-*p*-toluenesulfonamide *(2a)* in 50 ml of anhydrous ether, with cooling in ice. After 2 days, the *p*-toluenesulfonamide *(3a)* that has crystallized is removed by filtration, the ether is distilled off under vacuum at a low temperature, and the oily residue is taken up in 80 ml of petroleum ether. The solution is filtered and the petroleum ether is distilled off under vacuum. The thiirane remains behind as a yellow oil. Yield 10.1 g (46.5%). The thiirane can be purified by chromatography on silica gel (benzene as eluent), m.p. 104–105 °C.

cis-Dibenzoylstilbene [54]

4 g of crude 1,2-diphenyl-1,2-dibenzoylthiirane is dissolved in 50 ml of nitrobenzene and heated for 2 hours. The nitrobenzene is removed by steam distillation and the residue is recrystallized from ethanol. Yield 85%, m.p. 211 °C.

trans-Dibenzoylstilbene [54]

A solution of 3.4 g of triethyl phosphite in 40 ml of anhydrous ether is added dropwise to a boiling solution of 5 g of crude 1,2-diphenyl-1,2-dibenzoylthiirane in 40 ml of anhydrous benzene, and the mixture is heated for a further 4 hours. The ether is distilled off and the residue is recrystallized from 80% ethanol. Yield 85%, m.p. 231 °C.

Tetraethyl Ethylenetetracarboxylate [54]

A mixture of 0.1 mole of malonic ester, 0.01 mole of $AlCl_3$, and 0.1 mole of *N*-sulfinyl-*p*-toluenesulfonamide *(2a)* in 50 ml of nitromethane is heated for 6 hours. After cooling, the solution is filtered to remove crystals of the *p*-toluenesulfonamide *(3a)*, the nitromethane is removed by distillation under vacuum, and the residue is distilled at 10^{-2} mm Hg. Yield 38%, m.p. 52 °C.

1.2.5. Preparation of Ring Halogenated Aniline and Phenylenediamine Derivatives

The sulfinyl group has been found useful as a protective group for NH_2 in the halogenation of sensitive amines. Although the NSO group of *N*-sulfinylaniline *(1a)* is cleaved by chlorine or bromine in chloroform (the final products are 2,4,6-trihalogenoaniline and thionyl halide), chlorination in thionyl chloride as the solvent yields *N*-sulfinyl-2,4,6-trichloroaniline. Ring-halogenation of *m*- and *p*-phenylenediamine can also be achieved in this way. The resulting 2,4,6-trichlorinated or 2,3,5,6-tetrachlorinated *N*-sulfinyl derivatives can be hydrolysed to the amines with alkali or hot acid [85].

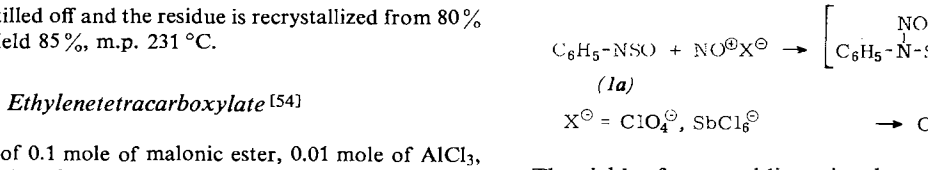
Procedure

N,N'-Disulfinyl-2,3,5,6-tetrachloro-p-phenylenediamine [85]

108 g (1 mole) of *p*-phenylenediamine is added in portions (over a period of 30 min) to 600 ml (8.25 moles) of $SOCl_2$, with stirring. During this addition, the temperature of the reactants is maintained at 50–65 °C in an oil bath at 50 to 55 °C. The mixture is stirred for a further 2 hours, and 281 g (7.92 moles) of chlorine passed through it at 55–65 °C for 4.5 hours. The chlorination is complete when chlorine begins to appear in the condenser. The mixture is cooled to 0 °C, and the *N,N'*-disulfinyl-2,3,5,6-tetrachloro-*p*-phenylenediamine that crystallizes is filtered off and recrystallized from CCl_4; yellow needles, yield 250 g (75%), m.p. 171 to 172 °C. Treatment with 15% NaOH at room temperature or with boiling hydrochloric acid leads to almost quantitative conversion into 2,3,5,6-tetrachloro-*p*-phenylenediamine, m.p. 224–225 °C.

1.2.6. Diazonium Salts and Sulfinamides

The reaction of *N*-sulfinyl compounds with polar or ionic, salt-like components can often be regarded as a primary reaction on one atom of the NSO system. Thus *Bott* [86] considers the formation of diazonium salts in the reaction of *(1)* with nitrosyl perchlorate, or hexachloroantimonate, in dichloroethane at −10 °C to 0 °C to proceed *via* an *N*-nitroso derivative:

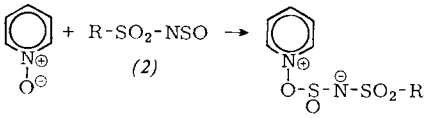


The yields of pure aryldiazonium hexachloroantimonates are higher than 90%.

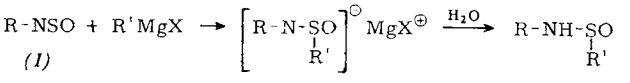
[85] *G. Ottmann* and *H. Hooks*, J. org. Chemistry *30*, 952 (1965).

[86] *K. Bott*, Angew. Chem. *77*, 132 (1965); Angew. Chem. internat. Edit. *4*, 148 (1965).

Only the S atom of the *N*-sulfinyl group is attacked in the reaction of *(2)* with pyridine *N*-oxides [40].



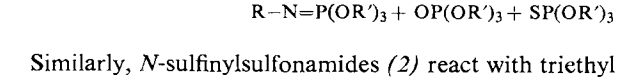
This type of reaction is probably also involved in the additions of organometallic compounds. Additions to *N*-sulfinylamines can be carried out with Grignard compounds [19,87] and with organolithium compounds [88]. Careful hydrolysis of the adducts gives good yields of sulfinamides.



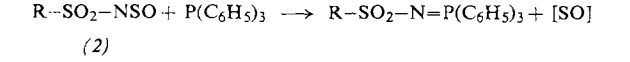
The only case in which poor yields (7% instead of 72–92%) indicate the effects of steric hindrance is the reaction of phenylmagnesium bromide with *N*-sulfinyl-t-butylamine; *N*-sulfinylmesidine, on the other hand, reacts normally [89].

With tertiary amines, *N*-sulfinylsulfonamides *(2)* first give a brown charge-transfer complex, which then loses SO_2 with self-condensation to form a sulfodiimide (cf. Section 2.1.2.).

N-Sulfinylaniline *(1a)* and dialkyl *N*-sulfinylphosphoramidates react with trialkyl phosphites to give iminophosphates, phosphates, and thiophosphates [90].



Similarly, *N*-sulfinylsulfonamides *(2)* react with triethyl phosphite, triphenylphosphine, triphenylarsine, and triphenylstibine to give iminophosphorane derivatives and their analogues [61,62].



2. Sulfodiimides

The chemistry of the sulfodiimides R–N=S=N–R′ is not yet so well developed as that of the *N*-sulfinylamines. Dialkyl- [8,91,92], diaryl- [78,93,95], disulfonyl- [96,97], and *N*-sulfonyl-*N*′-arylsulfodiimides [78,98] are known.

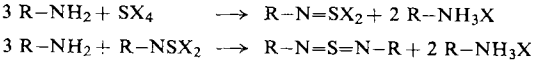
The stability of these compounds is strongly dependent on the organic residue [99]. Dialkylsulfodiimides decompose at, or slightly above, room temperature, only compounds containing tertiary groups being thermally stable [92]. Diaryl- and *N*-sulfonyl-*N*′-arylsulfodiimides change at high temperatures or on prolonged storage at room temperature, while disulfonylsulfodiimides are thermally stable.

Sulfodiimides are more sensitive to hydrolysis and more reactive than the corresponding *N*-sulfinylamines. Within the series of sulfodiimides, reactivity runs parallel to thermal stability.

2.1. Preparation of Sulfodiimides

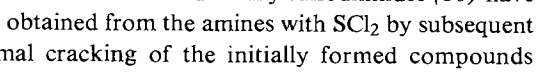
2.1.1. Dialkyl- and Diarylsulfodiimides

Dialkylsulfodiimides are prepared from alkylamines and sulfur tetrahalides at low temperatures [8,91].



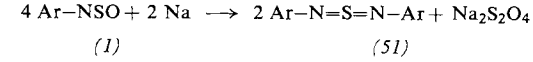
X = F, Cl

The much more stable di-t-alkylsulfodiimides *(50)* have been obtained from the amines with SCl_2 by subsequent thermal cracking of the initially formed compounds of the type $(R–NS)_x$ [92]:



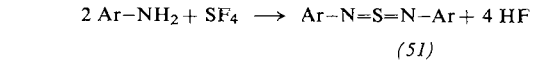
R = t-Alkyl *(50)*

Diarylsulfodiimides *(51)* were first prepared from the *N*-sulfinylamines *(1)* with sodium [93].

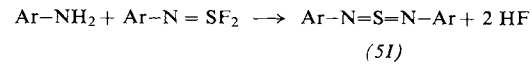


(1) *(51)*

Like the dialkylsulfodiimides, they are also formed in the reaction of SF_4 or aryliminosulfur difluorides with aromatic amines [94].

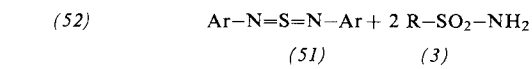


(51)



(51)

A very useful preparative method is the "transimidation" of the readily obtainable disulfonylsulfodiimides *(52)* with aromatic amines [95]



(52) *(51)* *(3)*

The deciding factor in this reaction (as in the analogous "transsulfinylation", cf. Section 1.1.1.) is the difference in basicity between the amine and the sulfonamide. This reaction can also readily be carried out in two steps [78].

[87] *A. Sonn* and *E. Schmidt*, Ber. dtsch. chem. Ges. *57*, 1355 (1924); *H. Gilman* and *H. L. Morris*, J. Amer. chem. Soc. *48*, 2399 (1926); *H. Gilman*, *J. E. Kirby*, and *C. R. Kinney*, *ibid. 51*, 2252 (1929).

[88] *A. Schönberg*, *A. Stephenson*, *H. Kaltschmitt*, *E. Petersen*, and *H. Schulten*, Ber. dtsch. chem. Ges. *66*, 237 (1933).

[89] *W. T. Smith jr.*, *Poo An Thio*, and *M. Grasley*, J. org. Chemistry *27*, 692 (1962).

[90] *J. Wieczorkowski*, Bull. Acad. polon. Sci. *13*, 155 (1965).

[91] *B. Cohen* and *A. G. McDiarmid*, Angew. Chem. *75*, 207 (1963); Angew. Chem. internat. Edit. *2*, 151 (1963).

[92] *D. H. Clemens*, *A. J. Bell*, and *J. L. O'Brien*, Tetrahedron Letters *1965*, 1487.

[93] *G. Leandri* and *P. Rebora*, Gazz. chim. ital. *87*, 503 (1957), wrongly described as azothiobenzenes (Ar–N=N(⟶ S)Ar) by the authors.

[94] *R. Cramer*, J. org. Chemistry *26*, 3476 (1961).

[95] *A. V. Kirsanov* and *E. S. Levtschenko*, USSR-Pat. (26th June 1963); Chem. Abstr. *60*, 11949c (1964).

[96] *E. S. Levtschenko* and *A. V. Kirsanov*, Ž. obšč. Chim. *32*, 2256 (1962).

[97] *W Wucherpfennig* and *G. Kresze*, Tetrahedron Letters *1966*, 1671.

[98] *E. S. Levtschenko* and *A. V. Kirsanov*, USSR-Pat. 154263 (July 24th 1963); Chem. Abstr. *61*, 1800a (1964).

[99] *E. S. Levtschenko* and *Ya. G. Bal'on*, Ž. org. Chim. *1*, 305 (1965).

1st step:

$$(R-SO_2-N)_2S + Ar^1-NH_2 \longrightarrow \underset{(52)}{R-SO_2-N=S=N-Ar^1} + R-SO_2-NH_2$$

In this (fast) step, both donor-substituted and acceptor-substituted anilines can be used. However, the course of the second (slow) step, which proceeds only with donor-substituted (strongly basic) amines, differs according to the amine component used in the first step.

2nd step:

a) Ar^1 = donor substituent, Ar^2 = donor substituent

$$R-SO_2-N=S=N-Ar^1 + Ar^2-NH_2 \longrightarrow Ar^2-N=S=N-Ar^1 + R-SO_2-NH_2$$

b) Ar^2 = acceptor substituent, Ar^2 = donor substituent

$$R-SO_2-N=S=N-Ar^1 + Ar^2-NH_2 \longrightarrow R-SO_2-N=S=N-Ar^2 + Ar^1-NH_2$$

Thus mixed diarylsulfodiimides can also be prepared by this reaction.

Dialkylsulfodiimides are bright yellow liquids, and those containing n-alkyl groups are very readily hydrolysed. Di-t-alkylsulfodiimides *(50)* are much more stable to hydrolysis. Diarylsulfodiimides *(51)* are orange to red liquids or low-melting solids having characteristic IR [94, 100] and UV spectra [94, 101]. They are slowly hydrolysed by water.

Procedures

Di-t-butylsulfodiimide ((50), $R = C(CH_3)_3$) [92]

A solution of 343 g (3.5 moles) of freshly distilled SCl_2 in 300 ml of anhydrous ether is added dropwise to 733 g (10 moles) of t-butylamine in 1250 ml of anhydrous ether at 5–10 °C. The mixture is allowed to stand for two days, and the t-butylamine hydrochloride that precipitates is filtered off and washed with ether. The filtrate is evaporated to dryness at 40 °C/0.1 mm Hg; 287 g of a yellow oil remain behind. 123 g of this oil is heated under reduced pressure. Decomposition begins at 63 °C. When the temperature reaches 160 °C, 72 g of a bright yellow oil has distilled over. Redistillation of this oil gives 70 g (56%) of pure di-t-butylsulfodiimide, b.p. 60–62 °C/15 mm Hg.

Diphenylsulfodiimide from N-Sulfinylaniline ((51), $Ar = C_6H_5$) [93]

A solution of 10 g of *N*-sulfinylaniline *(1a)* in 10 ml of anhydrous toluene is warmed with 3.2 g of Na powder (prepared by vigorous stirring of molten sodium in boiling xylene) until the exothermic reaction begins (the mixture begins to boil) and continues without further heating. When reaction has ceased, the mixture is heated for a further 15 hours, and is then cooled and filtered. The toluene solution is evaporated to dryness under vacuum at 30–40 °C, and the residue is distilled in a high vacuum. Yield about 40%.

Diarylsulfodiimides (51) from Sulfonylsulfodiimides [78]

a) 0.04 mole of arylamine in 20 ml of benzene is slowly added to a suspension of 0.02 mole of disulfonylsulfodiimide *(52)* in 30 ml of benzene. The reaction is complete within 3–4 days at room temperature but it can be accelerated by heating. The precipitated sulfonamide removed by is filtration and the filtrate is evaporated to dryness at 20–30 °C under vacuum. The diarylsulfodiimide is purified by vacuum distillation or by recrystallization from petroleum ether.

b) Diarylsulfodiimides can be obtained in 80% yield from 0.02 mole of *N*-sulfonyl-*N'*-arylsulfodiimide *(53)* in 20 ml of benzene and 0.02 mole of arylamine in 20 ml of benzene by the above procedure.

2.1.2. Disulfonyl- and *N*-Sulfonyl-*N'*-arylsulfodiimides

Disulfonylsulfodiimides *(52)* are formed by the action of tertiary amines or $AlCl_3$ on *N*-sulfinylsulfonamides *(2)* [97].

$$\underset{(2)}{2\,R-SO_2-NSO} \longrightarrow \underset{(52)}{R-SO_2-N=S=N-SO_2-R} + SO_2$$

Other syntheses use *N,N*-dichlorosulfonamides or arylsulfonyliminosulfur dichlorides *(44)* as starting materials [96].

$$2\,R-SO_2-NCl_2 + S,\ SCl_2,\ S_2Cl_2 \longrightarrow \underset{(52)}{R-SO_2-N=S=N-SO_2-R} + xCl_2$$

$$R-SO_2-NCl_2 + \underset{(44)}{R-SO_2-N=SCl_2} \longrightarrow \underset{(52)}{R-SO_2-N=S=N-SO_2-R} + 2\,Cl_2$$

$$\underset{(44)}{R-SO_2-N=SCl_2} + R-SO_2-NH_2 \longrightarrow \underset{(52)}{R-SO_2-N=S=N-SO_2-R} + 2\,HCl$$

N-Sulfonyl-*N'*-arylsulfodiimides *(53)* can be obtained by the reaction of disulfonylsulfodiimides *(52)* with one equivalent of arylamine [78].

$$\underset{(52)}{R-SO_2-N=S=N-SO_2-R} + Ar-NH_2 \longrightarrow \underset{(53)}{R-SO_2-N=S=N-Ar} + \underset{(3)}{R-SO_2-NH_2}$$

A second method is based on the use of arylsulfonyliminosulfur dichlorides *(44)* as starting materials [78].

$$\underset{(44)}{R-SO_2-N=SCl_2} + Ar-NH_2 \longrightarrow \underset{(53)}{R-SO_2-N=S=N-Ar} + HCl$$

Disulfonylsulfodiimides *(52)* are bright yellow substances which crystallize well (for IR spectra see [97]). They are extremely sensitive to hydrolysis and very reactive. *N*-Sulfonyl-*N'*-arylsulfodiimides *(53)* are yellow-orange solids; their reactivity and their sensitivity to hydrolysis are lower than those of the disulfonylsulfodiimides *(52)*.

Procedures

Disulfonylsulfodiimides (52) [97]

The *N*-sulfinylsulfonamide is dissolved in its own weight of anhydrous benzene, and 2.5 mole-% [based on *(2)*] of anhydrous pyridine (1:1 in benzene) is added. The mixture is

[100] *A. Foffani, G. Leandri, J. Zanon,* and *C. Carpanelli,* Tetrahedron Letters *1959*, Nr. 11, S. 21.

[101] *G. Leandri* and *A. Mangini,* Boll. sci. Fac. Chim. ind. Bologna *15*, 51 (1957).

allowed to stand overnight at room temperature, and the disulfonylsulfodiimide *(52)* that crystallizes is filtered off and washed with CCl_4. The yield is almost quantitative. The product may be recrystallized from benzene (R = aryl) or nitromethane (R = alkyl).

N-Arylsulfonyl-N'-arylsulfodiimides (53) [78]

A solution of 0.02 mole of arylamine in 20 ml of benzene is added slowly to a cooled suspension of 0.02 mole of bis(arylsulfonyl)sulfodiimide in 30 ml of benzene. The mixture is allowed to stand for 2–3 hours, the arylsulfonamide that crystallizes is removed by filtration, and the filtrate is evaporated to dryness under vacuum. A quantitative yield of the crude product is obtained.

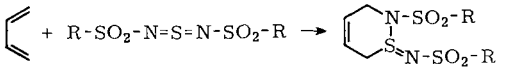
2.2. Reactions with Sulfodiimides

As might be expected, many of the reactions of sulfodiimides are similar to those of the *N*-sulfinylamines; however, in many other reactions, the sulfodiimides show a characteristically different behavior.

The only reactions of any preparative interest at present are those of the stable di-t-alkyl- *(50)*, disulfonyl- *(52)*, and *N*-sulfonyl-*N'*-arylsulfodiimides *(53)*.

2.2.1. Preparation of 1-Sulfonylimino-3,6-dihydro-1,2-thiazines

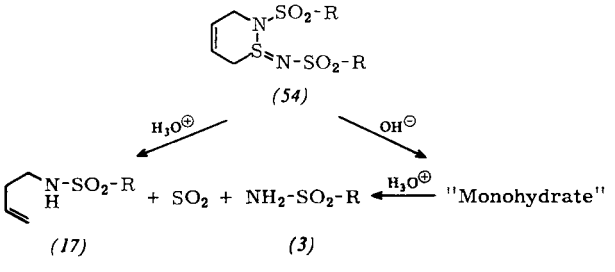
Di-*N*-sulfonylsulfodiimides *(52)* react even at room temperature with sterically unhindered dienes in solution with spontaneous liberation of heat and formation of 1-sulfonylimino-2-sulfonyl-3,6-dihydro-1,2-thiazines *(54)* [102].



(52) *(54)*

The structure of the heterocyclic compounds *(54)* was established from their IR spectra [97] and from degradation reactions [102].

Acid hydrolysis gives the *N*-alk-3-enylsulfonamide *(17)*, the sulfonamide *(3)*, and SO_2. Treatment with alkali solution [102] leads to the formation of "monohydrates" or their alkali metal salts, the structures of which are not yet known but which decompose on acid hydrolysis to form *(17)*, *(3)*, and SO_2.



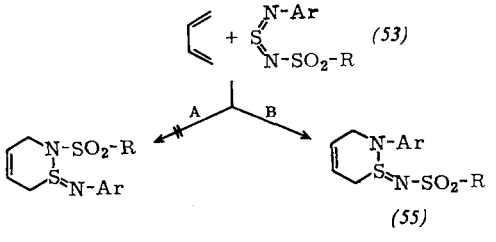
Thus the acid degradation proceeds similarly to that of the 2-sulfonyl-3,6-dihydro-1,2-thiazine 1-oxides *(12)* (cf. Section 1.2.2.1.).

[102] *E. S. Levtschenko* and *Ya. G. Bal'on*, Ž. org. Chim. *1*, 150 (1965).

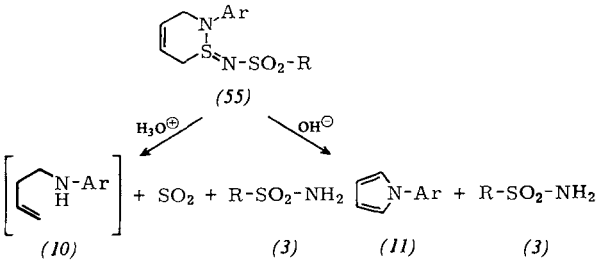
Table 3. Examples of sulfodiimides R'—N=S=N—R².

R¹	R²	M.p. (°C) or b.p. (°C/mm)	Ref.
CH_3	CH_3		[91]
n-C_4H_9	n-C_4H_9		[8]
t-C_4H_9	t-C_4H_9	167–169/760	[92]
		60–62/15	
t-Octyl	t-Octyl	88–90/0.15	[92]
C_6H_5	C_6H_5	123–124/0.6	[78,93,94]
o-CH_3—C_6H_4	*o*-CH_3—C_6H_4	126/0.01	[93]
m-CH_3—C_6H_4	*m*-CH_3—C_6H_4	132/0.01	[93]
p-CH_3—C_6H_4	*p*-CH_3—C_6H_4	48–50	[78,93]
o-Cl—C_6H_4	*o*-Cl—C_6H_4	138–140/0.01	[93]
m-Cl—C_6H_4	*m*-Cl—C_6H_4	45–47	[93]
p-Cl—C_6H_4	*p*-Cl—C_6H_4	60–61	[78,93]
p-Br—C_6H_4	*p*-Br—C_6H_4	106–107	[78,93]
o-$CH_3OC_6H_4$	*o*-$CH_3OC_6H_4$	89–91	[93]
p-$CH_3OC_6H_4$	*p*-$CH_3OC_6H_4$	46–47	[78,93]
o-$C_2H_5OC_6H_4$	*o*-$C_2H_5OC_6H_4$	106–108	[93]
p-$C_2H_5OC_6H_4$	*p*-$C_2H_5OC_6H_4$	66–68	[78,93]
p-$(CH_3)_2NC_6H_4$	*p*-$(CH_3)_2NC_6H_4$	96–98	[78,93]
o-C_6H_5—C_6H_4	*o*-C_6H_5—C_6H_4		[93]
p-C_6H_5—C_6H_4	*p*-C_6H_5—C_6H_4	144–146	[93]
$C_6H_5SO_2$	C_6H_5	94–95	[78,98]
$C_6H_5SO_2$	*p*-CH_3—C_6H_4	85–86	[78,98]
$C_6H_5SO_2$	*p*-$CH_3OC_6H_4$	134–136	[78,98]
$C_6H_5SO_2$	*m*-Cl—C_6H_4	66–67	[78]
$C_6H_5SO_2$	*p*-Cl—C_6H_4	120–123	[78,98]
$C_6H_5SO_2$	*m*-NO_2—C_6H_4	123–124	[78,98]
$C_6H_5SO_2$	*p*-NO_2—C_6H_4	140–141	[78,98]
$C_6H_5SO_2$	*p*-$(CH_3)_2NC_6H_4$	146–147	[78]
$C_6H_5SO_2$	*p*-CF_3—SO_2C_6H	112–113	[78]
CH_3SO_2	CH_3SO_2	122	[97]
$C_6H_5SO_2$	$C_6H_5SO_2$	110	[96,97]
p-CH_3—$C_6H_4SO_2$	*p*-CH_3—$C_6H_4SO_2$	120	[96,97]
p-$CH_3OC_6H_4SO_2$	*p*-$CH_3OC_6H_4SO_2$	147	[97]
p-F—$C_6H_4SO_2$	*p*-F—$C_6H_4SO_2$	129	[97]
p-Cl—$C_6H_4SO_2$	*p*-Cl—$C_6H_4SO_2$	142–144	[96,97]
p-Br—$C_6H_4SO_2$	*p*-Br—$C_6H_4SO_2$	160–162	[96,97]
o-NO_2—$C_6H_4SO_2$	*o*-NO_2—$C_6H_4SO_2$	131–133	[96]
m-NO_2—$C_6H_4SO_2$	*m*-NO_2—$C_6H_4SO_2$	147–148	[96]
p-NO_2—$C_6H_4SO_2$	*p*-NO_2—$C_6H_4SO_2$	227–229	[96]

The *N*-sulfonyl-*N'*arylsulfodiimides *(53)* react much less readily with dienes [99]; the components must be heated for some time in benzene. Two reactions (A and B) appear possible because of the unsymmetrical substitution of the dienophilic N=S=N system.



Degradation reactions show that the course followed is path B, with formation of *(55)*. Acid hydrolysis gives the sulfonamide *(3)*, SO_2, and a "basic fraction", from which the *N*-alk-3-enylaniline *(10)* has so far been isolated in only one case [99]. Alkaline hydrolysis gives the sulfonamide *(3)* and *N*-arylpyrroles *(11)* in a smooth reaction.



The acid and alkaline hydrolyses are completely analogous to those of the 2-aryl-3,6-dihydro-1,2-thiazine 1-oxides *(4)*.

As yet, no cycloadditions of diaryl- or dialkylsulfodiimides have been reported.

Procedures

1-Sulfonylimino-2-sulfonyl-3,6-dihydro-1,2-thiazines (54) [97]

0.02 mole of disulfonylsulfodiimide *(52)* is dissolved in 10 ml of warm benzene (in nitromethane when R = CH_3). The solution is cooled and 1.1 equivalents of freshly distilled diene are added. With low-boiling dienes it is recommended that the flask should be cooled with ice. The mixture is allowed to stand overnight, and the adduct that precipitates is filtered off and washed with ether. The yield is almost quantitative. The compounds can be recrystallized from a large quantity of alcohol or from nitromethane.

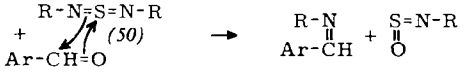
1-Benzenesulfonylimino-2-aryl-4,5-dimethyl-3,6-dihydro-1,2-thiazines [99]

0.02 mole of *N*-benzenesulfonyl-*N'*-arylsulfodiimide is boiled with 0.02 mole of dimethylbutadiene in 20 ml of benzene. Depending on the nature of the substituents in the aryl group, the reaction is complete within 15 min (NO_2, $SO_2N(CH_3)_2$) to 3 hours (OCH_3, Cl). If the adduct crystallizes on cooling, it is filtered off, washed with ether, and recrystallized. Otherwise the benzene is evaporated under vacuum and the crystalline residue is treated as described above.

2.2.2. Preparation of Carbodiimides

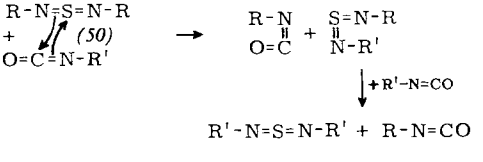
The only sulfodiimides whose reactions with polar multiple bonds have so far been investigated are the di-t-alkyl-substituted compounds *(50)* [103].

Sulfodiimides *(50)* (like the *N*-sulfinylsulfonamides *(2)*, cf. Section 1.2.3.1.) react with aromatic aldehydes to form imines.

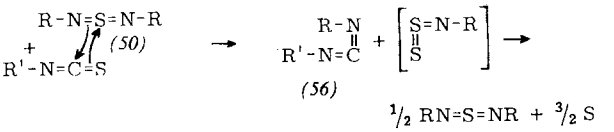


R = t-Alkyl

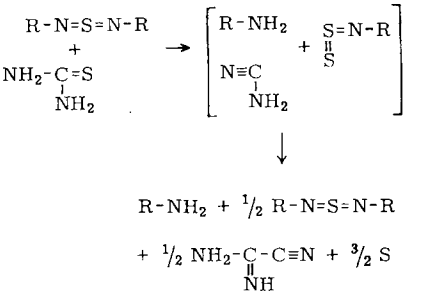
Reactions with cumulative double bond systems are also interesting. The nucleophilic center in isocyanates is the N atom, and one or both groups R (depending on the reactant ratio) are replaced.



In isothiocyanates, on the other hand, the nucleophilic center is the S atom, and carbodiimides *(56)* are formed.



The reaction with thiourea probably involves a similar primary reaction, the intermediate then being stabilized by proton shift.



Procedure

N-Phenyl-N'-tert-butylcarbodiimide ((56), R = C_6H_5, R' = $C(CH_3)_3$) [103]

6.8 g of di-t-butylsulfodiimide and 10.4 g of phenyl isothiocyanate are heated at 120 °C for 4 hours. Yield 72%, b.p. 90–92 °C/4 mm Hg.

2.2.3. Transimidations

The disulfonylsulfodiimides *(52)* react with arylamines to form *N*-sulfonyl-*N'*-arylsulfodiimides *(53)*, which can react with a second mole of arylamine to form diarylsulfodiimides *(51)*. These reactions have been discussed in Section 2.1.1.

This reaction is also used for the preparation of piazthioles [78] (cf. Section 1.2.4.3.). The disulfonylsulfodiimides react faster and under milder conditions (room temperature) than any other reagent used for the cyclization of diamines.

Procedure

Benzo-2,1,3-thiadiazole (piazthiole) (40) [78]

0.015 mole of *o*-phenylenediamine in 10 ml of benzene is slowly added to a solution of 0.015 mole of bis(benzenesulfonyl)sulfodiimide in 40 ml of anhydrous benzene. An intense red color appears, and then quickly disappears. After 2 hours, the benzenesulfonamide that has crystallized is filtered off and the filtrate is evaporated to dryness under vacuum. Yield quantitative, m.p. 43–44 °C.

We thank the "Fonds der Chemischen Industrie" and Schering AG., Berlin, for supporting our investigations. Our thanks are also due to Chemische Werke Hüls AG., Marl, to BASF, Ludwigshafen, to Farbwerke Hoechst, and to Farbenfabriken Bayer, Leverkusen, for generous gifts of chemicals.

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Translated by Express Translation Service, London

[103] *D. H. Clemens, A. J. Bell,* and *J. L. O'Brien,* Tetrahedron Letters *1965*, 1491.

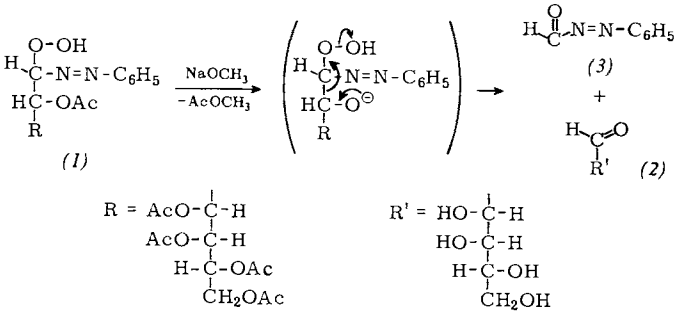
Formation and Degradation of 1-Phenylazo 1-Hydroperoxides Derived from Carbohydrates

By *Manfred Schulz* and *L. Somogyi*[*]

Geminal phenylazo-substituted organic hydroperoxides are formed by the action of oxygen on phenylhydrazones containing an NH group[1–5]. We have applied this reaction to both unacetylated and acetylated acyclic carbohydrate phenylhydrazones.

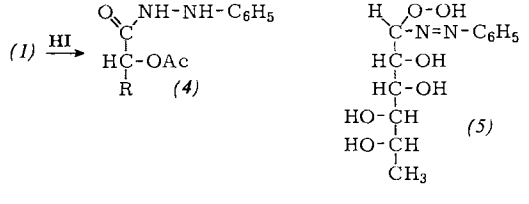
For instance, by passing oxygen into a benzene solution of penta-*O*-acetyl-D-galactose phenylhydrazone for 2 hr at room temperature we obtained 2,3,4,5,6-pentaacetoxy-1-phenylazo-D-*galacto*-hexyl hydroperoxide *(1)* in 80 % yield [m.p. 117–120 °C (decomp.); from benzene/petroleum ether; $[\alpha]_D^{21} = -30.8°$ (c = 1, in benzene)]. This compound crystallizes rapidly after treatment of the reaction mixture with petroleum ether. Its structure follows from elemental analysis and iodometric determination of the active oxygen, as well as from UV data: λ_{max} (in ethanol) = 217 mμ, ε = 11182; 275 mμ, ε = 11150; 412 mμ, ε = 153.

As in peroxyglycosides[6], the grouping $-O-\overset{|}{C}-\overset{|}{C}-O-O-$ proved liable to fragmentation. On treatment with 0.01 N methanolic $NaOCH_3$ at room temperature, compound *(1)* decomposes in a few hours to a sugar having one less carbon atom (D-lyxose) *(2)* as the main product, which can be isolated in 60 % yield (identified by paper-chromatographic comparison with authentic D-lyxose). *N*-Formyl-*N'*-phenyldiazene *(3)* should also be formed in this decomposition;



its hydrolysis products, methyl formate (identified by gas chromatography) and phenyldiazene (UV spectrum in 0.002 M methanolic $NaOCH_3$ solution: λ_{max} = 213 mμ, ε ≈ 8000; 273 mμ, ε ≈ 6700; 401 mμ, ε ≈ 58[7]) were identified.

On reduction with zinc and acetic acid, compound *(1)* regenerates the original hydrazone, and with sodium iodide in acetic acid gives penta-*O*-acetyl-*N*-phenyl-D-galactonohydrazide *(4)*[8] (yield 90 %).



2,3,4,5-Tetrahydroxy-1-phenylazo-L-*manno*-hexyl peroxide *(5)* [yield 60 %; m.p. 110–118 °C (decomp.); $[\alpha]_D^{22} = -71.0°$ (c = 1, in methanol); UV data: λ_{max} (in dioxane) = 240 mμ, ε = 7000; 272 mμ, ε = 7440; 400 mμ, ε = 92.6] is obtained from L-rhamnose phenylhydrazone by treatment with oxygen (in acetone; room temperature; 19 hr); it fragments to 5-deoxy-L-arabinose (yield 90 %; identified by paper-chromatographic comparison with authentic 5-deoxy-L-arabinose).

The following carbohydrates were similarly treated: D-glucose, D-xylose.

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[*] Dr. M. Schulz
Institut für Organische Chemie der Deutschen Akademie der Wissenschaften zu Berlin
X 1199 Berlin-Adlershof (Germany)
Dr. L. Somogyi
Institute of Organic Chemistry, University of Debrecen
Debrecen (Hungary)

[1] *M. Busch* and *W. Dietz*, Ber. dtsch. chem. Ges. *47*, 3277 (1914).
[2] *R. Criegee* and *G. Lohaus*, Chem. Ber. *84*, 219 (1951).
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[6] *M. Schulz* and *H. Boeden*, Tetrahedron Letters *1966*, 2843; *M. Schulz*, *H. Boeden*, and *P. Berlin*, Liebigs Ann. Chem., in press.
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Acid-Catalysed Oxidation of Isocyanides with Dimethyl Sulfoxide

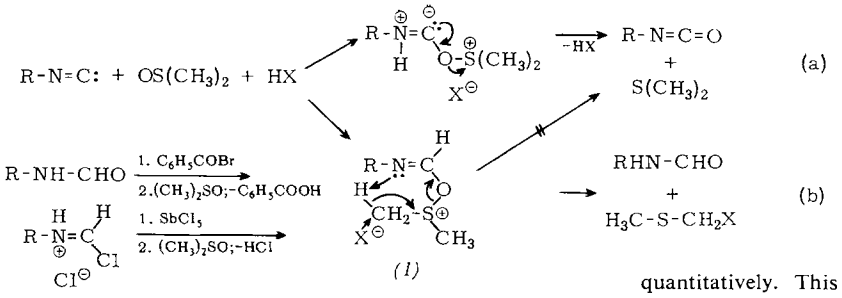
By *D. Martin* and *A. Weise*[*]

Pure dimethyl sulfoxide does not react with isocyanides. However, isocyanate and dimethyl sulfide are formed after about 24 hr if 5 mole-% of bromine is added to a boiling chloroform solution of an isocyanide and dimethyl sulfoxide[1]. This is presumably a chain reaction, involving primarily the isocyanide dibromide.

We have found that in oxidation of isocyanides with dimethyl sulfoxide, catalysis with Brönsted acids (*p*-toluenesulfonic acid; anhydrous HCl) or triphenylmethyl perchlorate is more convenient. The exothermic reaction requires only a short time for completion at 50 to 80 °C in the absence of a solvent. It gives the isocyanates in 50 to 90 % yield, together with dimethyl sulfide (40–60 %)[**] and relatively small amounts of resin.

This new method of oxidation helps to clarify the problem of whether the nitrogen or the carbon atom of the isocyanide group is the more basic: the smooth isocyanate formation is understandable only if we assume primary *N*-protonation of the isocyanide group (eq. a), as was postulated[2] for acid-catalysed reactions of isocyanides.

By model experiments[***] we have shown that the *O*-sulfonium formimidates *(1)* that would result from *C*-protonation do not decompose to isocyanates, dimethyl sulfide, and acid under comparable conditions, but, like the adducts of other nitrilium salts[3], react with dimethyl sulfoxide in accordance with the mechanism of the Pummerer reaction[4] to give amides and α-substituted dimethyl sulfides (eq. b); formamides were not found after reaction in the presence of catalytic amounts of acid. *C*-Protonation does occur to some extent when the isocyanide–dimethylsulfoxide mixture is added dropwise to an equimolar amount of anhydrous *p*-toluenesulfonic acid, but even then up to 50 % of isocyanate is formed.



Examples: A mixture of 50 mmole of isocyanide and 55 mmole of dimethyl sulfoxide is treated with 5 mmole of *p*-toluenesulfonic acid or 1 mmole of triphenylmethyl perchlorate. The temperature is kept at 50 to 80° by periodic cooling and two or three additions of a little acid; dimethyl sulfide distils off, and after disappearance of the isocyanide odor (about 30 min) the residue is fractionated in a water-pump vacuum. Products are tabulated below.

	Yield (%)	
	$(CH_3)_2S$	Isocyanate (b.p.)
n-C_4H_9	55	85 (115–120 °C)
Cyclohexyl	46	92 (62–68 °C/15 mm)
C_6H_5–CH_2	49	90 (88–91 °C/12 mm)
p-CH_3–C_6H_4	64	52 (75–78 °C/15 mm)

The behavior of isocyanides towards alkylating and arylating agents in dimethyl sulfoxide indicates that only "hard"[5] electrolytes tend to attack the nitrogen atom.

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[*] Dr. habil. D. Martin
Dipl.-Chem. A. Weise
Institut für organische Chemie der Deutschen Akademie der Wissenschaften zu Berlin
X 1199 Berlin-Adlershof (Germany)

[**] Quantitative isolation of the sulfide is impeded by its volatility (b.p. 38–40 °C).

[***] We prepared *(1)* with R = cyclohexyl and X = Br from *N*-cyclohexylformamide, benzoyl bromide, and dimethyl sulfoxide, and *(1)* with R = cyclohexyl and X = $SbCl_6$ from *N*-cyclohexylformonitrilium hexachloroantimonate and DMSO.

[1] *H. W. Johnson jr.* and *P. H. Daughhetee jr.*, J. org. Chemistry *29*, 246 (1964).

[2] *I. Hagedorn*, *U. Eholzer*, and *H. D. Winkelmann*, Angew. Chem. *76*, 583 (1964); Angew. Chem. internat. Edit. *3*, 647(1964); *I. Hagedorn* and *U. Eholzer*, Chem. Ber. *98*, 936 (1965).

[3] *D. Martin* and *A. Weise*, Liebigs Ann. Chem., in press.

[4] *F. G. Bordwell* and *B. M. Pitt*, J. Amer. chem. Soc. *77*, 572 (1955).

[5] *R. G. Pearsen*, J. Amer. chem. Soc. *85*, 3533 (1963).

Ligand Addition and Redox Reactions of Azido-Metal Complexes

By *W. Beck* and *W. P. Fehlhammer* [*]

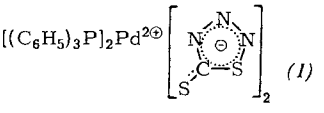
Metal carbonyls, *e.g.* $W(CO)_6$, react with azide ions, giving isocyanate complexes[1].

We have found that isocyanates also arise when azido-metal complexes are treated with free carbon monoxide. Thus when CO is passed at 20 °C into a chloroform solution of diazido-

$$M{-}CO + N_3^- \longrightarrow [M{-}NCO]^- + N_2$$
$$M{-}N_3 + CO \longrightarrow M{-}NCO + N_2$$

bis(triphenylphosphine)palladium(II), $[(C_6H_5)_3P]_2Pd(N_3)_2$[2], the isocyanate complex $[(C_6H_5)_3P]_2Pd(NCO)_2$ is obtained quantitatively. This pale yellow compound [decomp. at 216 °C; $\nu_{as}(NCO) = 2218$, $\nu_s(NCO) = 1347$ cm^{-1}, suspension in Nujol] is also obtained directly from $K_2[Pd(NCO)_4]$ and triphenylphosphine in ethanol/water[3]. A CO pressure of 200 atm (at 20 °C) is necessary for complete conversion of the platinum(II) compound $[(C_6H_5)_2P]_2Pt(N_3)_2$[2] into the analogous isocyanate complex [$\nu_{as}(NCO) = 2234$ cm^{-1}]. However, no cyanate could be detected after CO had been passed (at 200 atm and 20 °C) into an aqueous solution of sodium azide. The reaction $N_3^- \rightarrow NCO^-$ does occur when Pd(II) nitrate is added [1.5 g of NaN_3, 0.1 g of $Pd(NO_3)_2$, in water], the Pd(II) being reduced to metallic palladium.

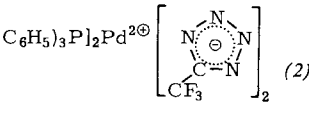
If an excess of carbon disulfide is allowed to act on solid $[(C_6H_5)_3P]_2Pd(N_3)_2$ for several days at 20 °C, CS_2 is added to the azide group and the complex *(1)* is formed. This pale yellow substance (decomp. at 119–120 °C) was also obtained from Pd(II) nitrate, $Na[CS_2N_3]$ ("azidodithiocarbonate")[4], and



(1)

$P(C_6H_5)_3$ in ethanol/water. The characteristic IR absorption bands of the coordinately bound 1,2,3,4-thiatriazole-5-thiolate ion lie at 1295(m), 1223(s), 1067(s), 1020(m), and 932(m) cm^{-1} (KBr disk). The decomposition products arising from *(1)* in chloroform solution at 20 °C give an intense IR band at 2095 cm^{-1} indicating an isothiocyanate complex.

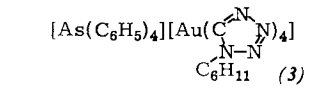
Reaction of $[(C_6H_5)_3P]_2Pd(N_3)_2$ with trifluoroacetonitrile in CH_2Cl_2 (1 atm, 0 °C, 1 hr) also leads to formation of a compound in which a five-membered ring system is bonded through a nitrogen to the palladium. This reaction is analogous to the 1,3-dipolar cycloadditions of organic azides[5].



(2)

The pale yellow tetrazolato complex *(2)* formed (decomp. at 258 °C) is sparingly soluble in CH_2Cl_2 and its IR spectrum (KBr disk) shows the bands of the 5-trifluoromethyltetrazolate anion[6]: 1507(s) ν(C–CF_3); 1242(s), 1191(s), 1182(m), 1168(s), 1156(s), 1143(s) $\nu(CF_3)$; 746 (s) $\delta(CF_3)$; 1401(w), 1312(w), 1040(s), and 1024(s) (ring vibrations).

A tetrazolato complex, possibly containing a metal-C bond, is also formed on treatment of $[As(C_6H_5)_4]$ $[Au(N_3)_4]$[2] with cyclohexyl isocyanide (molar proportions 1:4.5) in CH_2Cl_2 at 20 °C for about 1/2 hr. On addition of petroleum ether shiny, colorless leaflets of tetraphenylarsonium tetra-(cyclohexyltetrazolato)aurate(III) *(3)* are obtained [m.p. 184 °C (decomp.)]. The ^1H–NMR spectrum (in $DCCl_3$)



(3)

includes three signals (intensity ratio 5:1:10) which can be assigned to the 20 phenyl protons ($\tau = 2.4$), the four tertiary H atoms ($\tau = 5.2$), and the 40 methylene protons ($\tau = 8.3$) of

the cyclohexyl ring. The IR spectrum (Nujol suspension) contains the characteristic bands of 1-cyclohexyltetrazole, except for the ν(CH) vibration [7].

The red solution of $[As(C_6H_5)_4]$ $[Au(N_3)_4]$ in tetrahydrofuran rapidly becomes colorless in daylight, an intramolecular redox reaction occurring:

$$[As(C_6H_5)_4]\ [Au^{III}(N_3)_4] \xrightarrow[THF]{h\nu} [As(C_6H_5)_4]\ [Au^{I}(N_3)_2] + 3\,N_2.$$

The diazidoaurate(I) complex [decomp. at 127 °C; $\nu_{as}(N_3)$ = 2039 cm^{-1}, $\nu_s(N_3)$ = 1285 cm^{-1}, KBr disk] is precipitated in crystalline form by petroleum ether. It can also be obtained directly from Au(I)Cl, NaN_3, and $[As(C_6H_5)_4]Cl$ in CH_2Cl_2.

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[*] Doz. Dr. W. Beck
Dipl.-Chem. W. P. Fehlhammer
Anorganisch-Chemisches Laboratorium
der Technischen Hochschule
8 München 2 (Germany)

[1] *W. Beck* and *H. Smedal*, Angew. Chem. *78*, 267 (1966); Angew. Chem. internat. Edit. *5*, 253 (1966).

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[4] *F. Sommer*, Ber. dtsch. chem. Ges. *48*, 1833 (1915); *E. Lieber, C. N. Pillai, J. Ramachandran*, and *R. D. Hites*, J. org. Chemistry *22*, 1750 (1957).

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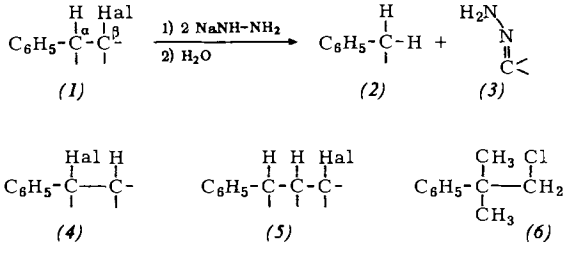
[7] *G. L. Gilbert* and *C. H. Brubaker jr.*, Inorg. Chem. *2*, 1216 (1963).

Cleavage of β-Halogeno-α-phenylalkanes by Sodium Hydrazide

By *Th. Kauffmann, W. Burkhardt*, and *E. Rauch* [*]

On reaction with sodium hydrazide, phenylalkyl halides of types *(1)*, *(4)*, and *(5)* [2] formally should be convertible by elimination of hydrogen halide into olefins that can be cleaved by the hydrazide [1]. If the elimination of HHal is faster than competing reactions, then the action of sodium hydrazide should lead to scission between the C atoms that are α and β to the phenyl group and thus to formation of a hydrocarbon *(2)* and a hydrazone *(3)*.

We have found that under the conditions of hydrazidolysis of C=C bonds [1] (in a hydrazine/ether mixture at 35 °C or in a hydrazine/benzene mixture at 60 °C; excess of sodium hydrazide) this cleavage does occur to a large extent with halides of type *(1)*. With *(4)* or *(5)* it occurs only to a small extent, the main reactions being replacement of the halogen by hydrogen, or a hydrazine group respectively.



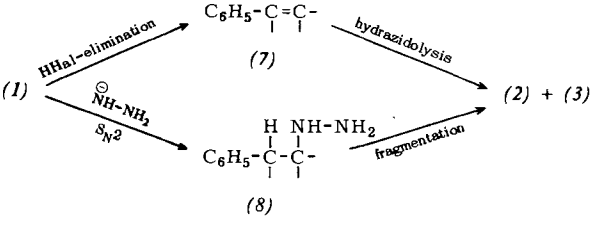
(1) *(2)* *(3)*

(4) *(5)* *(6)*

Reactant	Temp. (°C)	Yield (%) after 5 hr[3]
Type (1):		
Phenethyl chloride, bromide, iodide	60	Toluene 74, 80, 67
β-Methylphenethyl bromide	35	Ethylbenzene 67
α-Methylphenethyl chloride, bromide, iodide	35	Toluene 89, 85, 73
Type (4):		
α-Methylbenzyl bromide	35	Toluene 2, ethylbenzene 35
α-Ethylbenzyl bromide	35	Toluene 1, phenylpropane 41
Type (5):		
3-Phenylpropyl bromide	35	Toluene 16, 3-phenylpropylhydrazine 47, phenylpropane 6.

For cleavage of compounds of type *(1)* we must consider not only the route *via* the olefin *(7)*, but also that *via* the hydrazine derivative *(8)*, since hydrazines of this type decompose in the presence of sodium hydrazide according to *(8)* → *(2)* + *(3)* [4].

In favor of the route *via (7)* are the facts that β,β-dimethylphenethyl chloride *(6)*, which cannot yield a styrene derivative by elimination of HHal, gives no trace of isopropylbenzene on treatment with sodium hydrazide in ether at 35 °C or in benzene at 60 °C, but remains largely unattacked (22 % or 8 % resp. of t-butylbenzene being formed).



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[*] Prof. Dr. Th. Kauffmann, Dipl.-Ing. W. Burkhardt, and Dipl.-Ing. E. Rauch
Organisch-Chemisches Institut der Universität
Hindenburgplatz 55
44 Münster (Germany)

[1] Cf. *Th. Kauffmann*, Angew. Chem. *76*, 214 (1964); Angew. Chem. internat. Edit. *3*, 349 (1964); *Th. Kauffmann, H. Henkler, E. Rauch*, and *K. Lötzsch*, Chem. Ber. *98*, 912 (1965).

[2] When an olefin containing a β,γ-double bond with respect to a phenyl group is treated with sodium hydrazide, an α,β-double bond results which is subsequently cleaved.

[3] Molar ratio; halide: $NaNH{-}NH_2$: $NH_2{-}NH_2$ = 1:5:5–15.

[4] *Th. Kauffmann, K. Lötzsch*, and *D. Wolf*, Chem. Ber. *99*, 3148 (1966).

Stereoselective Synthesis of 1-Butene with Lithium Sulfate as Elimination Catalyst [1]

By *H. Noller, M. Rosa-Brusin*, and *P. Andréu* [*]

In our studies of the elimination of hydrogen halide on solid catalysts we have always obtained mixtures of the three linear butenes from n-butyl chloride or bromide, *cis* + *trans* 2-butene being formed in large excess [2]. Recently, however, using lithium sulfate and a microcatalytic technique (a pulse technique) at temperatures between 320 and 370 °C, we obtained 1-butene exclusively from n-butyl bromide [3]; at 390 °C some 10 %, and at 420 °C some 50 %, of 2-butene was formed.

A nitrogen stream (35 ml/min), saturated at 70 °C with n-butyl bromide, was passed through a horizontal glass tube (inner diameter 2 cm) holding *ca.* 50 g of catalyst, then through a

trap cooled in ice and water (to remove unchanged butyl bromide), and finally through a soda-lime tube (to remove HBr).

The lithium sulfate used as catalyst ($LiSO_4 \cdot H_2O$ cryst., Merck) is advantageously tempered for 11 hr at 160 °C[3]. The butenes produced were analysed by gas chromatography (column 3.5 m long, 1/4 inch diameter; packing, 30 % dinonyl phthalate on 60–80 mesh Chromopak from Curtin, USA; room temp.; carrier gas, 120 ml of He per min; flame ionization detector).

The 1-butene obtained on use of 45 g of lithium sulfate at 270 °C contained *ca.* 50 % of 2-butene; the selectivity is thus less on a preparative scale. The proportion of 2-butene can be kept below 10 % only by using a mixture of lithium sulfate 30 g and soda-lime 15 g (for removal of the HBr that favors isomerization) at 270 °C; under these conditions the conversion is about 20 % of the butyl bromide passed over the catalyst. At 300 °C the conversion is higher, but so is the proportion of 2-butene (*ca.* 30 %).

The composition of the product is almost unchanged when the experiment is run for several hours. A recirculating reactor of the type described by *Schwab* would probably be very suitable for continuous operation[4].

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[*] Prof. Dr. H. Noller
Licenciado en Química M. Rosa-Brusin,
and Dr. P. Andréu
Escuela de Quimica, Universidad Centrale de Venezuela
Caracas (Venezuela)

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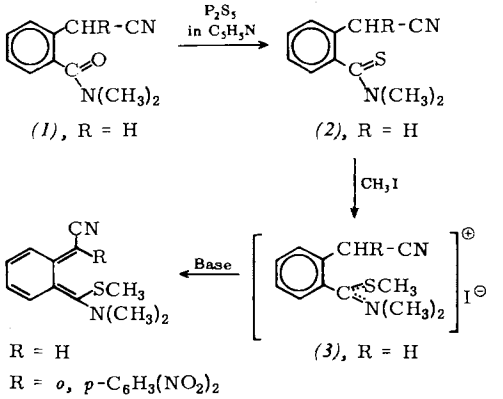
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[4] See, *e.g., G.-M. Schwab* and *G. Holz,* Z. anorg. Chem. *252*, 205 (1944); *G.-M. Schwab* and *N. Theophilides,* J. physic. Chem. *50*, 427 (1946); *R. Griffith* and *J. D. F. Marsh*: Contact Catalysis. Oxford University Press, London 1957, p. 116.

Stable *o*-Quinodimethanes [1]

By *R. Gompper, E. Kutter,* and *H. Kast* [*]

In contrast to their simple analogues, ω,ω-hetero-substituted (SR, NR_2, OR, or Hal) quinonemethides are stable[2]. The same structural principle[3] is incorporated in some stable *p*-quinodimethanes. Thus it was to be expected that suitable substituents would also stabilize *o*-quinodimethanes sufficiently to prevent the normal valence isomerization to bicyclo[4.2.0]octatrienes.



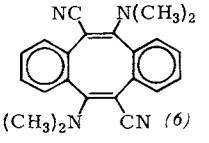
(1), R = H *(2)*, R = H

(4), R = H *(3)*, R = H

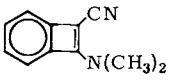
(5), R = *o*, *p*-$C_6H_3(NO_2)_2$

o-(Cyanomethyl)benzoic acid and PCl_5 in ether give the crystalline acid chloride (in CH_2Cl_2 an isoquinoline is formed[4]), which without further purification, is treated in benzene with aqueous dimethylamine, thus yielding the amide *(1)*[5] (a pale yellow oil, b.p. 128 °C/0.005 mm). Heating this amide with P_2S_5 in pyridine affords impure *o*-(cyanomethyl)thiobenzamide *(2)* (b.p. 140–145 °C/0.01 mm) as a deep red oil, which with methyl iodide yields the colorless quaternary salt *(3)* (m.p. 168–171 °C). If a solution of the salt *(3)* in dimethylformamide (DMF) at −40 °C is treated with a strong base (e.g. NaH, K t-butoxide, or C_2H_5MgI), it at once becomes deep blue; the following reactions, as well as the color[3], indicate the formation of the *o*-quinodimethane, 5-(cyanomethylene)-6-[(dimethylamino)(methylthio)methylene]-1,3-cyclohexadiene *(4)*.

If the temperature of the blue solution of compound *(4)* in DMF rises to −10 to 20 °C, the color changes to yellowish-brown, and if the mixture is then poured into water 5,11-dicyano-6,12-bis(dimethylamino)dibenzo[*a,e*]cyclooctatetraene *(6)* is isolated in *ca.* 50 % yield [colorless crystals, m.p. 236–238 °C; ν(CN) = 2195 cm^{-1}].



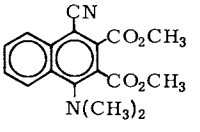
(6)



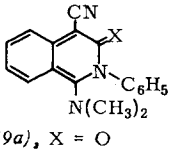
(7)

Elemental analysis, osmometric determination of the molecular weight in chloroform, and IR and NMR spectra confirm the structure given. We assume that compound *(6)* arises directly by dimerization of *(4)* and loss of CH_3SH from the primary product, since there is no indication of intermediate formation of the benzocyclobutadiene *(7)*. The *o*-quinodimethane *(5)*, which is stable even at room temperature, is obtained by treatment of *(4)* in DMF at −40 °C with 1-fluoro-2,4-dinitrobenzene, forming reddish-violet crystals with a golden-yellow sheen, m.p. 146–148 °C, λ_{max}(DMF) = 540 mμ.

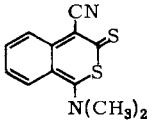
Compound *(4)* is the starting material for many cycloadditions (all effected in DMF at −40 °C, the reaction mixture subsequently being poured into water at 20 °C). Dimethyl acetylenedicarboxylate and *(4)* yield dimethyl 1-cyano-4-(dimethylamino)-2,3-naphthalenedicarboxylate (pale yellow needles, m.p. 131–133 °C; λ_{max}(DMF) = 377 mμ). 2,3-Dihydroisoquinolines *(9)* are formed in good yields on treatment of *(4)* with phenyl isocyanate [*(9a)*, orange prisms, m.p. 240–242 °C], phenyl isothiocyanate [*(9b)*, red



(8)



(9a), X = O
(9b), X = S
(9c), X = N-C_6H_5



(10)

prisms, m.p. 246–248 °C], and diphenylcarbodiimide [*(9c)*, dark-violet prisms, m.p. 234–236 °C]. Carbon disulfide and *(4)* react with formation of 4-cyano-1-(dimethylamino)benzo-[*d*]-α-dithiopyrone *(10)*.

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[*] Prof. Dr. R. Gompper, Dr. E. Kutter, and Dr. H. Kast
Institut für Organische Chemie der Universität
Karlstr. 23
8 München 2 (Germany)

[1] We thank the *Deutsche Forschungsgemeinschaft* and the *Fonds der Chemischen Industrie* for support of this work.

[2] *R. Gompper, R. R. Schmidt,* and *E. Kutter,* Liebigs Ann. Chem. *684*, 37 (1965); *R. Gompper* and *E. Kutter,* Chem. Ber. *98*, 1365 (1965); *R. Gompper* and *R.R. Schmidt, ibid. 98*, 1385 (1965).

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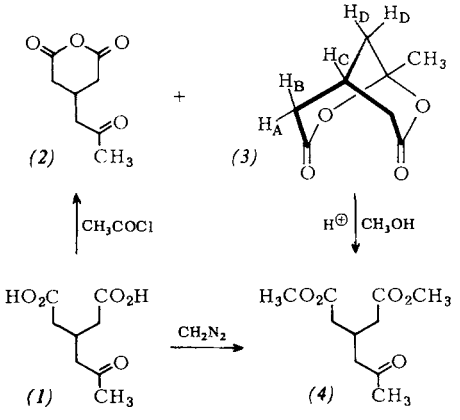
[4] *G. Simchen*, Angew. Chem. *78*, 674 (1966); Angew. Chem. internat. Edit. *5*, 663 (1966).

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Dehydration of 3-Acetonylglutaric Acid

By *E. Winterfeldt*[*]

The preparation of the anhydride *(2)* [1] by heating 3-acetonyl glutaric acid *(1)* with acetyl chloride (2 hr, *ca.* 51 °C) gives an approximately 20 % yield of a by-product that has a much higher melting point (170 °C) and is much less soluble in ether than *(2)*. The IR spectrum of this compound shows no anhydride band but has a broad carbonyl band at 1750 cm^{-1} and intense bands at 940, 1050, and 1130 cm^{-1}. Our assumption that the dilactone *(3)* had been formed was confirmed by elemental analysis and the NMR spectrum.



The signal of the methyl group appears as a singlet at τ = 8.28, and that of the two identical protons H_D as a broad singlet (half-width 4.5 Hz) at τ = 7.78 (intensity ratio 3:2), as expected since coupling with H_C is only slight. The protons H_A and H_B constitute a distorted AB quartet in which the two inner lines are almost superposed at τ = 7.25 (J_{AB} = 19 Hz); here also only slight coupling with H_C is observed.

The lactone *(3)* can be converted by methanolic hydrochloric acid into dimethyl 3-acetonylglutarate *(4)* (IR: 1730, 1150 cm^{-1}; NMR: τ_{OCH_3} = 6.39, τ_{OC-CH_3} = 7.90, τ = 7.4–7.7, intensity ratio 6:3:7), which is also obtained within 5 min when the dicarboxylic acid is allowed to react with diazomethane in ether at room temperature.

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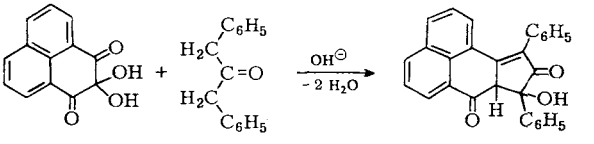
[*] Priv.-Doz. Dr. E. Winterfeldt
Organisch-Chemisches Institut der Technischen Universität
Hardenbergstr. 34
1 Berlin 12 (Germany)

[1] *E. Winterfeldt*, Chem. Ber. *97*, 2463 (1964).

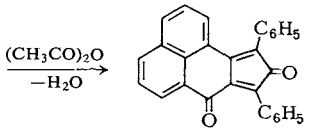
Synthesis of 7,9-Dioxo- and 7-Alkylidene-9-keto-derivatives of Cyclopenta[*a*]phenalene, and their Conversion into Substituted 7-Benz[*de*]anthrones

By *W. Ried* and *M. L. Mehrotra*[*]

7a,8-Dihydro-2-hydroxy-8,10-diphenylcyclopenta[*a*]phenalene-7,9-diones *(3)* are obtained in 60 to 70 % yield on treatment of 2,2-dihydroxy-1,3(2*H*)-phenalenedione *(1)* [1] with dibenzyl ketone *(2)*. [10 % methanolic KOH is added dropwise to a boiling anhydrous alcoholic solution of equimolar amounts of *(1)* and *(2)*, and the whole is boiled

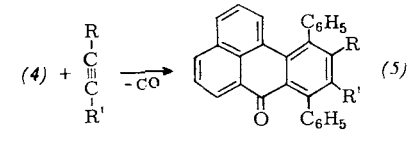


(1) *(2)* *(3)*, λ_{max} = 237; 337mμ
ε_{max} = 5,5 • 10^4; 1,62 • 10^4
(in CH_3OH)



(4), λ_{max} = 277,5; 375; 487,5mμ
ε_{max} = 2,5 • 10^4; 1,12 • 10^4; 1,3 • 10^4
(in CH_3OH)

for 1 h under reflux, whereupon the product *(3)* is precipitated [2]. Compound *(3)* forms pale yellow, shiny platelets m.p. 241–243 °C (softening from 233 °C), from anhydrous toluene.



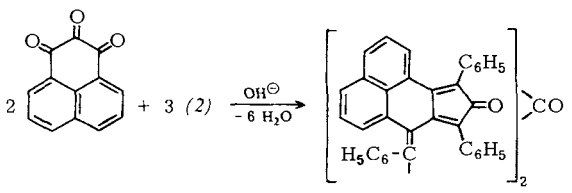
Compound *(3)* is dehydrated by acetic anhydride to 8,10-diphenylcyclopenta[*a*]phenalene-7,9-dione *(4)*, which crystallizes from the anhydride as black needles, m.p. 252 to 254 °C, and exhibits red halochromism in conc. H_2SO_4. Diene syntheses with *(4)* and alkynes leads to arylated 7-benz[*de*]anthrones *(5)* (cf. table).

(5) R	*(5)* R′	M.p. (°C)	Yield (%)	λ_{max} (mμ)	$\varepsilon_{max} \cdot 10^{-4}$
CO_2CH_3	CO_2CH_3	243–244	80	231; 239; 260; 272; 304; 317.5; 333.5; 402 (in CH_3OH)	5.65; 5.85; 2.32; 2.35; 1.2; 1.22; 1.45; 0.85
$CO-C_6H_5$	$CO-C_6H_5$	253–254	90	246; 405 (in CH_3OH)	4.45; 0.97
H	C_6H_5	303–304	75	300; 405 (in C_6H_6)	0.45; 0.27
or [a]					
C_6H_5	H				
$C\equiv C-C_6H_5$	C_6H_5	230–231	85	261; 327; 411 (in CH_3OH)	2.7; 2.32; 1.1
or [a]					
C_6H_5	$C\equiv C-C_6H_5$				

[a] The positions of the substituents have not yet been determined.

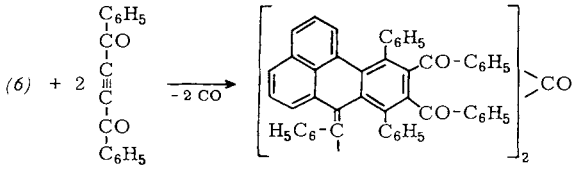
Treating 2 mol. equivalents of phenalene-1,2,3-triones with 3 mol. equivalents of dibenzyl ketone in boiling anhydrous ethanol in the presence of $NaOCH_3$ affords di-[α-(9-oxo-8,10-diphenyl-7*H*-cyclopenta[*a*]phenalen-7-ylidene)benzyl] ketone *(6)* in 20 to 30 % yield.

Compound *(6)* forms long black needles, m.p. 281–283 °C, from anhydrous toluene, and exhibits violet halochromism in conc. H_2SO_4. It reacts with 2 mol. equivalents of dibenzoylacetylene *(7)*, yielding bis-[α-(9,10-dibenzoyl-8,11-



(6), λ_{max} = 335; 573mμ
ε_{max} = 3,9 · 10⁴; 0,35 · 10⁴
(in C_6H_6)

diphenyl-7*H*-benz[*de*]anthren-7-ylidene)benzyl] ketone *(8)*. A 1:2 mixture of *(6)* and *(7)* is slowly heated in a little decanol until gas evolution begins and is kept at this temperature until decolorized, and then at 180 °C for a further 1 h. The product *(8)* crystallizes from ethyl acetate in pale yellow platelets, m.p. 281–282 °C.



(7)

(8), λ_{max} = 299; 329; 369; 379mμ
ε_{max} = 3,45 · 10⁴; 1,4 · 10⁴; 1,6 · 10⁴; 1,65 · 10⁴
(in C_6H_6)

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[*] Prof. Dr. W. Ried and Dipl.-Chem. M. L. Mehrotra
Institut für Organische Chemie der Universität
Robert-Mayer-Strasse 7/9
6 Frankfurt/M. (Germany)

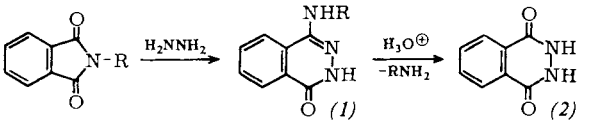
[1] *S. Errera*, Gazz. chim. ital. *43*, 583 (1913); *E.Yu. Gudrinietse, E.Ya. Dreimanis*, and *G.Ya. Vanag*, Ž. obšč. Chim. *26* [1], 289 (1956).

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Synthesis of 4-Amino-1-phthalazinones [1]

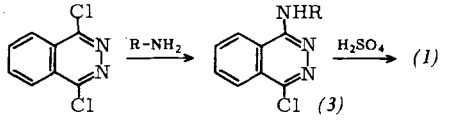
By *W. Flitsch* and *H. Peters* [*]

The Ing-Manske reaction of *N*-substituted phthalimides with hydrazine affords primary amines and 1,4-phthalazinedione *(2)* [2]. Except for the parent compound *(1a)* with R = H [4], 4-amino-1-phthalazinones *(1)*, which have been assumed to be intermediates in this reaction [3], have remained hitherto unknown.

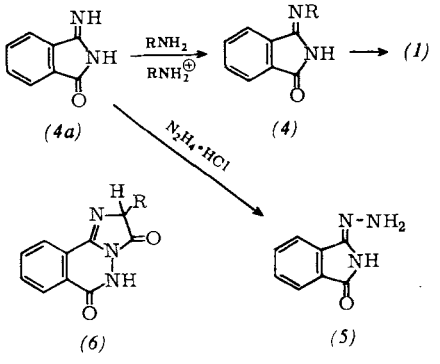


4-Amino-1-phthalazinones can be prepared in the following ways:

1. Reaction of 1,4-dichlorophthalazine [5,7] with primary amines and hydrolysis of the 1-amino-4-chlorophthalazines *(3)* by concentrated sulfuric acid, insofar as the group R is stable (*e.g.* H or CH_3).



2. A more generally useful synthesis is acid-catalysed transamination of 3-iminoisoindolin-1-one *(4a)* to yield 3*N*-substituted 3-iminoisoindoline-1-ones [6,8] and reaction thereof with hydrazine, which, contrary to the assumption made by *Elvidge* and *Linstead* [6], leads to 4-amino-1-phthalazinones *(1)*.



We used acid-catalysed reaction of compound *(4a)* and hydrazine to obtain the 3-hydrazonoisoindolin-1-one *(5)* described by *Elvidge* and *Linstead*. Compounds *(4c)* and *(4d)* react with hydrazine, affording imidazo[2,1-*a*]phthalazines *(6)* which are hydrolysed by alkali to the 4-amino-1-phthalazinones *(1d)* and *(1e)*. The structure of *(6)* was proved by elemental analysis and IR spectra.

The 4-amino-1-phthalazinones described are not converted into 1,4-phthalazinedione *(2)* either under the conditions of the Ing-Manske reaction (heating with dil. HCl) or by means of conc. HCl and thus cannot be intermediates in this reaction.

Compound	R	M.p. (°C)	Yield (%)	$\nu_{C=O}$ (cm^{-1})
(1a) [4]	H	265–266	57–66	1670
(1b)	CH_3	238	39	1650
(1c)	C_6H_5	258	3.4	1650
(1d)	CH_2CO_2H	200 (dec.)	78	1625, 1705 (Carboxyl)
(1e)	$CH(CH_3)CO_2H$	270 (dec.)	76	1620, 1695 (Carboxyl)
(3a) [7]	H	221–222	50	
(3b)	CH_3	223–224	75	
(3c)	CH_2CO_2H	130–140 (dec.)	57	
(4b) [6]	C_6H_5	168–169	74	1710
(4c)	$CH_2CO_2C_2H_5$	156–157	81	1700, 1740 (Ester)
(4d)	$CH(CH_3)CO_2C_2H_5$	148–149	79	1690, 1740 (Ester
(5)		195–205 (dec.)	55	1710
(6a)	H	270 (dec.)	65	1670, 1700 (Lactam)
(6b)	CH_3	230–231	57	1670, 1730 (Lactam)

Examples:

Method 1): *(3a)* is heated in 80 % H_2SO_4 at 150 °C for 1/2 h. On cooling and dilution, *(1a)* is precipitated; it was recrystallized from H_2O.

Method 2): 1 g of *(4a)* and 2 ml of 52 % hydrazine are dissolved in alcohol; *(1a)* is precipitated after *ca.* 12 h. *(4a)* is dissolved in hot alcohol and treated with an excess of aqueous hydrazine hydrochloride; *(5a)* separates and can be recrystallized from ethanol. *(6a)* can be prepared in the same way as *(4a)*, but from *(4c)* and hydrazine in ethanol; it was recrystallized from glacial acetic acid.

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[*] Priv.-Doz. Dr. W. Flitsch and Dipl.-Chem. H. Peters
Organisch-chemisches Institut der Universität
Hindenburgplatz 55
44 Münster (Germany)

[1] We thank the Landesamt für Forschung des Landes Nordrhein-Westfalen for support of this work.

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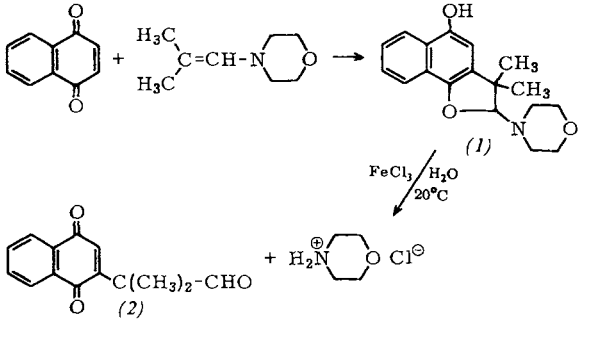
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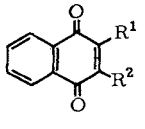
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Simple Method for Introduction of a Formylalkyl Group into Quinones

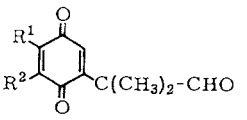
By *K. Ley* and *R. Nast* [*]

Enamines react smoothly with quinones, yielding 1:1 adducts [1]. Even in aqueous suspension, the resulting hydroxycoumarans *(1)* can be converted into formyl alkylquinones *(2)*, with loss of the amino group, by oxidizing agents such as $FeCl_3$, $CuCl_2$, nitric acid, and nitrous acid. Smooth oxidation requires that one of the positions *ortho* to the hydroxyl group in the coumaran *(1)* shall be substituted. Yields are greater than 70 %.





R^1	R^2	M.p. (°C)	Color of solid
H	$C(CH_3)_2$–CHO	91–92	Yellow
CH_3	$CHCH_3$–CHO	154–156	Yellow
H	1-Formyl-4-methyl-3-cyclohexenyl	140–142	Yellow



R^1	R^2	M.p. (°C)	Color of solid
$(CH_3)_3C$	H	87–88	Violet [a] (yellow in CH_3OH, CH_3CN)
CH_3	CH_3	60–62	Yellow
C_6H_5	H	142–143	Yellow
Cl	Cl	77–79	Yellow

[a] The solid compound gives an ESR signal.

Synthesis of compound (1):

149 g of isobutenylmorpholine is added dropwise to an ice-cooled suspension of 158 g (1 mole) of 1,4-naphthoquinone in 700 ml of methanol at 15–22 °C, with stirring. The mixture is stirred for 1 h at room temperature, and then filtered under suction; the crystalline filter cake is washed with 3 litres of methanol/water (2:1), and dried at 50 °C. Yield 224 g. M.p. 160–163 °C. The product can be used without further purification.

Synthesis of Compound (2):

540 g of $FeCl_3 \cdot 6H_2O$ in 750 ml of water is added dropwise to a well-stirred suspension of 299 g (1 mole) of compound *(1)* in 1 liter of water. Stirring is then continued for 1 h at room temperature and the mixture filtered. The filter-cake is washed with water, and recrystallized from iso-propanol. Yield 196 g = 86 %.

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[*] Dr. K. Ley and Dr. R. Nast
Wissenschaftliches Hauptlaboratorium
der Farbenfabriken Bayer AG.
509 Leverkusen-Bayerwerk (Germany)

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A New Synthesis of Aliphatic Isothiocyanates [1, 2]

By *J. C. Jochims* and *A. Seeliger* [*]

Carboxylic, phosphoric [3], and sulfonic acids [4] react intermolecularly with carbodiimides, yielding anhydrides; however, carbodiimide cleaves H_2S intramolecularly from dithiocarbamic acids, and isothiocyanates are obtained:

$$R{-}NH_2 + R'{-}N{=}C{=}N{-}R' + CS_2 \longrightarrow R{-}N{=}C{=}S + R'{-}NH{-}CS{-}NH{-}R'$$

This reaction, in a neutral aqueous medium at low temperature, can be used for the preparation of aliphatic isothiocyanates under milder conditions than are required for previously known isothiocyanate syntheses.

Experimental: 1/10 mole of a primary aliphatic amine is added to 1/10 mole of dicyclohexylcarbodiimide (or some other carbodiimide) and 40 ml of CS_2 in 100 to 200 ml of ether (or tetrahydrofuran) at −10 °C, with stirring, and the temperature is allowed to rise to 20 °C during 3 h. After the mixture has been kept for 12 h at room temperature it is filtered and the residue (dicyclohexylthiourea) washed with ether; the filtrate is concentrated and the alkyl isothiocyanate obtained (cf. table) is recrystallized or distilled in a vacuum. The poorer yields of 9-fluorenyl isothiocyanate are due to partial decomposition.

R–N=C=S R	Yield (%)	B.p. (°C/12 mm) or m.p. (°C)
Benzyl	90	125–126
$(C_2H_5O)_2CH-CH_2$	87	102–103
Phenylisobutyl	99	137–138
Diphenylmethyl	81	(59, from ethanol)
9-Fluorenyl	70	(91–92; from benzene/light petroleum)

In contrast to primary aliphatic amines, 1 mole of the more weakly basic α-naphthylamine uses only $^1/_2$ mole of carbodiimide under the usual conditions and 1,3-di-(α-naphthyl)-thiourea is obtained quantitatively.

The formation of the isothiocyanate thus depends on the relative velocities of competing reactions of the amine, namely, a) that with carbon disulfide to give the dithiocarbamic acid and b) that with the isothiocyanate formed to give the thiourea. With strongly basic aliphatic amines, reaction a) is faster and yields mainly alkyl isothiocyanates; with aromatic amines reaction b) is faster, yielding only the thioureas. However, even with aliphatic amines, reaction b) cannot be entirely suppressed, *i.e.* some 1,3-dialkylthiourea RHN–CS–NHR is formed and it is precipitated with the dicyclohexylthiourea. Therefore, when stoichiometric amounts are used the residual carbodiimide must be separated from the alkyl isothiocyanate by fractional distillation or washing with pentane; it is advantageous to begin with somewhat less than 1 mole of carbodiimide.

Attempts to prepare isocyanates by an analogous method gave ureas only.

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[*] Dr. J. C. Jochims and Frau A. Seeliger
Max-Planck-Institut für Medizinische Forschung,
Institut für Chemie
Jahnstr. 29
69 Heidelberg (Germany)

[1] We are very grateful to Prof. *R. Kuhn* for supporting this work.

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Metal Complexes of Diethylthiophosphinic Acid

By *W. Kuchen* and *H. Hertel*[*]

Metal complexes of diethylthiophosphinic acid show a greater tendency to associate in solvents free from electron donors than do the corresponding dithiophosphinato complexes[1,2]; the influence of various factors on the association thus becomes more evident. To prepare the complexes we used sodium diethylphosphinate, $(C_2H_5)_2P(S)ONa\cdot 3H_2O$, which was obtained as colorless leaflets (m.p. 58–59 °C) by neutralization of thiophosphinic acid[3] $(C_2H_5)_2P(S)OH$, evaporation, dissolution of the residue in acetone, and precipitation with ligroin.

Complexes of type *(1)* were precipitated when sodium diethylthiophosphinate was added to aqueous solutions of a metal salt, and they were recrystallized from 2-propanol. Complexes with Zn(II) (m.p. 186–188 °C), Cd(II) (m.p. 119–122 °C), In(III) (m.p. 133 °C), or Pb(II) (m.p. 99–102 °C) as the central atom formed colorless crystals which, as is shown by thermogravimetric analysis, melt with decomposition.

A mixture of stoichiometric quantities of $(C_2H_5)_2P(S)OH$ and $CoCO_3$ in boiling benzene gives, after several hours, a viscous, deep blue solution of the Co(II) complex, which is obtained as intensely blue crystals (m.p. 186–188 °C) from 2-propanol and forms mixed crystals with the Zn(II) complex.

All these complexes dissolve readily in organic solvents such as benzene, carbon tetrachloride, chloroform, alcohols, and acetone. Osmometric determination of the molecular weights shows that the *octahedral* In(III) complex is present only as a monomer in benzene over a wide range of concentrations (from *ca.* 0.005 to *ca.* 0.1 mole l^{-1}), whereas the *tetrahedral* complexes are strongly associated. With rising concentration the degree of association of the tetrahedral complexes approaches a limiting value which depends on the solvent (see Fig. 1) and on the central atom (see Table 1); extrapolation to infinite dilution always leads to the monomer. Viscometric studies[5] of the Co(II) and Zn(II) complexes in benzene disclosed a very steep rise in the reduced viscosity η_{spec}/c with rising concentration. The nature of the chalcogen atom also influences the association. For instance, the degree of association of the Cd(II) complexes increases in the order $Cd[(C_2H_5)_2P(Se)Se]_2 < Cd[(C_2H_5)_2P(Se)S]_2 < Cd[(C_2H_5)_2P(S)S]_2 < Cd[(C_2H_5)_2P(S)O]_2$ from 1.75 to 2.5 (at $c = 0.07$ mole/l, osmometrically in benzene at 37 °C).

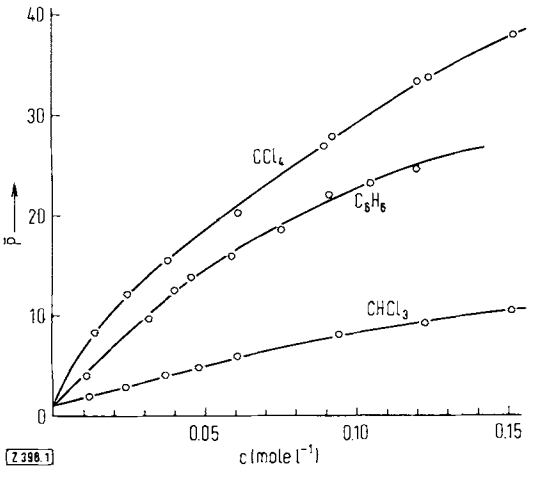
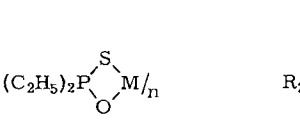


Fig. 1. Degrees of association $\bar{P}$ calculated from the osmometrically [4] determined apparent number average molecular weights of $Co[(C_2H_5)_2P(S)O]_2$ at 37 °C in CCl_4, C_6H_6, and $CHCl_3$ (mol. wt. of monomer 333.27).

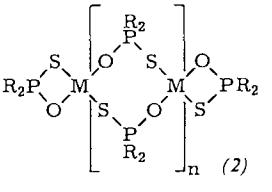
Table 1. Mean degree of association of complexes $M[(C_2H_5)_2P(S)O]_2$ in benzene at 37 °C.

mol/l	Cd(II)	Co(II)	Zn(II)
0.01	2.2	4.0	5.6
0.05	2.5	14.0	17.4
0.10	2.5	22.6	23.6
0.15	–	27.4	27.6

We assume that association involves formation of chelate bridges as in formula *(2)*, which was previously postulated or proved for metal complexes of the dialkyldithiophosphinic acids[1,2] and for phosphinic acids[6]. The influence of hybridization of the metal ions and the radii of the donor atoms, in particular, favor our view that bridged structures of low strain are formed for steric reasons[1]. That there is no tendency towards a higher coordination number on association could be shown for the Co(II) complex: the intensities and positions of the absorption maxima in the electronic spectra ($\lambda_{max} = 605$ mμ, $\log \varepsilon = 2.591$), measured for benzene and carbon tetrachloride solutions of various concentrations,



(1)



(2)

indicate in all cases tetrahedral coordination of the metal[7], which is clearly present also in the crystals since a magnetic moment of μ_{eff} = 4.63 B.M. was found[8].

The Co complex is monomeric in pyridine, which acts as an electron donor, the electronic spectrum (λ_{max} = 515 mμ, log ε = 1.496) here indicating octahedral coordination of the Co[7]. In agreement with this, we were able to isolate the pink bis(diethyl thiophosphinato)tetrapyridinocobalt(II), $[(C_2H_5)_2P(S)O]_2Co(C_5H_5N)_4$ (m.p. 63–64 °C; μ_{eff} = 4.98 B.M.[8]; non-electrolyte in pyridine), in which the phosphinato group acts as unidentate ligand.

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[*] Prof. Dr. W. Kuchen and Dipl.-Chem. H. Hertel
Institut für Anorganische Chemie und Elektrochemie der Rheinisch-Westfälischen Technischen Hochschule Aachen
Templergraben 55
51 Aachen (Germany)

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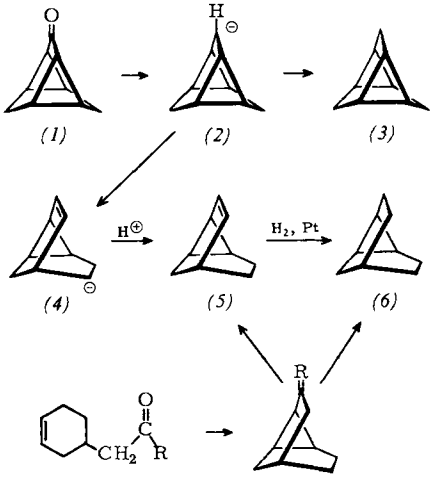
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Rearrangements of the Triasterane System [1]

By *U. Biethan*, *H. Klusacek*, and *H. Musso* [*]

The cyclopropane rings of triasterane *(3)* are parallel and particularly favorably situated for rearrangements induced by conversion of a methylene bridge into an anion, radical, cation, or carbene. For instance, the Wolff-Kishner reduction of triasteranone *(1)* gives 29 % of triasterane *(3)*, 8.5 % of bicyclo[3.3.1]nona-2,6- and -2,7-diene, as well as 0.9 %[2] of tricyclo[3.3.1.$0^{2,8}$]non-3-ene *(5)*[1]. The formation of *(5)* can be explained by homoallylic rearrangement of the anionic intermediate *(2)* to the anion *(4)* and protonation of the latter.

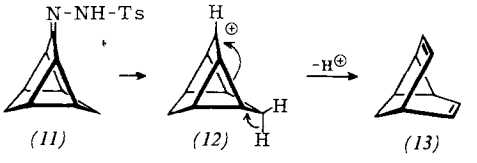


(1) *(2)* *(3)* *(4)* *(5)* *(6)*

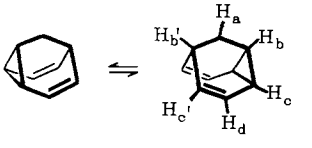
(7) R = Cl *(9)* R = O
(8) R = CHN_2 *(10)* R = N-NH-Tosyl

The olefin *(5)* can be hydrogenated over platinum in glacial acetic acid to the hydrocarbon *(6)* and thence further to bicyclo-[3.3.1.]- and -[3.2.2]-nonane[1]. The structures of the products *(5)* and *(6)* are proved by comparison with the products of the following syntheses. 3-Cyclohexenylacetic acid yields its acid chloride *(7)* (b.p. 90–92 °C/15 mm, 95 %) and thence a diazo ketone *(8)* which is decomposed by copper powder in boiling cyclohexane to yield the ketone *(9)* (colorless crystals, m.p. 92–94 °C, yield 52 %). Heating the tosylhydrazone *(10)* (m.p. 203–205 °C, 80 %) with sodium glycolate in ethylene glycol affords a crude product, 85 % of which is compound *(5)* and the remainder contains six compounds of unknown structure[3]. The compound *(5)* can be isolated from this mixture in 6 % yield[2] as colorless volatile crystals, m.p. 68–70 °C. Wolff-Kishner reduction of the ketone *(9)* gives the hydrocarbon *(6)* as colorless crystals with a pleasant smell (m.p. 128–129 °C, yield 63 %[2]).

According to the mechanism of the Bamford-Stevens reaction[4] the cation *(12)* should be accessible as a product from the tosylhydrazone *(11)* and should become stabilized by loss of a proton. If this hydrazone *(11)* (m.p. 202–204 °C, 79 %) is treated in the way described for *(10)*, then tricyclo-[3.3.1.$0^{2,8}$]nona-3,6-diene *(13)* is formed. The sublimed product (m.p. 37–44 °C, 57 %) contains 97 %[3] of *(13)* which, when purified by gas chromatography, forms light-sensitive, colorless crystals (m.p. 46 °C, 43 %[2]) with an unpleasant odour[5].



(11) *(12)* *(13)*



The NMR spectrum[6] of *(13)* in $CCl_4/CDCl_3$ at room temperature confirms the constitution assigned and indicates rapid exchange between the structures of equal energy content, for it shows only four signals in the intensity ratio 2:2:4:2, namely: H_a 1.06 ppm (triplet, J = 2.5 Hz), H_b 2.33 ppm (multiplet), H_c 3.97 ppm (triplet, J = 7.5 Hz), and H_d 5.63 ppm (triplet, J = 7.5 Hz).

Hydrogenation of *(13)* over platinum in glacial acetic acid leads, as in the case of *(3)*, to a mixture of *(6)* and bicyclo-[3.3.1]- and -[3.2.2]-nonane[3].

Compound *(8)* was not purified. Results obtained in the analysis of the other new compounds were consistent with the constitutions assigned. Compatible IR, NMR, and mass spectra were also obtained.

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[*] Dr. U. Biethan, cand. chem. H. Klusacek, and
Prof. Dr. H. Musso
Institut für Organische Chemie der Universität Bochum
Present address: Chemisches Institut der Universität
Bahnhofstr. 7
355 Marburg (Germany)

[1] Part III of Asteranes. – Part II: *H. Musso* and *U. Biethan*, Chem. Ber. *100*, 119 (1967).

[2] Yields after preparative gas chromatography: Wilkens Autoprep, column SE 30, 145 °C, H_2.

[3] Analytical gas chromatogram: Perkin-Elmer F 6, column 1 G 3, 140 °C, N_2.

[4] *L. Friedman* and *H. Shechter*, J. Amer. chem. Soc. *81*, 5512 (1959).

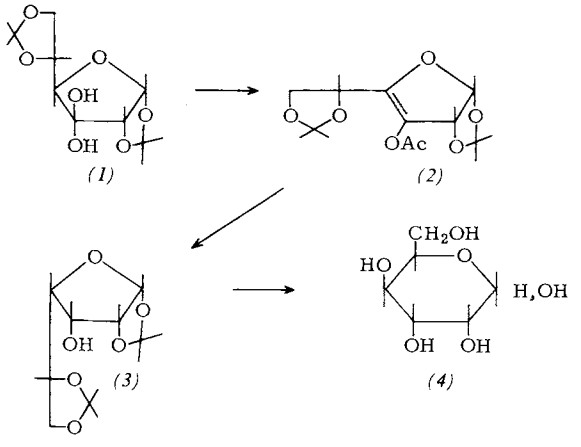
[5] According to a personal communication from Prof. *W. von E. Doering*, Wolff-Kishner reduction of tricyclo[3.3.1.0^{2,8}]nona-3,6-dien-9-one (barbaralone) gives a product consisting of a mixture of three substances, 30% of which is compound *(13)*. *(13)* (m.p. 30–31 °C) can be separated from the mixture by gas chromatography. The IR and NMR data for this product agree with those for ours.

[6] Varian A 60, tetramethylsilane as internal standard.

Synthesis of D-Gulose from D-Glucose

By *W. Meyer zu Reckendorf*[*]

The hydrate *(1)* of 1,2:5,6-di-*O*-isopropylidene-α-D-*ribo*-3-hexulofuranose, which is readily accessible from glucose[1], is, surprisingly, acetylated by acetic anhydride in pyridine (16 h, 60 °C) to the enol acetate *(2)* [yield 81 %, m.p. 62 to 63 °C, $[\alpha]_D^{20} = -33.0°$ (c = 1 in $CHCl_3$)]. The position of the double bond in *(2)* was established by the ^{1}H–NMR spectrum [τ values; solvent: $CDCl_3$ with tetramethylsilane as external standard: H–1 6.06; H–2 5.41; H–5 4.68; 2 H–6 4.09 (all doublets); CH_3CO 2.21 (singlet); 4 CH_3 1.39–1.54, $J_{1,2}$ 5.5 Hz], by results of the following experiments, and by steric considerations: the dioxolane ring does not permit a double bond between C–2 and C–3.



(1) *(2)* *(3)* *(4)*

Reduction of the product *(2)* with $NaBH_4$ in methanol occurs stereospecifically from the β-side, giving 1,2:5,6-di-*O*-isopropylidene-α-D-gulofuranose *(3)* [yield 60 %, m.p. 105–106 °C, $[\alpha]_D^{20} = +7.5°$ (c = 1 in $CHCl_3$)], which affords a quantitative yield of D-gulose *(4)* on hydrolysis with Lewatit S 100 H^+[2] (30 min, 90 °C). The product *(4)* was found to be pure on thin-layer chromatograms and was identified as the phenolhydrazone[3] [m.p. and mixed m.p. 142–143 °C (lit.[3] 143 °C) with a sample prepared from authentic D-gulose[4]].

The 5,6-*O*-isopropylidene group of *(2)* is labile in alkali and is removed by the $NaBH_4$ in a side reaction. This reaction is being investigated.

Contrary to statements in the literature[1], the hydrate *(1)* undergoes rapid and marked mutarotation in $CHCl_3$, this depending on loss of water of hydration. Simultaneously a strong positive Cotton effect becomes evident in the rotatory dispersion.

(1) in $CHCl_3$ (c = 10)			*(1)* in $CHCl_3$ (c = 10), dried by mol. sieve 3 A [a]	
λ (mμ)	[α] (°)	Lit. [1]	[α] (°)	Lit. [1]
589	+ 30.0 + 84.0	+44.5	+ 102	+107
349	+ 1095 (end val.)		+1412	
300	− 745 (end val.)		−1035	
258	− 431 (end val.)		− 625	
235			− 850	

[a] Produced by Union Carbide.

In water the rotation is constant, $[\alpha]_D^{20} = +32°$ (c = 1), with very small rotatory dispersion.

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[*] Dr. W. Meyer zu Reckendorf
Institut für Pharmazeutische Chemie der Universität
Hittorfstr. 58–62
44 Münster (Germany)

[1] *O. Theander*, Acta chem. scand. *18*, 2209 (1964); *P. J. Beynon, P. M. Collins*, and *W. G. Overend*, Proc. chem. Soc. (London) *1964*, 342; *K. Onodera, S. Hirano*, and *M. Kashimura*, J. Amer. chem. Soc. *87*, 4651 (1965); *P. J. Beynon, P. M. Collins, P. T. Doganges*, and *W. G. Overend*, J. chem. Soc. (London) (C) *1966*, 1131.

[2] Manufacturer: Farbenfabriken Bayer AG.

[3] *H. S. Isbell* in *R. L. Whistler* and *M. L. Wolfrom*: Methods in Carbohydrate Chemistry. Academic Press, New York 1962, Vol. 1, p. 135.

[4] I thank Dr. *H. S. Isbell*, National Bureau of Standards, Washington, for the supply of authentic D-gulose.

Synthesis of Indium Phosphide from Indium and Phosphorus Pentoxide

By *M. Kuisl*[*]

As an $A^{III}B^V$ compound, indium phosphide is of interest as semiconductor material[1]. It was first prepared by *Iandelli*[2] who heated the elements for 350 to 400 h in a sealed tube at 700 °C. We have found that phosphorus pentoxide reacts with indium, yielding indium phosphide, in an appreciably shorter time.

The reaction occurs at 850 °C within 8 h according to the equation:

$$3.5\ P_4O_{10} + 14\ In \longrightarrow 5\ In_2P_2O_7 + 4\ InP.$$

Indium turnings and phosphorus pentoxide are weighed into a quartz ampoule with exclusion of moisture and are mixed. The ampoule is then sealed and heated. The products can be separated by sublimation of the InP above 650 °C in a high vacuum. Use of non-stoichiometric proportions of the starting materials does not lead to any other indium phosphate. If more metal is used, the excess remains unattacked even after 100 h. If too much P_4O_{10} is present, phosphorus is formed and is deposited as a yellow or red film on the walls of the ampoule and it may inflame when the ampoule is opened. To obtain pure InP one thus starts with an excess of indium, since indium has a very low vapor pressure at 650 °C whereas at this temperature phosphorus can pass over into the sublimate.

InP was characterized by Debye-Scherrer diagrams. $In_2P_2O_7$ is formed as white crystals, which dissolve slowly in acids with evolution of gas; presence of a P_2O_7 anion is indicated by the IR spectrum as well as by elemental analysis (the IR bands lie within 20 to 30 cm^{-1} of those of $Na_4P_2O_7$, and the intensities are similar[3]). Indium is formally bivalent in the formula $In_2P_2O_7$, but, by analogy with In_2Br_4 and Ga_2Cl_4, a composition $In^{I}In^{III}P_2O_7$ can be assumed; ESR measurements seem to confirm this[4].

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[*] Dr. M. Kuisl
Allgemeine Electricitätsgesellschaft
AEG Telefunken
Forschungsinstitut
Postfach 627
79 Ulm (Germany)

[1] *H. Welker*, Z. Naturforsch. *7a*, 744 (1952); *8a*, 248 (1953).

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[3] *W. Bues* and *H. W. Gehrke*, Z. anorg. allg. Chem. *288*, 291 (1956).

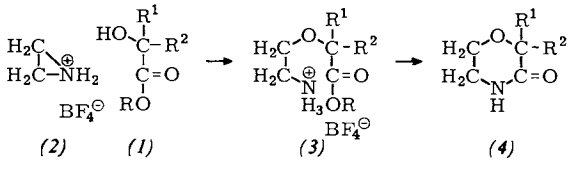
[4] I thank Prof. *H. Ch. Wolf* and Dr. *D. Schmid*, Technische Hochschule Stuttgart, for measurement and discussion of the ESR spectra.

Synthesis of Oxalactams (2-Morpholinones) from Aziridinium Tetrafluoroborates and Hydroxy Esters

By *E. Pfeil* and *U. Harder* [*]

The reactivity of the aziridinium cation towards the hydroxyl group of alcohols and phenols makes possible a simple synthesis of 2-alkoxyethylamines [1].

If the reaction is carried out with α-hydroxy esters *(1)* and aziridinium tetrafluoroborate *(2)*, one obtains first the salts *(3)* and then, by loss of alcohol, 2-substituted 3-oxapentane-5-lactams (2-morpholinones) *(4)* together with linear polyamides.



(2) *(1)* *(3)* *(4)*

R	R^1	R^2	*(4)*, M.p. (°C)	*(4)*, B.p. (°C/mm)	*(4)*, Yield (%)	*(4)*, IR νC=O (cm^{-1})
C_4H_{11}	H	H	106	142/7	33.6	1667
C_2H_5	CH_3	H	61–62	152/12	18.4	1667
CH_3	CH_3	CH_3	115	133/8	33.0	1672
C_2H_5	C_6H_5	H	144–145	—	27.6	1678, 1647

Although the yields are low the range of applicability and the simplicity of the process make it a useful route to the morpholinones which have hitherto been little investigated.

A compound of the type *(1)* is treated at 100 °C with one molar equiv. of the salt *(2)*. The mixture is heated for about 20 h at 100 °C, allowed to cool, and then dissolved in ether. Treatment with a two- to three-fold excess of piperidine or potassium ethoxide, extraction with ether, and distillation or recrystallization from cyclohexane yields the products *(4)*. The structures of the compounds produced are established by elemental analysis and IR spectra.

Ethyl DL-3-hydroxybutyrate gives analogously DL-3-methyl-4-oxahexan-6-lactam, b.p. 145–150 °C/10 mm, m.p. 109 °C, $\nu_{C=O}$ = 1678 cm^{-1}, in 29% yield.

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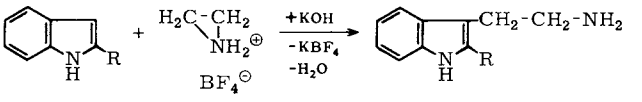
[*] Prof. Dr. E. Pfeil and Dr. U. Harder
Chemisches Institut der Universität
Bahnhofstr. 7
355 Marburg (Germany)

[1] *L. B. Clapp, E. A. Rick, W. B. Moniz,* and *V. B. Schatz,* J. Amer. chem. Soc. *77*, 5116 (1955); *U. Harder, E. Pfeil,* and *K. F. Zenner,* Chem. Ber. *97*, 510 (1964).

2-Aminoethylation of Indole and of 2-Methylindole

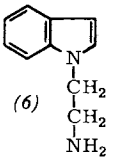
By *E. Pfeil* and *U. Harder* [*]

Aminoalkylated indoles are of importance because of their physiological properties and their use as intermediates in the synthesis of natural products, so that numerous multi-stage syntheses have been developed for them. We have succeeded in introducing the (protonated) aminoethyl group directly into the indole ring by means of the readily accessible [1] aziridinium tetrafluoroborate *(3)*, which reacts exothermally with indole *(1)* and 2-methylindole *(2)*. With the methyl compound *(2)* the reaction gives 2-methyltryptamine *(5)* in 80–90% yield, this being the simplest and fastest process for preparation of this substance.



(1) R = H *(3)* *(4)* R = H
(2) R = CH_3 *(5)* R = CH_3

The salt *(3)* and indole afford tryptamine *(4)*, 1-(2-aminoethyl)indole *(6)*, and numerous other products, including tryptamines with several aminoethyl side-chains. The ratio



(6)

of the yields of *(4)* and *(6)* depends on the temperature: at 70 °C one obtains 40% of *(4)* and 4% of *(6)*, but at 130 °C 20% of *(4)* and 20% of *(6)*.

The structures of the products are proved by elemental analysis and IR, NMR, and UV spectra, and by comparison with authentic material by thin-layer chromatography. The products can be separated by distillation or by chromatography on silica gel with chloroform-methanol-ammonia (85:15:2).

Tryptamine

23.4 g (0.2 mole) of indole is heated to 70 °C and treated, with stirring, with 26.3 g (0.2 mole) of the salt *(3)* over a period of 20 min; after a further 10 min the reaction is complete and the mixture solidifies. The bases are liberated by addition of 33.6 g (0.6 mole) of KOH in 50 ml of water. The mixture is then extracted with benzene for 20 h. Fractional distillation of the extract gives 12.9 g (40.3%) of tryptamine (b.p. 143–146 °C/0.75 mm, m.p. 118 °C; hydrochloride, m.p. 251–253 °C) as well as 1.3 g of 1-(2-aminoethyl)indole *(6)* [b.p. 125–126 °C/0.75 mm, n_D^{20} = 1.6092; IR, 3370 cm^{-1} (νNH_2); UV (ethanol), λ = 219 nm (ε = 28900), 273 (5080), 280 (5130), 292 (4100); ^{1}H–NMR: NH_2, τ = 9.25 (s); CH_2–NH_2, τ = 7.25 (t); CH_2–N(indole), τ = 6.15 (t); indole-β-H, τ = 3.50 (d); indole-α-H, τ = 2.95 (d); phenyl, τ = 2.85–2.50 (m); hydrochloride, m.p. 213–214 °C (decomp.); monopicrate (yellow), m.p. 211–212 °C; dipicrate (red), m.p. 160–162 °C].

2-Methyltryptamine

20.0 g (0.15 mole) of the salt *(3)* is added to 10.0 g (0.15 mole) of *(2)* at 110 °C. Liberation of bases with 25.2 g (0.45 mole) of KOH, in 50 ml of water, extraction for 10 h with benzene, and distillation gives 23.3 g (87%) of 2-methyltryptamine *(4)*, b.p. 155 °C/0.05 mm, m.p. 107 °C (picrate, m.p. 218 °C).

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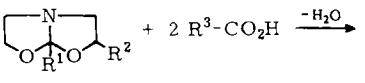
[*] Prof. Dr. E. Pfeil and Dr. U. Harder
Chemisches Institut der Universität
Bahnhofstr. 7
355 Marburg (Germany)

[1] *U. Harder, E. Pfeil,* and *K. F. Zenner,* Chem. Ber. *97*, 510 (1964).

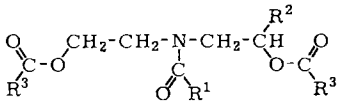
Reaction of Bicyclic Amide Acetals with Carboxylic Acids and their Anhydrides

By *R. Feinauer* [*]

Brechbühler et al. [1] recently reported a new method of esterification by treatment of carboxylic acids with acetals of *N,N*-dimethylformamide. The bicyclic amide acetals *(1)* [2], which have recently become readily accessible from epoxides and 2-oxazolines, react analogously with carboxylic acids or their anhydrides, yielding ester amides *(2)* of diethanolamine.



(1)



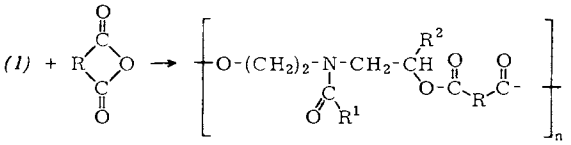
(2)

The components – a 5-fold excess of the acid or anhydride is used – are heated without a solvent for 2 h at 120 °C, and the ester amides are isolated by distillation. The products are viscous oils, whose structures can be established by elemental analyses, molecular-weight determinations, and by IR spectra.

R^1	R^2	R^3	*(2)*, Yield (%)	*(2)*, B.p. (°C/mm)	*(2)*, n_D^{20}
C_2H_5	C_6H_5	H	60	198/0.4	1.5152
C_2H_5	C_6H_5	CH_3	95 [a]	177/0.1	1.5052
C_2H_5	C_6H_5	C_2H_5	66	179/0.1	1.5038
C_2H_5	$CH_2OC_6H_5$	H	92	228–230/1.7	1.5159
C_2H_5	$CH_2OC_6H_5$	CH_3	92 [a]	205/0.3	1.5052
C_2H_5	$CH_2OC_6H_5$	C_2H_5	84	207/0.1	1.5055
C_6H_5	C_6H_5	CH_3	82	245/1	1.5450

[a] On use of acetic anhydride.

If equimolar amounts of the bicyclic amide acetals *(1)* are heated with dicarboxylic acid anhydrides *(3)* for 2 h at 120 to 140 °C with stirring and passage of dry nitrogen, a polyaddition to yield polyester amides of structure *(4)* occurs



(3) *(4)*

R	R^1	R^2	*(4)*, Yield (%)	*(4)*, Softening Pt. (°C)	*(4)*, $\overline{M}_n$ [a]
$-(CH_2)_2-$	C_2H_5	C_6H_5	96.6	65–73	9100
$-(CH_2)_2-$	C_2H_5	$CH_2OC_6H_5$	90.3	61–66	10500
$-(o\text{-}C_6H_4)-$	C_2H_5	C_6H_5	83.2	87–92	3850
$-(o\text{-}C_6H_4)-$	C_2H_5	$CH_2OC_6H_5$	94.5	75–83	5880
$-(o\text{-}C_6H_4)-$	C_6H_5	C_6H_5	71.0	134–138	4250
$-(o\text{-}C_6H_4)-$	CH_3	$CH_2OC_6H_5$	92.8	85–92	3640

[a] Mean molecular weight from vapor pressure osmotic measurements.

rapidly, even in the absence of a catalyst. These polymers are purified by reprecipitation from chloroform/ether (1:10 v/v) and their structures determined by elemental analyses, molecular-weight determinations, and IR spectrometry.

If dicarboxylic acids are used in place of the anhydrides *(3)*, condensates of structure *(4)* but with lower molecular weights are obtained. If the temperature is raised or the reaction time prolonged, these polymers react by transamidation with loss of monocarboxylic acid R^1COOH to cross-linked resins.

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[*] Dr. R. Feinauer
Forschungslaboratorien der Chemische Werke Hüls AG
437 Marl (Germany)

[1] *H. Brechbühler, H. Büchi, E. Hatz, J. Schreiber,* and *A. Eschermoser,* Helv. Chim. Acta *48*, 1746 (1965).

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Synthesis of *N*-(Fluorosulfonyl)iminosulfur Difluoride

By *O. Glemser, H. W. Roesky,* and *P. R. Heinze*[*]

Fluorosulfonamide *(1)*, prepared by ammonolysis of sulfuryl difluoride[1], reacts with tetrafluorosulfur at room temperature in the presence of sodium fluoride as HF-trapping agent, to yield 72% of *N*-(fluorosulfonyl)iminosulfur

$$\underset{(1)}{FSO_2NH_2} + SF_4 \longrightarrow \underset{(2)}{FSO_2N{=}SF_2} + 2\,HF$$

difluoride *(2)*. Its ready accessibility makes the product *(2)* suitable for preparation of further N,S compounds.

Compound *(2)* is a colorless liquid that is decomposed by traces of water with loss of HF; b.p. 105.5 °C (with partial decomposition), m.p. 77–78 °C.

Its composition is proved by the results of elemental analysis and determination of the molecular weight [164 (cryoscopically in benzene); calc 167].

The ^{19}F–NMR spectrum of *(3)* includes the triplet expected for the FSO_2 group and a doublet (spin-spin coupling of the F atoms) for the SF_2 group. N–F coupling is not observed at room temperature. The nitrogen merely broadens the bands, but at −50 °C sharper signals are obtained. The coupling constant is $J_{FF} = 9$ Hz.

	Chemical shifts (ppm) [a]			
	30 °C	−50 °C	Multiplicity	Intensity
δSF_2	−40.0	−35.7	Doublet	2
δSF	−62.2	−44.0	Triplet	1

[a] With respect to Freon 11 (CCl_3F) as external standard.

The IR spectrum of a capillary film in the NaCl region shows strong bands at 1443, 1258, 1222, 848, 795, 735, and 684 cm^{-1}, which are ascribed to the seven possible stretching vibrations, and other strong bands at 552, 473, 408, and 305 cm^{-1}, which are ascribed to deformation vibrations.

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[*] Prof. Dr. O. Glemser, Dr. H. W. Roesky,
and Dipl.-Chem. P. R. Heinze
Anorganisch-Chemisches Institut der Universität
Hospitalstr. 8–9
34 Göttingen (Germany)

[1] *R. Appel* and *G. Eisenhauer,* Z. anorg. allg. Chem. *310*, 90 (1961).

The Structure of the Juvenile Hormone

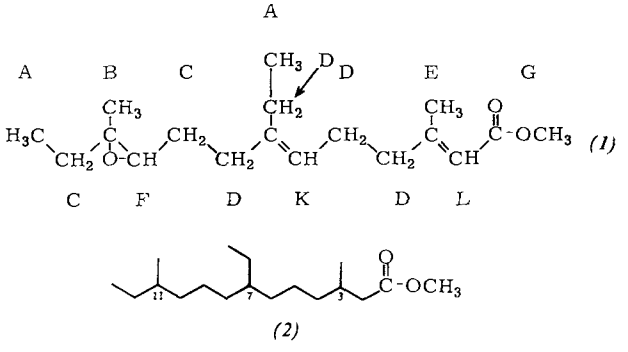
By *H. Röller, K. H. Dahm, C. C. Sweely,* and *B. M. Trost*[*]

The postembryonic development of insects is controlled by the molting hormone (ecdysone)[1], the juvenile hormone and an adenotropic factor (brain hormone). Previously we have isolated the juvenile hormone from abdomens of adult male *Hyalophora cecropia*, the giant silkworm moth[2].

Catalytic hydrogenation of 20 μg of juvenile hormone *(1)* in ethanol with palladium black gave a product *(2)* which has the empirical formula $C_{18}H_{36}O_2$ as calculated from its mass spectrum (molecular ion at *m/e* 284). The most abundant fragments at *m/e* 101 and 74 and the ion at M–31 show the presence of a methoxycarbonyl group on an aliphatic chain with a methyl branch at C-3. The mass spectrum provided no evidence of another functional group. Ions of relative high intensity at *m/e* 143, 185, and 153 (185–32) indicate an ethyl or dimethyl branch at C-7. The mass spectrum of *(1)*

contains the molecular ion at *m/e* 294 and fragments at *M*−18, *M*−31, and *M*−32. Comparison with *(2)* gives the empirical formula $C_{18}H_{30}O_3$ for *(1)*. Therefore, the hormone *(1)* has three double bonds or rings which can be hydrogenated and an oxygen that is easily eliminated. Catalytic hydrogenation of 30 μg of *(1)* with a poisoned catalyst (palladium on barium sulfate with triethylamine) gave several products with molecular ions at *m/e* 296 and 298. One spectrum shows an abundant ion at *m/e* 211 (298−87) indicating loss of the fragment $C_5H_{11}O$.

Cleavage of 15 μg of *(1)* with osmium tetroxide and periodic acid gave levulinic aldehyde which has been identified by gas chromatography. Another cleavage product has a peak in the gas chromatogram corresponding to a homologue of levulinic aldehyde.



(2)

The NMR-spectrum of 200 μg of *(1)* contains the signals (δ values with tetramethylsilane as internal standard): (A) 0.96 ppm, triplet, 6 H; (B) 1.16 ppm, singlet, 3 H; (C) 1.22–1.70 ppm, unresolved multiplet, 4 H; (D) 1.80–2.30 ppm, broad adsorption; (E) 2.12 ppm, narrow doublet, *J* 0.8 Hz, (D) and (E) together 11 H; (F) 2.46 ppm, triplet, 1 H; (G) 3.59 ppm, singlet, 3 H; (K) 4.96 ppm, unresolved multiplet, 1 H; (L) 5.46 ppm, broad singlet, 1 H.

Since the positions of branches and of double bonds have been determined by mass spectrometry and cleavage, the juvenile hormone can be identified as methyl 10-epoxy-7-ethyl-3,11-dimethyl-2,6-tridecadienoate. From the coupling constant J_{EL} and the chemical shift of E, the conjugated double bond has the *trans* configuration. The halfband width of the proton K signal compared with the absorption of similar terpene protons suggests the *trans* configuration also for the second double bond. Nothing can be said about the stereochemistry of the oxirane ring.

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[*] Dr. H. Röller and Dr. K. H. Dahm
Dept. of Zoology, University of Wisconsin
1117 West Johnson Street
Madison 53706, Wisc. (U.S.A.)
Dr. C. C. Sweely
Dept. of Biochemistry and Nutrition
Graduate School of Public Health
University of Pittsburgh
Pittsburgh 15313, Pa. (U.S.A.)
Dr. B. M. Trost
Dept. of Chemistry, University of Wisconsin
1112 West Johnson Street
Madison 53706, Wisc. (U.S.A.)

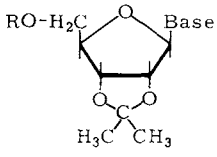
[1] *P. Karlson, H. Hoffmeister, H. Hummel, P. Hocks,* and *G. Spiteller,* Chem. Ber. *98,* 2394 (1965); *R. Huber* and *W. Hoppe,* Chem. Ber. *98,* 2403 (1965); *U. Kerb, P. Hocks, R. Wiechert, A. Furlenmeier, A. Fürst, A. Langemann,* and *G. Waldvogel,* Tetrahedron Letters *1966,* 1387; *J. B. Siddall, A. D. Cross,* and *J. H. Fried,* J. Amer. chem. Soc. *88,* 862 (1966).

[2] *H. Röller* and *J. S. Bjerke,* Life Sciences *4,* 1617 (1965); *H. Röller, J. S. Bjerke, D. W. Norgard,* and *W. H. McShan,* Proceedings of the International Symposium on Insect Endocrinology, Brno, Czechoslovakia, 1966, Academic Press New York and London (1967).

Detection of Hydrogen Bridges between Inosine and Other Nucleosides by NMR Spectroscopy

By *K. H. Scheit* [*]

Occurrence of a hydrogen bridge can be recognized in the NMR spectrum of a compound by a shift of the signals of the protons concerned to lower field strengths [1]. *Penman et al.* [2] and *Miles et al.* [3] were thus able to demonstrate hydrogen bridges between guanosine and cytidine, between thymine and adenine, and between uracil and adenine. 4-Thiouridine and inosine are present in t-RNS as rare nucleosides; their function has not yet been clarified. We have tried to determine with which nucleosides 4-thiouridine and inosine can associate by means of hydrogen bridges. For detection of weak hydrogen bridges it is essential to use an inert solvent such as deuterochloroform ($CDCl_3$). We therefore prepared the protected nucleosides *(1)*–*(6)* which are sufficiently



(1) Base = Adenine, R = $-CO-CH_3$
(2) Base = Uracil, R = $-CO-CH_3$
(3) Base = 4-Thiouracil, R = $-CO-CH_3$
(4) Base = Hypoxanthine, R = $-CO-CH_3$
(5) Base = Cytosine, R = $-CH(OC_2H_5)-CH_3$
(6) Base = Guanine, R = $-CH(OC_2H_5)-CH_3$

soluble in deuterochloroform. The NMR spectra of mixtures, each of two nucleosides, in $CDCl_3$ were compared with the spectra of the components at the same concentrations, and in some cases we found a shift of the NH signals to lower field strengths. This shift (interaction shift) denotes a hydrogen bridge between the bases of the nucleosides.

	Concn. (mole l^{-1})	Interaction shifts (τ-values) [b]
(1) + *(2)* [a]	0.4	ANH_2 −0.38; UN^3-H 3.34 [c]
	0.2	ANH_2 −0.56; UN^3-H −3.08
(1) + *(3)*	0.4	ANH_2 −0.38; TUN^3-H −2.90
	0.2	ANH_2 −0.54; TUN^3-H −2.70
(1) + *(4)*	0.4	ANH_2 −0.18; HN^1-H +0.1
	0.2	ANH_2 −0.28; HN^1-H no signal
(2) + *(4)*	0.4	HN^1-H +0.37; UN^3-H 0.75
	0.2	HN^1-H +0.32; UN^3-H −0.55
(2) + *(3)*	0.4	UN^3-H −; TUN^3-H −
(3) + *(4)*	0.4	HN^1-H +0.35; TUN^3-H −1.42
	0.2	HN^1-H +0.32; TUN^3-H −1.22
(3) + *(5)*	0.4	CNH_2 −; TUN^3-H −
(3) + *(6)*	0.4	GN^1-H −; GNH_2 −; TUN^3-H −

[a] Molar ratios 1:1 in all cases.

[b] Perkin-Elmer apparatus, 32.4 °C; tetramethylsilane ($\tau CH_3 = 10$) as internal standard. Negative values denote a shift to lower field strengths, positive values a shift to higher field strengths.

[c] ANH_2 = Adenine-6-NH_2; UN^3-H = Uracil-N^3−H; TUN^3-H = 4-Thiouracil-N^3−H; HN^1-H = Hypoxanthine-N^1−H; CNH_2 = Cytosine-4-NH_2; GN^1-H = Guanine-N^1−H; GNH_2 = Guanine-2-NH_2.

The table shows that 4-thiouridine *(3)* in $CDCl_3$ can associate with adenosine *(1)* and with inosine *(4)* but not with cytidine *(5)* or guanosine *(6)*. 4-Thiouridine has the same specificity as uridine in respect of its formation of hydrogen bridges with other nucleosides [2]. Inosine *(4)* apparently associates with adenosine *(1)* as well as with uridine *(2)*. The ability of the nucleobase hypoxanthine to form hydrogen bridges with purines and pyrimidines may be one reason for the presence of inosine in t-RNS. From the values of the

interaction shifts it may be concluded that the hydrogen bridges of adenosine-inosine, uridine-inosine, and 4-thiouridine-inosine are weaker than those of adenosine-uridine, and adenosine-4-thiouridine.

Received: December 14th, 1966; revised: December 23rd, 1966 [Z 405 IE]
German version: Angew. Chem. 79, 190 (1967)

[*] Dr. K. H. Scheit
Max-Planck-Institut für experimentelle Medizin
Chemische Abteilung
Hermann-Rein-Strasse 3
34 Göttingen (Germany)

[1] *J. A. Pople, W. G. Schneider,* and *H. J. Bernstein*: High Resolution Nuclear Magnetic Resonance. McGraw-Hill, New York 1959, p. 5400.

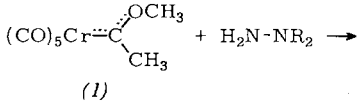
[2] *L. Katz* and *J. Penman*, J. mol. Biol. *15*, 220 (1966).

[3] *R. R. Shoup, H. T. Miles,* and *E. D. Becker*, Biochem. biophys. Res. Commun. *23*, 194 (1966).

Novel Rearrangement Processes of Transition Metal Carbene Complexes

By *E. O. Fischer* and *R. Aumann* [*]

The reaction of (methoxymethylcarbene)pentacarbonylchromium(0) *(1)* [1] with substituted hydrazines of the type H_2N-NR_2, in water-free ether at room temperature, produces acetonitrilepentacarbonylchromium(0) *(2)* in high yield. The compound, which crystallizes as yellow platelets (m.p. 71 °C), gives IR and NMR spectra which are identical with those of the complex formed [2] from $Cr(CO)_6$ and CH_3CN



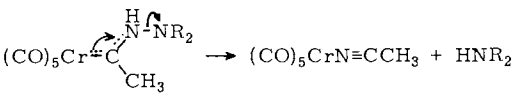
(1)

$$(CO)_5CrN{\equiv}CCH_3 + CH_3OH + HNR_2$$

(2)

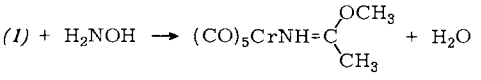
R = CH_3, C_6H_5

It is probable that the reaction proceeds *via* the hydrazinomethylcarbene complex *(3)*, which immediately loses the amine group.



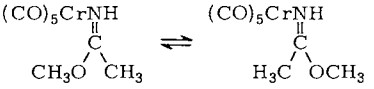
(3)

The reaction of anhydrous hydroxylamine with *(1)*, in ether at room temperature, produces the yellow (methyl acetimidato) pentacarbonylchromium(0) *(4)* in almost quantitative yield.



(4)

The structure of this novel complex was established by elemental analysis, NMR-, IR-, and mass spectra [3]. The methyl acetimidate can be split off by thermal decomposition of the compound at 200 ° and subsequently identified by gas chromatography. We assume that the ligand is bound at the nitrogen since Cr—N fragments are observed in the mass spectrum. The compound *(4)* exists in two forms which are in equilibrium with each other. NMR measurements at different temperatures showed that the two forms interconvert reversibly. The isomer ratio of the compounds *(4a)* and *(4b)* is 1.1:1 at 30 °C; 1.8:1 at 50 °C and 2:1 at 70 °C.



(4a) *(4b)*

The NMR spectrum [4] of the compound *(4a)* (saturated solution in C_6D_6 measured relative to the proton signal of the solvent at 436 Hz) shows two signals of equal intensity at 142 Hz and 100 Hz; the NMR spectrum of the compound *(4b)* shows two signals at 167 Hz and 44 Hz respectively.

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[*] Prof. Dr. E. O. Fischer and Dipl.-Chem. R. Aumann
Anorganisch-Chemisches Laboratorium der
Technischen Hochschule
Arcisstr. 21
8 München 2 (Germany)

[1] *A. Maasböl*: Dissertation, Technische Hochschule München, 1965.

[2] *W. Strohmeier* and *K. Gerlach*, Z. Naturforsch. *15b*, 622 (1960).

[3] Measurements by *J. Müller*.

[4] Recorded at 60 MHz.

CONFERENCE REPORTS

Drying of Paint Films in Steam

W. Funke and *K. Hamann*, Stuttgart (Germany)

Films of baking enamel are usually hardened by heat or infrared radiation. An attempt has been made to achieve cross-linking with superheated steam led over the laquered samples.

Considerable acceleration of the setting process was observed with binding agents which are cross-linked by condensation reactions. Thus the setting times of phenolic, urea, and melamine resins were shortened by 80%, or for the same setting time the necessary temperature was correspondingly reduced. Similar results were obtained for water-soluble baking enamels based on these binding materials. However, with films containing binders that dry oxidatively, drying is delayed by steaming. This result can be explained as being due to lack of the oxygen needed for hardening.

The acceleration of drying by superheated steam is probably caused by the rapid heating due to heat liberated on condensation of steam on the surface and to faster removal of solvent from the film.

Lecture at Freudenstadt (Germany), Sept. 29th, 1966 [VB 26a IE]
German version: Angew. Chem. 79, 192 (1967)

Adsorption on, and Desorption from, Pigments

K. Nollen, Stuttgart (Germany)

Isotherms for adsorption of substances of low molecular weight (fatty acids, amines) from organic solvents on oxide pigments can be described approximately by the Langmuir equation up to certain concentrations.

Studies of desorption showed that the adsorption is not reversible: some of the adsorbed material cannot be desorbed. The

amount of material that resists desorption depends on the temperature, solvent, and pigment and, above a certain concentration, is independent of the amount adsorbed. After adsorption of acid the amount resisting desorption is greater the more basic the pigment. It must thus be assumed that at least part of the non-desorbable acid is bound chemically to the pigment surface.

Reactive compounds do not lose their reactivity when firmly bound to the surface. For instance, the acrylic or methacrylic acid that cannot be desorbed from titanium dioxide (rutile) copolymerizes with styrene. The polymer, which is firmly bound to the pigment surface by its carboxyl groups, was identified by elemental analysis and IR spectroscopy.

Lecture at Freudenstadt (Germany), Sept. 29th, 1966 [VB 26b IE]
German version: Angew. Chem. 79, 192 (1967)

Autoxidation of Polyepoxides

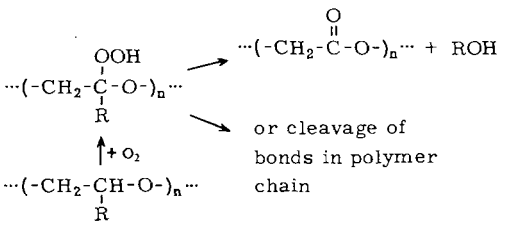
L. Dulog, Mainz (Germany)

Substituted polyethylene oxides of the general formula $(-CH_2-CHR-O-)_n$ have been prepared from the monomers by use of modified organometallic catalysts, such as partly hydrolysed aluminum alkyls subsequently treated with acetylacetone. In each case the polymers have been separated by solvent-extraction, *e.g.* with ether or acetone, into a tactic and an atactic fraction. The difficultly soluble or insoluble fractions are the isotactic ones according to X-ray diffraction and IR spectra. This is in agreement with literature data.

Isotactic polypropylene oxide, isotactic poly-1-butene oxide, and isotactic polystyrene oxide, as well as polyethylene oxide were subjected in undiluted form to autoxidation in air as well as in oxygen at temperatures from 50 to 150 °C and for times from a few minutes to several hours. Degradation of the substituted polyethylene oxides sets in at once (recognizable by a loss in weight), with simultaneous decrease in the molecular weight (observable as a decrease in solution viscosity); cross-linking does not occur. Only small amounts of volatile products are formed from polyethylene oxide and there is barely any decrease in molecular weight; degradation occurs at higher temperatures (*ca.* 145 °C) than for the substituted polymers.

The volatile products were identified by gas chromatography. The first to volatilize from substituted polyethylene oxides are the alcohols ROH derived from the substituent R, the methyl ketones $R-CO-CH_3$ isomeric with the monomer, and the secondary alcohol $R-CHOH-CH_3$ formally derivable from these by reduction. Water was the only volatile product observed to be formed from polyethylene oxide.

The mechanism of the oxidation with molecular oxygen can be interpreted as formation and decomposition of ether hydroperoxides in the first step:



Lecture at Freudenstadt on September 29th and 30th, 1966 [VB 26c IE]
German version: Angew. Chem. 79, 192 (1967)

Symposium on Heterocyclic Chemistry

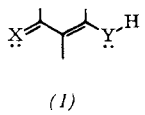
The Institut für Organische Chemie of the Technische Hochschule Stuttgart (Germany) was host to the 1st German Symposium on Heterocyclic Chemistry from the 5th to the 7th of October, 1966.

From the lectures:

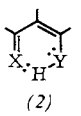
The Aromatic Character of Six-Membered Ring Chelates

E. Daltrozzo and *K. Feldmann*, Munich (Germany)

Compounds of type *(1)* can form hydrogen-bridged chelates *(2)* containing a six-membered ring in which the bridging hydrogen can be replaced by metals.



(1)

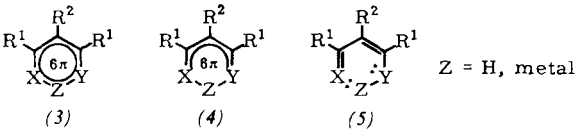


(2)

X,Y = NR, PR O, S etc.

Such cyclic 6 π-electron systems may be classified as being either cyclically conjugated *(3)* or not cyclically conjugated *(4)*. The characteristic difference between the aromatic *(3)* and the "quasiaromatic"[1] system *(4)* is in the shift of the NMR signals of the ring protons which is caused by the ring current.

[1] Nomenclature according to *D. M. G. Lloyd* and *D. R. Marshall*, Chem. and Ind. *1964*, 1760.



(3) *(4)* *(5)*

Z = H, metal

The possibility of aromatic *(3)* or "quasiaromatic" character *(4)* has been investigated in a series of H-bridged and metal chelates of structure *(5)* (X = Y = NR or O; R^1, R^2 = H, alkyl, aryl, or aralkyl). In all cases, UV and NMR results, when compared with those for model substances in which the existence of cyclic or non-cyclic π-electron conjugation is established, favor structure *(4)*, *i.e.* π-electron interaction does not occur across the bridging atom Z.

This is the case for (a): the H-bridged chelates (Z = H; X = Y = NR, where R = benzyl, phenyl, C_2H_5, or cyclohexyl; R^1, R^2 = H, alkyl, or aryl)[2,3], (b): the cyclic acetylacetonates [Z = H, Be, Zn, Al, Ga, In, Sc, Y, Co(III), Zr(IV), Th(IV), $SnCl_2$, $SnBr_2$, SnI_2, or Rh] for which aromatic character has often been suggested, and (c): for compounds *(5)* with X,Y = NR and Z = Li, Na, K, Cs, MgR_2, BR, ZnR_2,

[2] *L. C. Dorman* recently (Tetrahedron Letters *1966*, 459) assigned aromatic character to *N*-(3-benzylimino-1-methyl-1-butenyl)benzylamine (X = Y = N–CH_2–C_6H_5, R^1 = CH_3, R^2 = H). The conclusions drawn from the UV and NMR spectra of this compound and its salts are erroneous.

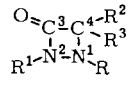
[3] Bases of type *(1)* exist as *cis-trans* equilibrium mixtures *(1)* ⇌ *(2)* and the position of the equilibrium is strongly dependent upon both the nature of the substituents and the solvent. The same is true also for the metal derivatives. This should be borne in mind when discussing the aromatic character of these compounds.

etc., in which N and C^{α} are in aromatic rings as in, *e.g.* di-2-pyridyl-, di-2-quinolyl-, and di-9-phenanthridinyl-methane. The term "quasiaromatic" was applied to compounds of structure *(4)* primarily because of their ready electrophilic substitution. S_E reactions are, however, no criterion for aromatic character, as is shown by the many examples of S_E reactions now known for polymethines (cyanines) and even for polyenes. There is thus no reason to designate the ring structure *(4)* as quasiaromatic; compounds containing it belong rather to the polymethine series.

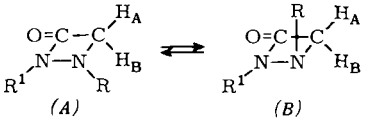
Preparation and Reactions of Diazetidine Derivatives

E. Fahr, W. Fischer, H. P. Flemming, A. Jung, K. H. Keil, K. Königsdorfer, J. Markert, Liselotte Sauer, F. Scheckenbach, and *R. Thiedemann*, Würzburg (Germany)

A number of 1,2-diazetidinones of types *(1a)* to *(1c)* have been prepared by addition of azo compounds to ketenes. IR spectroscopic investigation of the 1,2-diazetidinones *(1b)* has shown that the CO stretching vibration band lies between 1780 and 1785 cm^{-1} and is influenced by the substituent on the phenyl nucleus R^3, as is the ^1H–NMR signal of the C^4–H group.



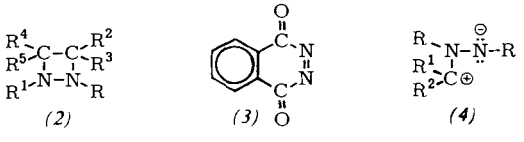
(1a), $R^2 = R^3 = H$
(1b), $R^2 = H, R^3$ = substituted phenyl
(1c), R^2, R^3 = substituted phenyl etc.



(A) *(B)*

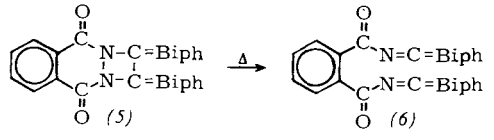
Inversion at the N^1 atom *(A)* ⇌ *(B)* was proved by the temperature-dependence of the NMR spectra[4] of the 1,2-diazetidinones; it occurs relatively slowly (coalescence temperature for R = *o*-, *m*-, and *p*-CH_3–C_6H_4 between 262 and 280 °K).

1,2-Diazetidines *(2)* were prepared by the reaction of cyclic α-oxoazo compounds, *e.g.* *(3)*, with indene. Study of the



(2) *(3)* *(4)*

products of reaction of azopyridine or azoquinoline with diazo compounds, in which diaziridines or 1,2-diazetidines should result [5], showed that deep red azomethine imines *(4)* were formed[6]. Only in one case – treatment of diazofluorene with compound *(3)* – could we identify a diazetidine derivative *(5)*; it is thermally unstable and isomerizes to *(6)*.



(5) *(6)*

Biph = 2,2'-Biphenylylene

[4] With the collaboration of Dr. *A. Mannschreck*, Heidelberg (Germany).

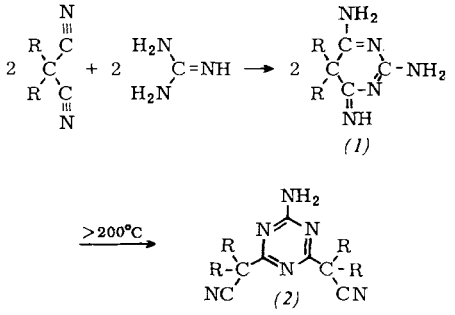
[5] *M. Colonna* and *A. Risaliti*, Atti Accad. naz. Lincei, Rend., Cl. Sci. fisiche, mat. natur *26*, 248 (1959); Chem. Abstr. *54*, 3420 (1960); Gazz. chim. ital. *89*, 2493 (1959).

[6] See also *A. R. Katritzky* and *S. Musierowicz*, J. chem. Soc. (London) C *1966*, 78.

Syntheses of Triazines, Pyrimidines, and Pyridines from Nitriles

H. J. Kabbe, Leverkusen (Germany)

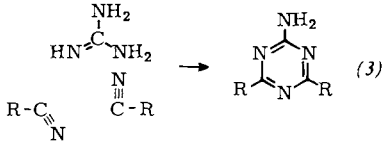
Barbiturates *(1)* are accessible from guanidine and dialkylmalonodinitriles; they rearrange above 200 °C to 2-amino-1,3,5-triazines *(2)*.



(1)

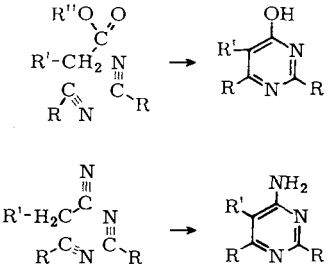
(2)

An alkoxide-catalysed synthesis of 2-amino-1,3,5-triazines *(3)* from numerous aliphatic, aromatic, and heterocyclic nitriles with guanidine is based on this reaction. Yields of up to 80 % are obtained.

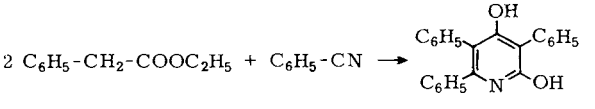


(3)

If esters (or nitriles) of the general formula R'–CH_2–COOR'' (R'–CH_2–CN) are used in place of guanidine, 4-hydroxy- or 4-amino-pyrimidines, respectively, are obtained; for this reaction the particularly reactive heterocyclic nitriles, such as 2- and 4-pyridinecarbonitriles or 2-furancarbonitrile, are generally used as the nitrile.



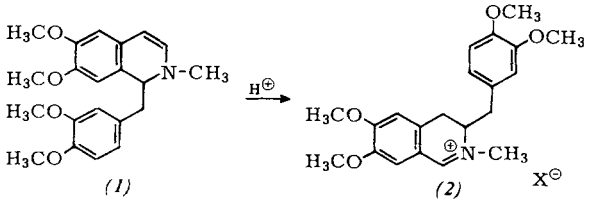
On the other hand, 3,5,6-triphenyl-2,4-pyridinediol is obtained from, *e.g.*, benzonitrile and ethyl phenylacetate:



Rearrangement of Dihydroisoquinolines

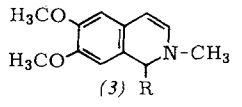
J. Knabe, Saarbrücken (Germany)

We have found that 1,2-dihydro-2-methylpapaverine *(1)* rearranges to *(2)* under the influence of dilute acids.



(1) *(2)*

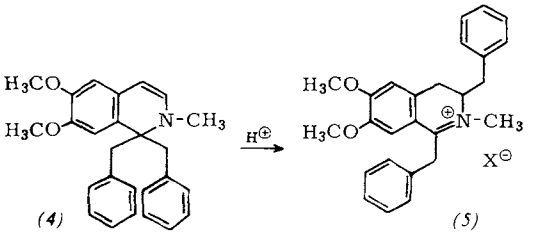
The 1-benzyl derivative corresponding to *(1)* also rearranges in a similar, unusual reaction. However, 1-alkyl-1,2-dihydro- and 1-phenyl-1,2-dihydro-isoquinoline *(3a)–(3d)* disproportionate in dilute acid to 1-substituted isoquinolinium salts and the corresponding tetrahydroisoquinolines.



(3) R

(a), R = C_6H_5
(b), R = n-C_4H_9
(c), R = CH_3
(d), R = CH_2-CH_2-C_6H_5

Treatment of 1,1-dibenzyl-1,2-dihydro-2-methylisoquinoline *(4)* with acid gives the 1,3-dibenzyl-3,4-dihydro-2-methylisoquinolinium salt *(5)*; but 1,1-diethyl-1,2-dihydro-6,7-dimethoxy-2-methylisoquinoline dimerizes.



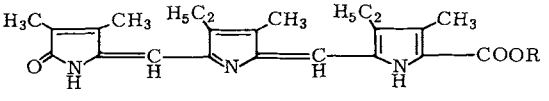
(4) *(5)*

To clarify the mechanism of the rearrangement *(1)* → *(2)*, a mixture of *(1)* and the corresponding tetraethoxy compound was made to react. Four rearrangement products were formed (structures proved by synthesis), thus proving that the rearrangement is intermolecular.

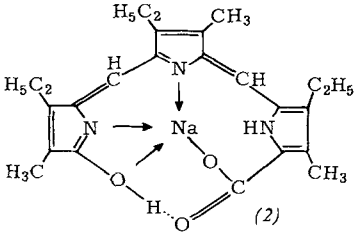
Metal Complexes of Oxotripyrrene-α-carboxylic Acid Derivatives

H. Plieninger, B. Kanellakopulos, and *K. Stumpf,*
Heidelberg and Karlsruhe (Germany)

When a chloroform solution of the deep purple acid *(1)* is shaken with aqueous alkali hydroxide, the acid does not pass into the aqueous phase; the latter remains colorless while the chloroform layer turns violet. If the chloroform solution is then evaporated in the presence of methanol, Na, K, Rb, Cs, and even ammonium salts are obtained as fine needles. The crystalline salts are then barely soluble in chloroform or other organic solvents, and are insoluble in water. Analysis of the Na salt indicates a 1:1 complex and on the basis of its remarkable properties we assigned to it the structure *(2)* containing coordinately quadrivalent Na.



(1), R = H
(1a), R = C_2H_5



(2)

In the Ca, Sr, and Ba salts, which were prepared similarly, one bivalent metal ion is bound to two oxopyrrenic acid molecules. Measurements with solutions of radioisotope-labeled Na, Ca, Ba, and Sr hydroxides and stoichiometric amounts of oxopyrrenic acid in chloroform showed that the ions of alkaline-earth metals pass completely, and the ions of alkali metals only partly, into the organic phase.

The positions of the UV absorption bands of the salts differ only slightly from those of the free acid. The IR carbonyl absorption of the ester *(1a)*, the acid *(1)*, and the salts is at 1720 cm^{-1}; the absence of carboxylate absorption for the "salts" indicates an undissociated chelate, as does the chemical behavior.

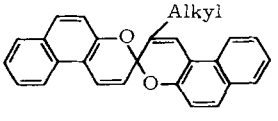
With Cu, Co, Cd, Ni, Mn, and, particularly, Zn ions the color of oxotripyrrene-α-carboxylic acid shows a shift towards blue and complex salts are formed whose UV and IR spectra are quite different from those of the salts with alkali and alkaline-earth metals. The zinc complex of ethyl oxotripyrrene-α-carboxylate *(1a)*, which gives a blue solution, contains the components in the ratio 1:1 and has strong red fluorescence. The acid *(1)* is suitable for detection of zinc in μg quantities; it is not yet known to what extent other metals interfere.

Isomerism of Spirans

C. Schiele, Ulm (Germany)

Consideration of Dreiding models indicates that asymmetrically substituted spiropyrans should be obtainable in four stereoisomeric forms.

In agreement with this expectation, work with 3-substituted spirobi(2*H*-benzopyrans) and 2-substituted spirobi(3*H*-naphtho[2,1-*b*]pyrans) such as *(1)* has led to isolation of such previously unknown stereoisomers by fractional crystallization [7]. The products were identified by IR spectroscopy [8].

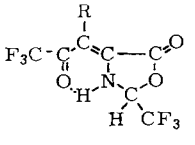


(1)

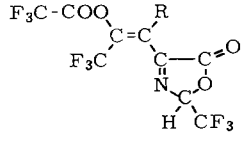
Preparation of Heterocyclic Compounds by Treatment of Amino Acids with Trifluoroacetic Anhydride

W. Steglich and *V. Austel,* Munich (Germany)

On treatment of α-amino acids with an excess of trifluoroacetic anhydride, various types of compounds result according to the reaction conditions and the nature of the amino acid. Substituted 4-trifluoroacetylmethylene-2-trifluoromethyl-5-oxazolidinones *(1)* and enol trifluoroacetates *(2)* are



(1)
R = H, CH_3, C_6H_5

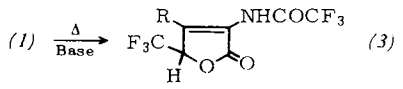


(2)

formed from alanine, 2-aminobutyric acid, and phenylalanine. On prolonged heating, alanine further affords the doubly trifluoroacetylated oxazolidinone *(1)* with R = $COCF_3$. The steric arrangement about the C=C double bond is not yet known.

When warmed with weak bases the oxazolidinones *(1)* rearrange to 2(5*H*)-furanones *(3)*. Compounds *(3)*, R = H or $COCF_3$, can also be prepared directly from alanine

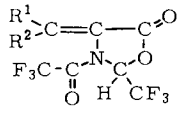
[7] *C. Schiele et al.*, Z. Naturforsch. *21b*, 292 (1966).
[8] *G. Arnold*, Z. Naturforsch. *21b*, 291 (1966).



(1) (3)

and trifluoroacetic anhydride. Furanones *(3)* with R = COOR′ are particularly easily formed from aspartic β-esters[9]. A small amount of 4-ethyl-3-trifluoroacetamido-2,5-bis(trifluoromethyl)furan is obtained alongside *(2)*, R = C_2H_5, when norvaline is used.

N-Trifluoroacetylated 4-alkylidene-2-trifluoromethyl-5-oxazolidinones *(4)* are formed when an excess of trifluoroacetic anhydride reacts with amino acids such as valine, isoleucine, and leucine that are branched in the β- or γ-position.

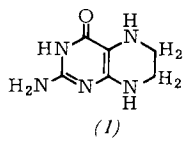


(4)

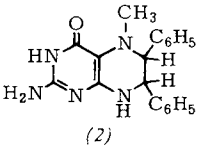
Phenyl-hydroxylation with Tetrahydropterin as Activator. — A Model for the Enzymic Synthesis of Tyrosine

M. Viscontini, Zürich (Switzerland)

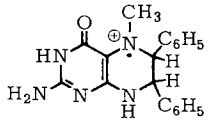
An aqueous solution of tetrahydropterin *(1)* (pH 6.9) is readily oxidized by atmospheric oxygen. If phenylalanine, Fe ions, and either ethylenediaminetetraacetic acid or pyrophosphate are added to this solution, oxidation occurs in such a way that one oxygen atom is added to the phenylalanine molecule and then a 2:1:1 mixture of *o*-, *m*-, and *p*-tyrosine is formed.



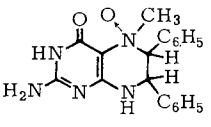
(1)



(2)



(3)



(4)

If, instead of tetrahydropterin *(1)*, tetrahydro-5-methyl-6,7-diphenylpterin *(2)* with Fe^{3+} is used in the solution, formation of an unstable complex is first observed and then, after two hr, an addition product is precipitated for which we propose the structure *(4)*. We assume that on complex formation an electron is transferred from *(2)* to Fe^{3+}, that a radical cation *(3)*[*] is formed, and that this radical adds an oxygen atom that was activated by the complexed Fe^{2+}.

On the basis of these results a novel theory of chemical and enzymic hydroxylation has been developed, involving formation of radical cations of *(1)* and of the *N*-oxide of *(1)*, rearrangement to the hydroxylamine from *(1)*, and subsequent formation of radicals of *(1)* and OH. This theory differs from the so-called mixed oxidation mechanism. The whole process may possibly occur in a complex composed of EDTA or pyrophosphate, Fe^{2+} or Fe^{3+}, *(1)*, oxygen, and phenylalanine, transfers and migrations of electrons playing a central role. If in this complex the EDTA or pyrophosphate is replaced by an apoenzyme, an enzymic reaction results in which asymmetry and stereochemistry may exert an influence on the specific course of the hydroxylation.

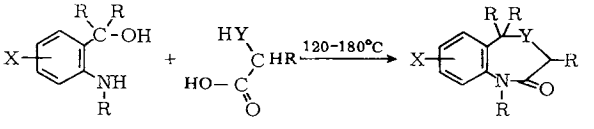
[9] *H. Tanner*, Dissertation, Technische Hochschule München, 1963.

[*] *P. Hemmerich*, Universität Basel, recently demonstrated the existence of these radical cations by ESR measurements on *(2)*.

A Simple Synthesis of 2,3,4,7-Tetrabenzo-1,4-thiazepin-3-one

K. H. Weber and *K. H. Hauptmann*. Ingelheim (Germany)

In a search for psychotropic benzazepines a remarkably simple single-stage synthesis of 2,3,4,7-tetrahydrobenzo-1,4-thiazepin-3-ones *(3a)* and oxazepin-3-ones *(3b)* was discovered. These compounds were obtained in up to 98 % yield on melting 2-alkylamino-, 2-arylamino-, or 2-heteroarylaminobenzyl alcohols *(1)* with 2-mercapto or 2-hydroxy carboxylic acids *(2)*.



(1) *(2)* *(3a)*, Y = S; *(3b)*, Y = O

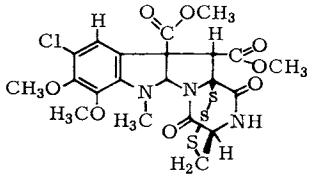
Since benzyl alcohol itself and 2-nitrobenzyl alcohol do not react with the SH group of 2-mercapto carboxylic acids under the above conditions, a salt-like intermediate is invoked to explain the mechanism. The yields depend greatly on the basicity of the amino group and the ease of exchange of the hydroxyl group of the substituted benzyl alcohols; as expected 2-hydroxy carboxylic acids, do not react so well.

[VB 32 IE]

German version: Angew. Chem. *79*, 153 (1967)

SELECTED ABSTRACTS

An unusual eight-membered ring with 3 adjacent sulfur atoms – Sporidesmin C – has been isolated by *R. Hodges* and *J. S. Shannon*. It is one of the metabolites of the fungus *Pithomyces chartarum*, which are responsible for liver damages and face eczema of sheep grazing on New Zealand pastures.



(1)

The structure was proved by degradation, NMR spectra, and particularly, mass spectrometry. / Austral. J. Chem. *19*, 1059 (1966) / –Bu. [Rd 561 IE]

***endo*-Dicyclopentadiene undergoes intermolecular rearrangement to form *exo*-dicyclopentadiene,** as has been shown by *J. E. Baldwin* with the aid of dicyclopentadiene in which an H has been replaced by a D in one of the rings. If the reaction were intramolecular, the isomerized product should remain monodeuterated, whereas an intermolecular reaction could also give doubly deuterated dicyclopentadiene. The latter is found to be the case with the *endo* compound. The labeling

in the *exo* compound does not change under the conditions of the reaction (solution in cyclohexane in a pressure tube at 196 °C). / J. org. Chemistry *31*, 2442 (1966) / –Bu. [Rd 562 IE]

A change in the specificity of chymotrypsin was produced by *H. Weiner*, *W. Batt*, and *D. E. Koshland* by chemical modification of the enzyme. Chymotrypsin contains two methionine units, one of which is three (Met 3) and the other 15 (Met 15) amino acids away from the serine, which is the reactive group in the active site. Met 3 lies on the surface of the protein molecule, while Met 15 is situated in the interior; neither is essential to the enzymatic activity. Met 3 can be oxidized to the sulfoxide by H_2O_2 at pH 3 without additives, whereas Met 15 is oxidized only in the presence of 8 M urea. Differences between the mono- (M) and disulfoxide (D) enzymes and the native enzyme (N) include: N hydrolyses the methyl ester of acetyltyrosine three times as rapidly as M and four times as rapidly as D, and hydrolyses acetyltyrosinamide six times as rapidly as M and 400 times as rapidly as D. Benzyloxycarbonylphenylalanylleucine is hydrolysed twice as rapidly by N as by M and 59 times as rapidly as by D. / J. biol. Chemistry *241*, 2687 (1966) / –Hö. [Rd 566 IE]

The conditions for the binding of tRNA on ribosomes were studied by *C. G. Kurland*. Ribosomes from *Escherichia coli* were purified, *inter alia*, by ammonium sulfate fractionations until they no longer contained either GTP or the transferases. The binding of tRNA required only the presence of mRNA (poly-U) at a suitable salt concentration (2×10^{-2} M $MgCl_2$). The addition of GTP or transferases neither accelerated the binding of tRNA nor increased the quantity bound. No qualitative or quantitative differences were observed in the binding of phenylalanyl-tRNA and deacylated tRNA. Thus the function of the cofactors GTP and transferases I and II required for the poly-peptide synthesis is to form the peptide linkages after the ribosome/mRNA/tRNA complex has been formed. / J. molecular Bio. *18*, 90 (1966) / –Hö [Rd 571 IE]

Apophosphorylase b from rabbit muscle has been studied by *E. H. Fischer et al.* The holoenzyme contains pyridoxal phosphate (PyP), and after conversion into phosphorylase a (phosphorylation by phosphorylase b kinase and ATP), it catalyses the phosphorolysis of glycogen to glucose-1-phosphate. The PyP can be removed from phosphorylase b in imidazole citrate buffer (unfolding of the protein to expose the PyP) by cysteine (removal of PyP). The apoenzyme can be crystallized in the presence of Mg^{2+}, AMP, and 2-mercaptoethanol. Unlike the holoenzyme, it tends to associate at low temperatures or at high salt concentrations, and is more labile than the holoenzyme. Incubation with PyP leads to the holoenzyme, which is indistinguishable from native phosphorylase b. Apophosphorylase b is enzymatically activated to phosphorylase a just as rapidly as phosphorylase b, the measurement being carried out after subsequent recombination with PyP. / Biochemistry *5*, 2108 (1966) / –Hö. [Rd 572 IE]

Ribulosediphosphate carboxylase from spinach leaves has been purified to a homogeneous state in ultracentrifugation experiments by *J. M. Paulsen* and *M. D. Lane*. The enzyme catalyses the reaction of ribulosediphosphate with CO_2 (or bicarbonate) to give two molecules of 3-phosphoglycerate, *i.e.* the CO_2 fixing step in the Calvin cycle in plants. The cofactor is Mg^{2+}. The incorporation of ^{14}C was used to determine the activity. The enzyme accounts for about 15 % of the total soluble protein in spinach leaves. It was purified by two ammonium sulfate precipitations and chromatography on DEAE cellulose and on hydroxyapatite. Sedimentation coefficient: 21.0 S; molecular weight by the sedimentation equilibrium method: 557000 ± 16000; molecular activity *in vitro* at 30 °C and pH 7.8 is 1300 moles of CO_2/mole of enzyme min. / Biochemistry *5*, 2350 (1966) / –Hö. [Rd 573 IE]

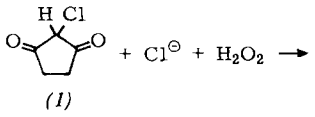
$$^{2\ominus}O_3POCH_2\text{–}CO\text{–}HCOH\text{–}HCOH\text{–}CH_2OPO_3^{2\ominus} + HCO^{\ominus}_3 \rightarrow 2\ {}^{\ominus}OOC\text{–}HCOH\text{–}CH_2OPO_3^{2\ominus} + H^{\oplus}$$

Aminopeptidase B, an *exo*peptidase with a hitherto unknown specificity, has been isolated from rat liver and enriched by a factor of 1100 by *V. K. Hopsu*, *K. K. Mäkinen*, and *G. G. Glenner*. The enzyme splits off *N*-terminal lysine and arginine; the only exception found so far was the cleavage of Gly-L-Lys. The substrates used in the activity tests were arginyl- and lysylnaphthylamides. There is no stereospecificity towards L and D forms. Gel filtration on Sephadex G 100 gives a molecular weight of about 95500, and the optimum pH is about 7. The enzyme is very specifically activated by chloride, and inhibited by complexing agents, heavy metal ions, and disulfide and thiol reagents. After treatment with complexing agents, no reactivation by metal ions was observed. / Arch. Biochem. Biophysics *114*, 557, 567 (1966) / –Hö. [Rd 574 IE]

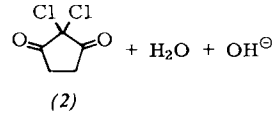
An extraintestinal protease of bluebottles (*Calliphora erythrocephala* Meigen) has been found by *J. G. Moser*. The larvae of the flies can be kept on agar under sterile conditions. Over a period of about 100 hours they excrete a protease with their feces, whose total activity is about 100 times as high as the protease activity present in the larvae after this time, and whose specific activity is about 350 times as high as in the remainder of the larval extract. The protease differs significantly from trypsin and chymotrypsin in its specificity and in its marked sensitivity to acids. The flat pH optimum is between 7.2 and 9.4. In the oxidized B chain of insulin the following peptide linkages were cleaved: Ser-His, His-Leu, Leu-Val, Gly-Phe, and Phe-Phe. Azocasein is broken down with roughly the same kinetics as by trypsin. *N*-α-Benzoyl-arginine-β-naphthylamide (trypsin substrate) is not attacked. The maximum specific activity after concentration is comparable with that of trypsin. / Biochem. Z. *344*, 337 (1966); Umschau *66*, 570 (1966)/–Hö. [Rd 575 IE]

The enzymatic transfer of sulfur from cysteine to tRNA has been studied by *R. S. Hayward* and *S. B. Weiss* and by *M. N. Lipsett* and *A. Peterkofsky*. tRNA from *Escherichia coli* contains bases with thiol groups, as well as other uncommon bases. It has been shown that the sulfur is incorporated only when the synthesis of the tRNA molecule is complete. One of the sulfur acceptors is undoubtedly the uracil residue which is converted into the 4-thiouracil residue. The sulfur transfer requires the presence, not only of cysteine tRNA, but also of a protein fraction that has been concentrated by ultracentrifugation and ammonium sulfate fractionation, as well as magnesium ions, ATP, and pyridoxal phosphate. / Proc. nat. Acad. Sci. USA *55*, 1161, 1169 (1966) / –Hö. [Rd 576 IE]

Chloroperoxidase has been purified and crystallized by *L. P. Hager*, *D. R. Morris*, and their co-workers, and its specificity towards halides has been studied. Chloroperoxidase from *Caldariomyces fumago* is a glycoprotein having a molecular weight of about 42000 and containing iron(III) protoporphyrin IX as the prosthetic group. The enzyme catalyses the *C*-halogenation of acceptors such as β-keto acids, cyclic diketones, and substituted phenols. A suitable optical test is the conversion of 2-chloro-1,3-cyclopentanedione *(1)* into 2,2-dichloro-1,3-cyclopentanedione *(2)*, which leads to the disappearance of the high UV absorption of *(1)*. [*(1)* λ_{max} =



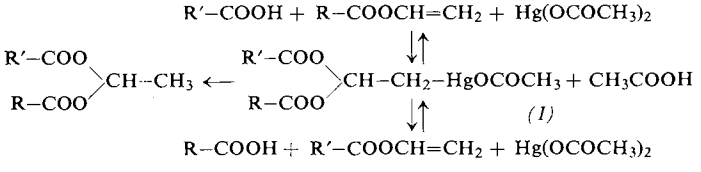
(1)



(2)

242, 248 mμ, ε = 20000; *(2)* λ_{max} = 277 mμ, ε = 160]. The molecular activity is 67000 mole/min/mole of enzyme for chloride, and is twice as high for bromide. Iodide also reacts, but interference occurs in this case as a result of the formation of elementary iodine. Fluoride acts as an inhibitor. / J. biol. Chemistry *241*, 1763, 1769 (1966) / –Hö. [Rd 584 IE]

The Hg(II)-catalysed vinyl exchange between vinyl acetate and carboxylic acids, according to *H. Lüssi*, proceeds by an acid-catalysed addition of Hg(II) acetate to the vinyl double bond. The organomercury intermediate *(1)* was isolated and identified. The transvinylation of carboxylic acids with vinyl esters proceeds in accordance with the following scheme:



/ Helv. chim. Acta *49*, 1684 (1966) / –Ma. [Rd 585 IE]

A method for the study of the polarity of the microenvironment of the active site in chymotrypsin has been described by *J. Kallos* and *K. Avatis*. If the *p*-nitrobenzenesulfonyl (nisyl) group is attached to the serine unit of the active center, it gives a spectrum similar to those of nisyl esters in cyclohexane. The spectrum of the nisylchymotrypsin changes when the protein is reversibly unfolded by gentle heating: it then resembles the spectra of nisyl esters in water. The serine in the native enzyme is evidently situated in a hydrophobic region, and can be reversibly exposed to the polar external environment. / Biochemistry *5*, 1979 (1966) / –Ma. [Rd 586 IE]

The histochemical detection of thiol groups can be achieved with 4-iodoacetamido-1-naphthol, which reacts with SH groups in proteins to form thioethers; these thioethers form a blue dye with diazotized 4-amino-2,5-bisethoxybenzanilide. A blue dye is also formed by the two reagents, but this can be easily washed out with organic solvents. Thus regions containing SH groups can be accurately located in histological preparations. *K. C. Tsou* and *A. M. Seligman* synthesized 4-iodoacetamido-1-naphthol from 4-amino-1-naphthol; this was converted into the 4-chloroacetamido compound, from which the end product was obtained by treatment with NaI [overall yield 20 %; pink crystals having m.p. 199 °C (aqueous methanol)]. / J. med. Chemistry *9*, 640 (1966) / –De. [Rd 587 IE]

Myxinol disulfate is the principal bile salt of the hagfish (Myxinidae) as was found by *G. A. D. Haslewood*. The Myxinidae (very primitive vertebrates) have very large gallbladders. A crystalline alcohol, myxinol, m.p. 206 °C, $[\alpha]_D$ = –15° (3β, 7α, 16α, 27-tetrahydroxy-5β-cholestane) was isolated from the hag species *Eptatretus stoutii* and *Myxine glutinosa*. This compound occurs in both species as the 3,27-bis-sulfate ester, which could be separated in the form of the Na salt (crystals from methanol), m.p. 195 °C (dec.). The salt has a very bitter taste. The Ba salt melts at 147 to 148 °C with decomposition. / Biochem. J. *100*, 233 (1966) / –De. [Rd 588 IE]

4-Hydroxy-2,3-dimethyl-2,3-dihydro-3-furanone *(1)*, an aroma component of the pineapple, has been synthesized by *D. W. Henry* and *R. M. Silverstein* by base-catalysed condensation of dimethyl oxalate and dimethyl glycolate to form the dimethyl ester of 3,4-dihydroxy-2,5-furandicarboxylic acid, conversion into the 3,4-bisbenzyloxy compound, reduction with $LiAlH_4$ to the 2,5-bishydroxymethyl derivative, and hydrogenation (Pd-C) of the dibenzoate. Compound *(1)* forms crystals having m.p. 75–78 °C. When stored under nitrogen at low temperatures *(1)* is stable for some months, whereas at room temperature in air it changes within 1–2 days into a viscous oil having a different odor. The same compound was obtained by *A. Hofmann* and *C. H. Eugster* by hydrogenolysis of acetylformoin with Pd-C/H_2 in water. / J. org. Chemistry *31*, 2391 (1966); Helv. chim. Acta *49*, Special Volume Emile Cherbuliez, 53 (1966)/–De. [Rd 589 IE]

The half-lives of the ^{129}Sn nuclear isomers were checked by *P. Chu* and *J. A. Marinsky*. These authors confirmed the existence of a nuclear isomer having $\tau_{1/2} \approx 6$ to 7 min, which had already been found by *Hagebø* and by *Dropesky* and *Orth*, but they found no evidence of the isomer having $\tau_{1/2} \approx 1$ hour postulated by *Hagebø*. After irradiation of a sample of $UO_2(NO_3)_3 \cdot 6H_2O$ with neutrons for one minute, the solution of the sample was worked up by a new method using NaI + $HClO_4$ with the addition of an Sn(IV) carrier, and ^{129}Sn was separated *via* a benzene phase. In this way it was possible to establish the existence of an isomer having $\tau_{1/2}$ = 2.0 min. These two short half lives of ^{129}Sn fit excellently with the linear log $\tau_{1/2}$-mass number relationship required for isotopes having the same spin and the same parity (^{123}Sn, ^{125}Sn, ^{127}Sn). / J. inorg. nuclear Chem. *28*, 1339 (1966) / –WG. [Rd 596 IE]

Two new syntheses of secondary phosphine sulfides are described by *Ludwig Maier*. Dialkylamino-dialkyl- and -diarylphosphines in boiling benzene react almost quantitatively with H_2S to form secondary phosphine sulfides.

$$R_2P{-}NR_2 + 2\ H_2S \rightarrow R_2P(S)H + R_2NH_2SH$$

These sulfides can also be obtained in high yields from thiophosphites and organometallic compounds. Addition of secondary phosphine sulfides to olefins or condensation with dialkylaminomethanols leads to the formation of unsymmetrical tertiary phosphine sulfides. Examples:

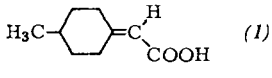
$(CH_3)_2P(S)H$, b.p. 48–50 °C/0.4 mm (yield 94 %);
$(C_6H_5)(C_2H_5O)P(S)H$, b.p. 120–127 °C/0.2 mm (54 %);
$(CH_3)_2$ (n-$C_{14}H_{29}$)PS, b.p. 186–190 °C/0.2 mm (100 %);
$(C_6H_5)_2$(cyclo-C_6H_{11})PS, m.p. 180–185 °C (77 %). / Helv. chim. Acta *49*, 1249 (1966) / –WG. [Rd 597 IE]

The preparation and structure of open-chain and cyclic polyphosphines have been described by *L. Maier*. For example, the new triphosphine $CH_3P[P(C_6H_5)_2]_2$, m.p. 130–134 °C, is obtained by the reaction of $(C_6H_5)_2PH$ with $CH_3P[N(CH_3)_2]_2$ in xylene. The structures of several known cyclic polyphosphines were corrected on the basis of molecular weight determinations and X-ray analyses. For example, $(C_6H_5P)_n$ (m.p. 149–150 °C) exists, not as a four-membered ring, but as an equilateral five-membered ring having the approximate symmetry C_s. The compound $(C_6H_5P)_6$ (m.p. 190 °C), in which the six P atoms are arranged as a six-membered ring in the chair form with the phenyl groups in the equatorial position, crystallizes in at least four forms. / Helv. chim. Acta *49*, 1119 (1966) / –WG. [Rd 598 IE]

The selective cleavage of substituted phenylthio (phenylsulfenyl) protective groups in peptide syntheses has been reported by *W. Kessler* and *B. Iselin*. The *o*-nitrophenylthio group is extremely suitable for the protection of α-amino groups, particularly in complicated peptides that also contain acid-labile groups such as t-butoxycarbonyl for the protection of the side chain of trifunctional amino acids. The *o*-nitrophenylthio groups can be easily removed by nucleophilic reagents; *e.g.* $O_2N-C_6H_4-S-Lys[COOC(CH_3)_3]-OCH_3$ can be cleaved by HCN/acetic acid, SO_2/methanol/water, or thioacetamide/acetic acid to give $HLys[COOC(CH_3)_3]-OCH_3$. The use of this method in peptide synthesis on a support as described by *Merrifield* is still associated with technical difficulties. / Helv. chim. Acta *49*, 1330 (1966) / –WG.

[Rd 599 IE]

The absolute configuration of the enantiomeric 4-methylcyclohexylideneacetic acids has been determined by *H. Gerlach*.

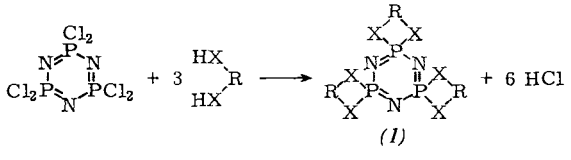


(1)

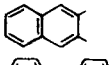
The substance *(1)* was resolved into enantiomers in 1909 by *W. H. Perkin et al.* The absolute configuration was established by correlation with (–)-isoborneol. The acid that is dextrorotatory in benzene and alcohol ($[\alpha]_{546} = +95°$ (c = 1.2; ethanol)) has *S*-chirality and the levorotatory acid has *R*-chirality. / Helv. chim. Acta *49*, 1291 (1966) / –WG.

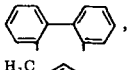
[Rd 600 IE]

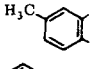
Novel phosphonitrile heterocycles were obtained by *H. R. Allcock* and *R. L. Kugel* in the reaction of phosphonitrilic chloride with diols, dithiols, and diamines in the presence of $(C_2H_5)_3N$.



(1)

(1a): R =  , X = O

(1b): R =  , X = O

(1c): R =  , X = S

(1d): R =  , X = NH

(1a): colorless crystals, m.p. 335–336 °C (benzene). *(1b)*: white crystals, m.p. > 300 °C; can be recrystallized from xylene at 200 °C in a closed vessel. *(1c)*: colorless crystals m.p. 255–257 °C (toluene or xylene). *(1d)*: m.p. > 300 °C (aqueous acetone), insoluble in hexane, benzene, toluene, dioxane, CCl_4, and H_2O, slightly soluble in acetone, acetonitrile, and methyl ethyl ketone. The yields of *(1a)* and *(1d)* are 62 and 72 % respectively. The compounds were all characterized by analysis and by their IR, UV, and ^{1}H-NMR spectra. No evidence of interaction of the π electrons of the cyclotriphosphazane system with lone pairs of the ligands X was found. / Inorg. Chem. *5*, 1016 (1966) / –Sch. [Rd 601 IE]

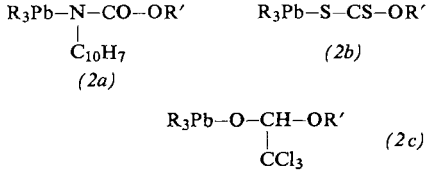
The crystal structure of dimethyltin difluoride was described by *E. O. Schlemper* and *W. C. Hamilton* as an example of octahedral coordination of tin. $(CH_3)_2SnF_2$ forms tetragonal crystals, space group I4/mm, a = 4.24, c = 14.16 Å (two formula units per unit cell). The structure consists of an infinite two-dimensional network of tin atoms and bridging fluorine atoms, with the methyl groups above and below the plane of the network. The interatomic distances are: Sn–C (2.08 ± 0.01 Å) and Sn–F (2.12 ± 0.01 Å). The crystal structure is similar to that of SnF_4. / Inorg. Chem. *5*, 995 (1966) / –Sch. [Rd 602 IE]

Additions to the lead-oxygen bond have been observed by *A. G. Davies* and *R. J. Puddephatt*. Thus novel lead-nitrogen, lead-oxygen, and lead-sulfur compounds are formed in accordance with

$$\underset{(1)}{R_3PbOR'} + A{=}B \rightarrow \underset{(2)}{R_3Pb{-}A{-}B{-}OR'}$$

$R = C_6H_5$, $R' = CH_3$

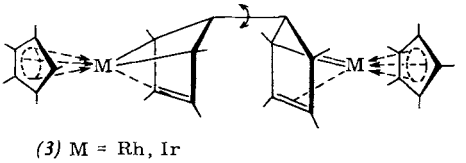
For example *(2a)* is formed from methoxytriphenyllead and AB = 1-naphthyl isocyanate, dec. p. 135–141 °C; *(2b)* is formed from *(1)* and AB = CS_2, m.p. 93–95 °C; *(2c)* is formed from *(1)* and AB = Cl_3CCHO, dec.p. 96–100 °C. The compounds are all sufficiently stable for osmometric molecular weight determinations. They are monomeric in



(2a) *(2b)* *(2c)*

0.02–0.04 M benzene solution. *(1)* reacts exothermally with hexachloroacetone in benzene. Chromatographic product recovery gives triphenyllead chloride (about 40 %), trichloromethyltriphenyllead (yield 60 %, m.p. 171–171.5 °C), and methyl trichloroacetate. The reaction with tribromoacetaldehyde yields tribromomethyl-triphenyllead having m.p. 135–140 °C. / J. organometallic Chem. *5*, 590 (1966) / –Sch. [Rd 603 IE]

Monomeric and dimeric dicyclopentadienylrhodium and -iridium have been described by *E. O. Fischer* and *H. Wawersik*. The uncharged compounds $Rh_2(C_5H_5)_4$ *(1)* and $Ir_2(C_5H_5)_4$ *(2)* were prepared for the first time by the reduction of $[Rh(C_5H_5)_2]PF_6$ and $[Ir(C_5H_5)_2]PF_6$ with molten sodium metal. *(1)* is formed in 8 % yield as an orange-yellow crystalline substance; it sublimes above 120 °C in high vacuum, decomposes above 140 °C, and is sparingly soluble in benzene, toluene, carbon disulfide, and chloroform and insoluble in hexane, methanol and water. The solid compound is moderately stable in air, but is sensitive to oxidation and to heat in solution. *(2)* is a pale yellowish substance (3 % yield), which sublimes in the monomeric form at 200 °C, and decomposes at normal pressure above 230 °C. It is sparingly soluble in benzene, toluene, and chloroform, and insoluble in hexane, methanol, and water, The paramagnetic compounds are monomeric at the temperature of liquid nitrogen only and in the gas phase above about 150 °C, and dimerize at room temperature to give the diamagnetic metal(I) complexes *(3)*. The structure was confirmed by IR and ^{1}H–NMR spectra. / J. organometallic Chem. *5*, 559 (1966) / –Sch.



(3) M = Rh, Ir

[Rd 604 IE]

Handbuch der Lebensmittelchemie (Manual of Food Chemistry). By *J. Schormüller*. Vol. II, Part 1: Analytik der Lebensmittel. Physikalische und physikalisch-chemische Untersuchungsmethoden (Analysis of foodstuffs. Physical and physico-chemical methods of investigation). Springer Verlag, Berlin-Heidelberg-New York 1965. 2nd ed., xxiv, 944 pp., DM 236.–

Physical and physico-chemical methods are of great value in the investigation of foodstuffs. Very far-reaching changes in methods have taken place since the publication of the first edition of the manual. Consequently, the first volume[*], which is devoted to the components of foodstuffs, is followed by a second volume on the analysis of foodstuffs. The 31 chapters follow the same scheme. The book starts with a theoretical introduction to the field, and this is followed by a description of the apparatus and its use, and notes on special problems of food chemistry.

H. Werner first describes sampling and associated questions (13 pp.). The descriptions are assisted by a number of good schematic drawings. The physical concept of density and its determination in liquids, solids, and gases is described by *A. Mahling* (26 pp.). The term "specific gravity" is avoided because of the confusion of the terms. The same author contributes articles on viscosity (20 pp.) and the ultracentrifuge (24 pp.). Theoretical explanations are skilfully linked with practical instructions in these articles. The same is true of the two chapters by *H. Wollenberg*, 'Ultracentrifugation, Dialysis, and Electrodialysis" (26 pp.) and "Phenomena at Phase Boundaries" (32 pp.). Theoretical explanations of the melting point, solidification point, and boiling point, and a description of the apparatus used for their determination are contributed by *H. J. Henning* (33 pp . Some mention of zone melting, which has proved an excellent method for the purification of substances would have been desirable here.

In his discussion of solubility (23 pp. *H. J. Henning* discusses open questions as well as known facts. *K. Volz* contributes a short paper on calorimetry (5 pp.). In line with the frequent use of pH measurements, these and all related questions are discussed at length by *D. Berndt* (34 pp.). Mention is also made of older methods that are less common in food chemistry. The redox potential is discussed in general and from the point of view of biology and food chemistry by *W. Heimann* and *K. Wisser* (40 pp.). The chapter is supplemented by seven tables. *K. E. Slevogt* discusses conductometry and dielectrometry (37 pp.).

In the reviewer's opinion, *K. Pfeilsticker*'s chapter (42 pp.) on emission spectral analysis passes beyond the scope of food analysis in places. The principles, technique, and value of flame photometry in the analysis of foodstuffs are described by *W. Diemair* and *K. Pfeilsticker*. Light-absorption measurements in the visible and ultraviolet regions and infrared spectra (47 pp.), color measurements (7 pp.), and luminescence analysis (20 pp.) are explained well by *J. Eisenbrand*. The reader is introduced to optical polarimetry, polarization, and (briefly) rotatory dispersion by *J. Flügge* (40 pp.). Interferometry is mentioned by *J. Eisenbrand* (5 pp.). The important topic of polarography is discussed by *W. Diemair* and *K. Pfeilsticker* (18 pp.). A good survey of the history and techniques of paper chromatography is contributed by *A. Grüne* (45 pp.), who also refers briefly to labeling with radioactive isotopes. In connection with *G. Wohlleben*'s chapter on column chromatography (9 pp.), special mention should be made of the discussion of the suitability of various inorganic and organic adsorbents. Ion exchangers and molecular sieves are also briefly described. Thin-layer chromatographic analysis (24 pp.) is discussed by *A. Seher*, starting with a short introduction and proceeding to consider various groups of substances that are of interest in food chemistry. Corresponding to the great importance of gas chromatography, *F. Drawert* (69 pp.) not only discusses in detail the theory and the structure of individual instruments and parts of instruments, but also presents many items of general interest. The chapter is supplemented by a large number of examples of applications. Electrophoresis (20 pp.) is discussed by *H. D. Behlitz*, who describes, not only methods, but also applications to various classes of substances. The authority on multiplicative distribution, *E. Hecker*, presents a concise survey of this special field (31 pp.). The increasingly important task of detecting radionuclides in foodstuffs is discussed by *K. G. Bergner* and *P. Jägerhuber* (38 pp.). The topics covered include sampling, methods of measurement, and evaluation of the measurements. The authors finally offer suggestions for the equipment of a laboratory. Under the heading "Microscopy", *H. Freund* (41 pp.) discusses microscopes, (including the electron microscope), accessories, and techniques. The microscope specimens and the staining of bacteria specimens is described by *F. Walter* (37 pp.). The calibration of measuring instruments is surveyed by *H. Johannsen* (19 pp.). *H. Ramb* presents an introduction to the fundamentals of refractometry, technical refractometry, and the application of this method to special foodstuffs (34 pp.). In the last chapter, *K. Feiling* discusses nephelometry (7 pp.). The subject index covers 29 pages.

Each chapter is accompanied by an extensive bibliography, and in almost every case by a comprehensive list of journal references. The literature is covered up to 1964. The present volume is a valuable aid to anyone who is concerned with food chemistry and who wishes to use the latest methods in his work.

C. H. Brieskorn [NB 534 IE]

[*] Cf. Angew. Chem. *78*, 398 (1966); Angew. Chem. internat. Edit. *5*, 431 (1966).

HMO – Hückel Molecular Orbitals. By *E. Heilbronner* and *P. A. Straub*. Springer-Verlag, Berlin-Heidelberg-New York 1966. 1st ed., 816 pp., loose leaf DM 72.–.

It is becoming an increasingly established practice, in seeking for an understanding of the properties of molecules and in discussing possible reaction mechanisms, to turn to the results of Hückel molecular orbital (HMO) calculations rather than to write out resonance structures, as was formerly common. A systematic application of the HMO method in chemical practice seems possible only if there is no need to carry out a HMO calculation in each individual case and one may simply look up its results. The present set of tables, with a short but clear introduction on their use, is therefore very welcome.

It is not very important to the experimental chemist to understand the conditions and limitations under which the HMO theory can be derived from quantum mechanics. It is more important that he should be able to use the results of HMO calculations, and to draw chemically relevant conclusions from molecular diagrams, from the scheme of the orbital energies, and possibly also from the polarizabilities and other numerical values. This requires not only study of a textbook of MO theory, but also a certain amount of experience, and this experience can probably be built up more rapidly with the aid of the present tables.

It should be noted tha the HMO method applies only to the π-electron systems of unsaturated compounds, so that it cannot be expected to provide answers to questions specifically concerned with σ bonds. The number of possible π-electron systems is so great that it would be futile to hope for completeness. However, about 800 systems are tabulated in the book, starting with simple chains and rings, and progressing to very complex combinations of rings of various sizes and branched chains. It includes the most important

kata- and *peri*-condensed aromatics as well as many of their 5- and 7-membered ring analogues.

If one is interested in hydrocarbons that are not included in the tables, then one has simply to punch cards according to Fortran program published with the book and send it, together with data cards, to the nearest computer center.

Compounds containing hetero atoms are not included. This is understandable, since the choice of suitable heteroatom parameters is not easy, and since, for this reason as well as others (for example, because the $\sigma-\pi$ interaction is more pronounced in heteromolecules), the numerical values obtained by the HMO method for heteromolecules must be regarded much more critically than those obtained for alternant hydrocarbons.

Nevertheless, the tables can also be used for heteromolecules. To a first approximation, these can be replaced by the isoelectronic hydrocarbons, while the approximate molecular diagrams can be easily calculated (i.e. by multiplications and additions) in higher approximation from the given numerical values, particularly from the "polarizabilities". Similarly, additional cross bonds and even a possible bond alternation can be easily taken into account by means of perturbation theory. Useful as the "polarizabilities" are for expressing "perturbations" in the molecule, it is quite another question whether they will find much practical application and hence whether the space given to them is justified.

Finally, it should not be forgotten that more accurate MO calculations (*e.g.* by the Pariser-Parr method) are supposed to reproduce the HMO diagram qualitatively, but not quantitatively. However, even the most accurate calculations possible today are still far from the "ultimate truth", and in any case, this still does not detract from the usefulness of the HMO method.

The loose-leaf presentation has the advantages that the order can be changed as desired, and that new sheets can be inserted; however, it also has some disadvantages. For example, the mechanism of the reviewer's copy was damaged in transit.

W. Kutzelnigg [NB 567 IE]

Einführung in die Allgemeine Pharmakologie (Introduction to General Pharmacology). By *S. DeJong*. From the 2nd Dutch edition, translated into German by *F. Hohensee*. Urban & Schwarzenberg, München-Berlin 1965. 1st Edit. xv, 200 pp., 24 illustrations, board DM 19.80.

This booklet by the well-known Dutch pharmacologist is an attempt "to write in general terms a pharmacology for readers who know nothing of the subject"

The author gives a 20-page introduction on drugs, poisons, and stimulants (tobacco, alcohol, *etc.*) and the historical development of pharmacological research. A further 22 pages are devoted to a description of the fate of a physiologically active substance in the body after introduction in various ways, of its distribution and elimination.

The next 50 pages deal with differences in sensitivity between races and sexes, hypersensitivity, tachyphylaxis, habituation and addiction, and the cumulation of drugs; "cumulation" here refers only to the retention of a substance, and "addiction" is regarded only as psychic dependence (including that on cigarettes), while physical dependence with withdrawal symptoms is referred to as "habituation". Surprisingly, the term "drug idiosyncrasy' is used instead of the usual "sensitization", *eg.* to penicillin

In the discussion of differences in sensitivity, much too little reference is made to biological dispersion to suit the needs of beginn rs.

The difference in sensitivity is mentioned only in the testing of insulin, where "the American rabbit requires three times as much insulin as in Europe", and "the effect of insulin on rabbits varies with the time and with the weather". It would have been more useful to the beginner (for whom the book is intended) to give some examples of the difference in sensitivity of different animals to the same substance, and the resulting difficulty of applying conclusions drawn from animal experiments to humans.

Another 50 pages are devoted to a description of the relation between dose and effect with the aid of curves, the terms "probit" and "probability paper" being explained. The well-known "CT product" is given for the action as a function of time, but unfortunately is illustrated with the action of CO, which in view of the unpredictable after-effects following prolonged exposure to CO probably has nothing to do with the "CT product".

Isobolic curves are given for the combined action of substances that can reinforce or weaken each other in their action. This is followed by a number of examples illustrating "Chemical Constitution and Pharmacological Action", which show only how little is known about this subject.

A 20-page chapter shows how pharmacological effects can be calibrated and how drugs are tested for side effects (particularly for pyrogenic action), and a short note is given on the toxicological examination of drugs.

The problem of a "general pharmacology" is evident in this book. In order to understand it, one must have considerable previous knowledge, and it is impossible to agree with the author when he stresses the undemanding nature of this text. The whole book is a rather abstract affair, and the reviewer fears that, particularly among those with no medical training, it will be more confusing than useful, or may foster the misconception that the ability to manipulate terms constitutes some understanding of pharmacology. The book will make enjoyable reading for those who are experienced in pharmacological or toxicological animal experiments or in clinical pharmacology.

H. Oettel [NB 542 IE]

Manometrische Methoden und ihre Anwendung in der Biologie und Biochemie (Manometric Methods and their Use in Biology and Biochemistry). By *Arnošt Kleinzeller et al.* VEB Gustav Fischer Verlag, Jena 1965; Tschechoslowakischer Verlag für medizinische Literatur, Prague 1965. 2nd ed., 601 pp., 147 illustrations, paper DM 75.60.

The second edition, the first to appear in German, was edited by *A. Kleinzeller* and written in collaboration with seven Czechoslovakian and one English author. It contains the following chapters: 1. Warburg manometric apparatus; theory and use. 2. Methods of measurement using the Warburg apparatus. 3. Differential manometers and their use. 4. Volumetric respirometers. 5. Microrespirometers. 6. Van Slyke manometric instrument. 7. The use of electrochemical methods for the study of tissue respiration. 8. Theory of buffers and their preparation; retention. 9. Media for animal tissues. 10. Processing and preparation of biological material for manometric metabolism studies. 11. Manometric measurement of the activity of enzymes and the use of inhibitors. 12. Thunberg technique and related methods 13. The use of manometric methods in metabolic studies and interpretation of the results. 14. Analytical manometric methods.

The reader is surprised by the full and detailed treatment of the theory and use of a method whose history began with a lecture by *E. Warburg* to the *Preaßische Akademie der Wissenschaften* in 1900, and which, particularly in the hands of *O. Warburg*, has made such a significant contribution to our present knowledge of cell physiology. A particularly welcome feature of this book is the fact that the authors not only deal with pure manometry, but also describe the polarographic method for the determination of oxygen, which is an important complement to the classical method, and report at length on methods for the manipulation of biological material. Detailed procedures and lists of references dating up to 1965 are given for each technique, so providing an extremely valuable aid to both beginners and advanced workers in the field of cell physiology and enzymology.

B. Hess [NB 517 IE]

Advances in Heterocyclic Chemistry. Vol. 5. Edited by *A. R. Katritzky*, *A. J. Boulton*, and *J. M. Lagowski*; Academic Press, New York-London 1965. 1st ed., xiv, 395 pp., 395 illustrations, $16.00.

In the first article (67 pp.), *R. Zahradník* deals with theoretical considerations on the electronic structure, the resulting reactivity, and a number of physical properties of heterocyclic sulfur compounds. Starting with the model for the atomic orbitals of sulfur, calculations of the molecular orbitals for sulfur compounds are presented, and comparisons are drawn with corresponding carbocycles.

The second article (49 pp.) by *K. Zahradník* and *J. Koutecký* covers theoretical studies on the physical properties and reactivity of nitrogen heterocycles ("azines"). This article presents lucidly a tabular collection of spectral data, polarographic half-wave potentials, π-electron densities, basicities, and chemical reactivities of mono-aza heterocycles with a completeness that is unequalled elsewhere.

F. Kurzer is responsible for the article on 1,2,3-thiadiazoles (85 pp.), a class of substances that has been closely studied only in the last ten years. The syntheses developed during this time are described, those discovered by *J. Goerdeler* being particularly outstanding. Other chapters deal with the chemical and physical as well as physiological and pharmacological properties of these compounds.

R. A. Heacock wrote the article on aminochromes (85 pp.), the deep-red to violet oxidation products of 3,4-dihydroxyphenylethylamine and its derivatives (dopa amines). The possibilities of formation, the methods of preparation, and the mechanism of formation are discussed. The physical behavior, and especially chromatographic and spectral data, are presented clearly. The chemical properties, stability, and rearrangement and condensation reactions are described at length. Detailed reference is also made to the importance of the aminochromes in medicine and biology, particularly for the formation of melanine in the dark pigments or the adrenochrome metabolism.

B. S. Thygarajan discusses the aromatic quinolizines (23 pp.). He describes in detail the syntheses of the known quinolizine derivatives, the possible reactions, and the ultraviolet and infrared spectra.

The last contribution (50 pp.) by *N. Kochetkov* and *A. M. Likhosherstov*, presents a digest of 125 original publications on advances in pyrrolizidine chemistry. The syntheses described are backed up by numerous clear formulae. One chapter is devoted to the relative and absolute configuration and stereochemical transformations of the pyrrolizidine bases. The reactions and ring cleavages are reported at length. The section closes with a discussion of the biogenesis of naturally-occurring pyrrolizidines from ornithine or β-hydroxyornithine.

The book contains a balanced blend of theoretical and preparative results from research on special heterocycles. The layout of the book is again outstanding, so that it is a worthy successor to the earlier volumes, and will be a useful source of information for anyone who is interested in heterocycles.

W. Ried [NB 530 IE]

Comprehensive Biochemistry. Edited by *M. Florkin* and *E. H. Stotz*. Vol. 16: Hydrolytic Reactions; Cobamide and Biotin Coenzymes[1]. Elsevier Publishing Company, Amsterdam-London-New York 1965. 1st ed. XII, 267 pp. 10 illustrations, 37.50 Dutch florins (by subscription, 30.00 Dfl.).

Of the many reactions of enzymes a few are selected as examples and treated here in exemplary fashion; these are the reactions of the hydrolases, the action of which as acid-base catalysts has been largely elucidated in recent years, and those of the isomerizing and carboxylating enzymes that use cobamides and biotin as cofactors. A deeper insight into the arrangement of the active site of esterases has been obtained, mainly by variation of the structure of the substrate and by means of inhibitors; this is discussed by *Oosterbaan* and *Jansz*. The role of phosphatases in the synthesis and degradation of cell substances is described by *Morton* (in an article published posthumously) with his usual lucidity. A particularly topical section which, like the others, contains interesting aspects based on the personal experience of the author *(Cunnigham)*, deals with the serine proteases. Considerable space in this section is devoted to the views on the formation of active enzyme-substrate complexes, which have already been extended to other enzyme mechanisms, and the chemical and physical principles underlying these ideas are discussed.

The chapter on the cobamide (B_{12}) coenzymes, in which the essentials are presented concisely and authoritatively by *Weisbach*, *Peterkofsky*, and *Barker*, is a masterpiece of selective writing. A somewhat less balanced section is that on biotin carboxylases by *Ochoa* and *Kaziro* However, the discussion also includes all the necessary detail.

This volume is again undoubtedly well presented. However, consideration of the further progress of the enterprise raises the question of whether the completeness of this work, for which a high price must be paid, is not a luxury. The volumes should not be included in a single treatise, where there is always a desire to complete the series, but which will nevertheless not become a comprehensive manual of biochemistry; they should instead have been published as monographs, from which one could select those required, and which could be more easily kept up-to-date by publication of new editions.

L. Jaenicke [NB 539 IE]

[1] Cf. Angew. Chem. *76*, 868 (1964).

Advances in Organic Chemistry. Methods and Results. Vol. 5. Edited by *R. A. Raphael*, *E. C. Taylor*, and *H. Wynberg*. John Wiley & Sons. Ltd., New York-London-Sydney 1965. 1st Edit., vii, 337 pp., several figures and tables, cloth, 105s.

In volume 5[*] of "Advances in Organic Chemistry", *A. J. Parker* reports on the use of dipolar aprotic solvents, *R. McCrindle* and *K. H. Overton* on the chemistry of cyclic diterpenoids, and *M. Tichý* on the determination of intramolecular hydrogen bonds by IR spectroscopy and the application of such data to stereochemistry.

Parker's article (46 pp.; 232 references, of which no. 232 appears in the list of references but not in the text) is a careless piece of work and contains many mistakes. The content of the publications on which the article is based is reviewed (often distortedly) in a loose sequence instead of coordinated to form a unified picture. Consequently, there is considerable repetition with different references, while other topics are discussed in unsuitable places (*e.g.* the reaction of mercaptides with oxygen appears under "Dipolar Aprotic Solvents as Reactants", and the formation of alkyl nitrates is given as an example of the reaction $RX + R'_2N^{\ominus} \rightarrow NRR'_2 + X^{\ominus}$); with the result that the original sense is often lost (*e.g.* p. 27: preparation of nylon from isocyanates). The main value of this article would therefore lie in the reference list, but for its careless compilation: 60 references are incorrect, data on the publishers rudimentary (*e.g.* Elsevier, New York"), abbreviations of journals are sometimes inconsistent and journals that are translated into English are referred to only as the English translation. The work cited occasionally does not deal with the topic in connection with which it is referred to.

McCrindle and *Overton* review 237 papers in 67 pages. The terse discussion does not always follow *Fieser*'s "Style Guide for Chemists", and occasional incorrect (*e.g.* p. 74 under the chemistry of dihydrorosenonolactone, p. 51, two methyl groups missing; note a) of Tables I to IV is not relevant) or incomprehensible presentation (p. 80, formula of podototarin) makes it necessary to consult the original literature (spot checks indicate that the references are almost free from errors). The use of unaccustomed abbreviations is not conducive to easy reading.

Tichý deals almost exclusively with shifts in the positions of OH bands as a result of hydrogen bonding, and scattered data from 339 publications are presented on 184 pages (mainly in tables). Errors leading to distortion of meaning are comparatively rare [formulae *59* and *78* do not agree with their legends; on p. 145 *63d* appears instead of *63b*; on p. 282 one finds 2-(3,4,6- (better: 2-(2,4,5-) instead of 2-(3,4,4-trimethoxyphenyl)ethanol; on p. 157 the value of $\Delta\nu$(OH) for 2-hydroxybenzonitrile is omitted; on pages 234 and 273, the OH groups are omitted from the azomethine and biaryl formulae; a wrong formula is given on p. 178 for ascaridole glycol; the bottom formula on p. 278 (as in the original publication) carries one CH_3 group too many]. Some names of authors are also quoted wrongly (nos. 161, 209, 276, 338). On p. 200, *Tichý* uses the numbering given by *McCrindle* and *Overton* for labdandiol, while on pages 121 and 132 he uses the old system.

The reproduction of steric formulae is very arbitrary, and even includes bold dotted bonds. As before, the external presentation is excellent. *G. P. Schiemenz* [NB 577 IE]

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[*] For reviews of Vols. 3 and 4 cf. Angew. Chem. *77*, 599, 687 (1965); Angew. Chem. internat. Edit. *4*, 614, 725 (1965).

Industrial Chemicals. By *W. L. Faith, D. B. Keyes*, and *R. L. Clark*. John Wiley & Sons, Inc., New York-London-Sydney 1965. 3rd Edit., 852 pp., 190 s.

137 of the most important industrial chemicals are decribed in alphabetic order. These include 83 organic substances and 54 inorganic substances as well as a few elements, such as oxygen, hydrogen, and chlorine. The emphasis is placed on base chemicals and intermediates. Organic "end-products" include aspirin, penicillin, polyethylene, and polypropylene.

Under each substance the book presents a brief but very lucid description of the current technical production processes (with flow diagrams and "recipes"), and the important properties, commerical grades, producers in the U.S.A., and prices are given. Processes that are important for several products, such as the oxo process and hydrodealkylation, are discussed under one of the products for which they are used. (A more detailed index would have made it easier to find such processes. For example, the alfol process is mentioned under "decyl alcohol", synthesis gas is described under hydrogen, and the oxidation of hydrocarbons under acetaldehyde; none of these processes is mentioned in the index).

The industrial chemist will be particularly interested in the "Economic Aspects". Here he will find data on the present market importance of a product, the production (in the U.S.A.) since 1944, and the prospects for further development. These sections also contain information about the relationship between production costs and plant size, the economics of combination with other processes, and the position of a product in relation to competing products.

The book offers students, teachers, and industrial chemists a wealth of facts and suggestions. Many readers may be disappointed that no literature or patents are cited. However, this was the only way in which the size and cost of the book could be kept within reasonable limits.

H. Buchholz-Meisenheimer [NB 573 IE]

Catalytic Hydrogenation (Techniques and Applications in Organic Synthesis). By *R. L. Augustine*. Marcel Dekker, Inc., New York 1965. 1st ed., xii, 188 pp., several illustrations, bound $8.75.

Considerable progress has been made in recent years in catalytic hydrogenation, particularly in selective and partial hydrogenations, for which a large number of new catalysts have been discovered. Despite the existence of a number of handbooks, the literature in this field is not easy to survey. A number of authors have recently described the subject in relatively short monographs. Among these, *Augustine* stands out for his conciseness and lucidity.

The sub-title suggests that the book is intended mainly for the preparative organic chemist, with the object of assisting with hydrogenation problems; this is achieved with the aid of short hydrogenation procedures set in bold type. However, reference to the original publication often is unavoidable. Nevertheless, the brevity is a decisive aid to clarity. This is also assisted by the division of the material into: 1. Apparatus and general technical instructions (but only for the laboratory scale), 2. catalysts and general hydrogenation conditions, and 3. instructions for hydrogenations and hydrogenolyses, arranged according to functional groups, though many problems here are dealt with in a few sentences. An appendix describes the preparation of a number of common catalysts; more examples would have been welcome here.

The book may also be of interest to the hydrogenation specialist for quick orientation, though the specialist would prefer a stronger emphasis on patent literature. However, the book will be a useful aid to chemists working in the laboratory and in general research, and above all to the newcomer to the field of catalytic hydrogenation. It is concisely and clearly written, and if it is regarded as an introduction to the problems of catalytic hydrogenation, it probably serves its purpose. *M. Reich* [NB 525 IE]

The Alkaloids, Chemistry and Physiology. By *R. H. F. Manske*. Vol. VIII[1]: The Indole Alkaloids. Academic Press Inc., New York-London 1965. 1st Edit., 861 pp., bound $ 32.00.

Between 1949 and 1955, *R. H. F. Manske H. L. Holmes*, together with other well-known authors, collected the existing knowledge on the chemistry and physiology of the alkaloids n a five-volume handbook. This work became one of the most important sources of information on these natural products, and is still unsurpassed in this field. The supplementary volumes VI and VII were published in 1960. The present volume, which is particularly extensive, is devoted to the results obtained since 1960 on the indole alkaloids. The rapid development of this group of alkaloids is indicated by the size of the relevant chapters: 138 pages in Vol. II, a supplement of 200 pages in Vol. VII, and now 861 pages in Vol. VIII. This growth is due to the fact that the indole derivatives form one of the most extensive and medically most useful groups of alkaloids. Thus some 600 indole alkaloids are now known, and 50 to 100 are isolated for the first time and their structure elucidated every year. Examples of therapeutically important indole alkaloids are reserpine and the ergot and curare alkaloids.

The editor, *R. H. F. Manske*, and the eleven co-authors have made an ideal selection of material for this supplement to a handbook. The content is largely new and contains only as much material from the earlier volumes as is required to make the chapters independent. In this way the 22 chapters of the volume give impressive evidence of how much as been achieved in five years, how many new alkaloids have been elucidated, and what modern methods have been used in their elucidation. The authors themselves have made a decisive contribution to these successes.

The synthesis and stereochemistry of ergotamine are a climax of the chapter by *A. Stoll* and *A. Hofmann* on ergot alkaloids, which has grown from 28 pages in Vol. VII to 53 pages in the present volume. The description of the curare alkaloids, by *A. R. Battersby* nd *H. F. Hodson*, has also expanded considerably. In this section, due attention is paid to the elucidation of the dumeric alkaloids of calabash curare by the authors and by the research groups of *H. Schmid* and *Th. Wieland*.

The editor has written five excellent chapters on the calycanthacea and other alkaloids studied by him. This section also includes the elucidation, completed by *R. B. Woodward* and at the same time by X-ray analysis by *M. Robertson*, of

calycanthine, which is remarkable for its unusual 6-membered ring structure.

E. Schlittler describes the progress achieved in the chemistry of reserpine (which was elucidated by this author) and similar indole alkaloids. The reader learns from competent sources how *Woodward*'s total synthesis of reserpine, described in Vol. VII, has in the meantime been modified in such a way that this therapeutically active alkaloid is now as readily obtainable by synthesis as from varieties of *Rauwolfia*.

In four chapters on vinca, iboga, pentaceras, and ajmaline alkaloids, *W. I. Taylor* describes the isolation and structure elucidation of a large number of new alkaloids. These chapters also describe one of the first triumphs of mass spectrometry, which has made an outstanding contribution in this field through the work of *K. Biemann* and *C. Djerassi*. This is particularly true in the case of the detailed description of the aspidosperma alkaloids by *B. Gilbert*.

G. F. Smith, *E. Coxworth*, and *W. I. Taylor* describe the strychnos alkaloids, physostigmine, and the biogenetically important cinchonamine, fields that are now essentially complete. *J. E. Saxton* describes recent achievements in the field of the gelsemium and other alkaloids in six outstanding reviews.

Owing to the arrangement of the handbook, which was established 16 years ago, only relatively little attention could be given to advances in biogenitic studies.

There can be no doubt that in the supplementary volume VIII the editor and co-authors have produced one of the best and most stimulating monographs on the chemistry of natural products. The book will be read not only by chemists, botanists, and pharmacologists engaged in the alkaloid field, but also by all those who are interested in important mechanistic and stereochemical results and in modern methods of structure elucidation.

B. Franck [NB 540 1E]

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Hydrophobic Interactions

BY G. NÉMETHY[*]

Recent advances in theoretical and experimental studies of hydrophobic interactions are reviewed. The theory of water structure as applied to hydrophobic bonding, theoretical estimates for the free energy of unfolding of proteins, and the statistical mechanical theory of hydrophobic bonding in polyamino acids are summarized. Experimental estimates of the thermodynamic parameters of the hydrophobic bond can be obtained from solubility and dimerization data of low molecular weight compounds. Recent studies of the interaction of proteins with nonpolar solutes are discussed. Hydrophobic bonds can also be important in various other kinds of interactions involving proteins. The observed effect of urea is mentioned, although no theoretical interpretation of this effect is available yet. In conclusion the methods available for the detection of hydrophobic interactions are reviewed.

Introduction

In recent years the role of hydrophobic bonding in the maintenance of the secondary and tertiary structure of proteins (and of other macromolecules) in aqueous solution has become increasingly clear. The term "hydrophobic bonding", or more properly "hydrophobic interaction", describes the tendency of nonpolar groups to associate in aqueous solution, thereby reducing the extent of contact with neighboring water molecules. This behaviour does not arise from unfavorable energetics of the nonpolar group-water contact. On the contrary, the enthalpy of formation of a hydrophobic bond is destabilizing ($\Delta H^\circ > 0$). The formation of hydrophobic bonds is favored only because of an entropy effect: the water molecules become more ordered around exposed nonpolar solutes. When the hydrophobic bond is formed the order decreases, resulting in a favorable entropy and hence free energy of formation.

Hydrophobic bonding is often invoked in the interpretation of various observed anomalies in protein structure and reactivity. Undoubtedly, hydrophobic interactions are one of the most important effects in the stabilization of the conformation of proteins in aqueous solution. Nevertheless, restraint must be exercised in the use of this concept when experimental data are to be interpreted. Hydrophobic bonds cannot be the sole important noncovalent interaction in proteins, even though they can make a large or even the predominant contribution to the stabilization of particular conformations. They are not sufficiently specific in character to force the establishment of a unique structure: in the interaction of nonpolar groups with each other, there is little restriction upon the number of interacting groups, their mutual orientation, and the extent of their contact. Therefore, specific folding into a unique conformation presumably requires the interplay of several types of noncovalent interactions.

Theoretical Treatments of the Hydrophobic Bond

The consideration of hydrophobic bonding cannot be separated from the study of the structure of liquid water. In this connection, the most important feature of the structure of liquid water is the ability of its molecules to form spatially extended networks (clusters), by means of intermolecular hydrogen bonding (Fig. 1). Various theoretical and experimental approaches to the determination of water structure were reviewed by *Némethy* and *Scheraga*[1], and by *Kava-*

[*] Dr. G. Némethy
The Rockefeller University
New York, N.Y. 10021 (U.S.A.)

[1] *G. Némethy* and *H. A. Scheraga*, J. chem. Physics *36*, 3382 (1962).

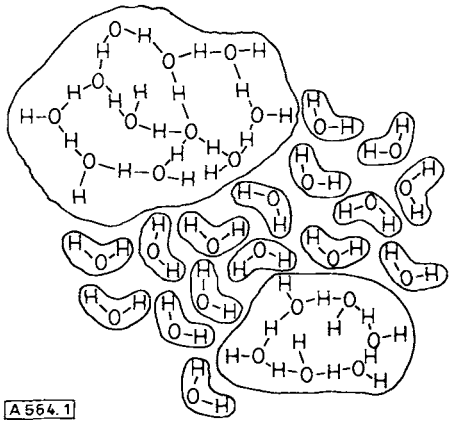


Fig. 1. Schematic representation of the structure of liquid water according to the theory of *Némethy* and *Scheraga* [1]. Hydrogen-bonded clusters and regions of non-hydrogen-bonded molecules are shown.

nau [2]. Since then, several further proposals for the structure of liquid water have been published with the aim of providing an improved description of the structure, *e.g.*, by postulating a variety of interacting multimolecular structures [3,4], or by generalizing [5,6] the use of various energy levels introduced in the theory of *Némethy* and *Scheraga* [1]. In interpretations of some recent infrared or Raman spectroscopic data, it was suggested [7–9] that the fraction of broken hydrogen bonds is small (below 10 %), *i.e.* much below earlier estimates [1,2]. Some of the problems arising in the interpretation of various observations in terms of water structure have been summarized by *Frank* [10].

Even though the details of the intermolecular structure in liquid water are still a subject of controversy, this does not detract from the prevalent picture of the effects of nonpolar solutes on water structure and on the nature of hydrophobic bonding. All evidence supports the early suggestion by *Frank* and *Evans* [11], treated later in more detail by *Kauzmann* [12] and by *Némethy* and *Scheraga* [13], that structural order increases near nonpolar solutes. Thermodynamic parameters and solubility data for various nonpolar substances can be best reconciled with the assumption that the number of hydrogen bonds per mole of water is increased near nonpolar solutes. It has been shown [13] that the presence of highly hydrogen-bonded water molecules in the immediate neighborhood of nonpolar solute molecules is favored because of the possibility of increasing the number of attractive intermolecular (van der Waals) contacts (Fig. 2). This

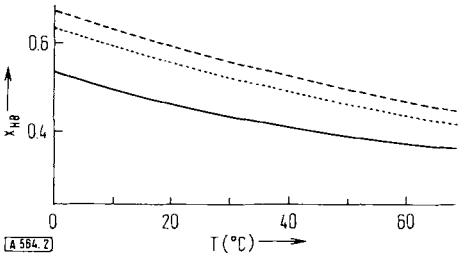


Fig. 2. The fraction of unbroken hydrogen bonds x_{HB} at various temperatures in pure water (——) and in the first layer of water molecules around aliphatic (- - - -) and aromatic (····) hydrocarbon molecules. (x_{HB} = 1 for perfectly crystalline ice.) Calculated from the theory of *Némethy* and *Scheraga* [13].

results in a stabilization of hydrogen-bonded water networks or clusters. Since this effect leads to the immobilization of more water molecules than in pure water, it results in a negative excess entropy of solution [13] and hence a large positive free energy of solution (Fig. 3), as observed. The enthalpy gained

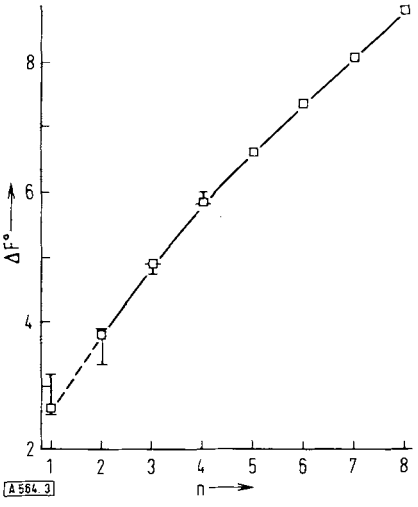


Fig. 3. Comparison of experimental (I) and theoretical (□) excess free energies (kcal/mol) of solution for the normal aliphatic hydrocarbons in water at 25 °C. *n* is the number of carbon atoms in the hydrocarbon. The curve is drawn through the theoretical points calculated by *Némethy* and *Scheraga* [13].

from the formation of the new hydrogen bonds and from the increased number of van der Waals contacts explains [13] the observation that aliphatic hydrocarbons dissolve exothermally in water.

Hydrophobic bonding can be considered essentially as the partial or complete reversal of the solution process for a hydrocarbon in water (Fig. 4). As pointed out by *Kauzmann* [12], the stable conformations of a protein in aqueous solution will be those in which nonpolar groups can come into contact with each other and are thus partially or completely removed from water [14]. This process will be accompanied by

[2] *J. L. Kavanau*: Water and Solute-Water Interactions. Holden-Day, San Francisco 1964.

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[6] *J. H. Griffith* and *H. A. Scheraga*, Abstr. 150th Meeting American Chem. Society, Atlantic City, September 1965, p. 18-I.

[7] *T. T. Wall* and *D. F. Hornig*, J. chem. Physics *43*, 2079 (1965).

[8] *W. A. P. Luck*, (a) Ber. Bunsenges. physik. Chem. *69*, 626 (1965); (b) *W. Luck*, Fortschr. chem. Forsch. *4*, 653 (1964).

[9] *K. A. Hartman, jr.*, J. physic. Chem. *70*, 270 (1966).

[10] *H. S. Frank*, (a) Natl. Acad. Sci-NRS U.S.A., Publ. *942*, 141 (1963); (b) Federat. Proc. *24*, Suppl. *15*, S-1 (1965).

[11] *H. S. Frank* and *M. W. Evans*, J. chem. Physics *13*, 507 (1945).

[12] *W. Kauzmann*, Advances Protein Chem. *14*, 1 (1959).

[13] *G. Némethy* and *H. A. Scheraga*, J. chem. Physics *36*, 3401 (1962).

[14] *G. Némethy* and *H. A. Scheraga*, (a) J. physic. Chem. *66*, 1773 (1962); (b) *67*, 2888 (1963).

a large negative free energy change (ΔF°), composed of a large positive entropy component (ΔS°) and zero or a small, positive enthalpy component (ΔH°), as calculated by *Némethy* and *Scheraga* [14]. The value of ΔH° is near zero for aromatic groups and positive for aliphatic groups near room temperature [14]. The free energy ΔF° describes the tendency of the non-polar groups to adhere to each other, and thus represents the strength of the hydrophobic bond.

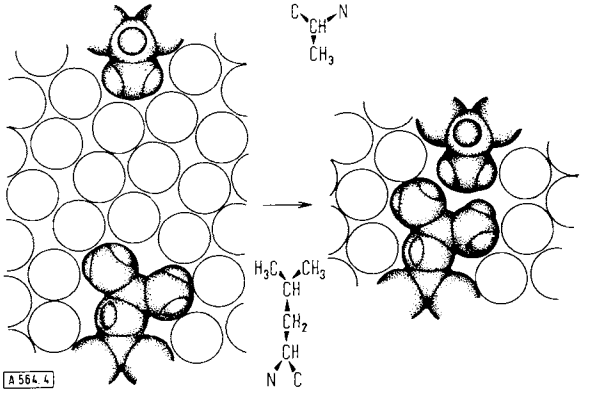


Fig. 4. Schematic representation of the formation of a hydrophobic bond between exposed alanyl and leucyl side chains on a protein. The two side chains approach each other until they touch, so that the number of nearest neighbor water molecules (shown schematically by circles, without indicating the structure) is reduced [14].

In other polar solvents, nonpolar groups also may tend to contact each other, but this happens because the energy of solvent-solvent and solute-solute interactions is more favorable than that of solvent-solute interactions. Such lyophobic [15] interactions are enthalpy-driven.

This character of hydrophobic bonds is evidenced in their temperature dependence: at low temperatures, hydrophobic bonds become stronger as the temperature increases [14,16]. The maximum strength is reached at a certain temperature which is estimated [14] to be near 58 °C for aliphatic side chains and near 42 °C for aromatic side chains.

The partial molal volume of a hydrocarbon is much smaller in aqueous solution than in nonpolar solvents ($\Delta V^\circ < 0$ for the solution process). This can be explained [13] in terms of the specific structural arrangement of water around the nonpolar solute molecules. The formation of hydrogen-bonded water aggregates is accompanied by a volume increase. However, the inert solute molecules occupy part of the cavities occurring in these water structures, resulting in a net decrease of the total volume. Conversely, the formation of hydrophobic bonds is accompanied by a volume increase [14].

A different interpretation of the effects of non-polar groups in water was proposed by *Klotz* [17,18]. According to his view, the formation of regions of ordered water in ice-like sheaths ("hydrotactoids" [18]) in the vicinity of nonpolar groups is favored, because such a structure would be stabilized by these non-polar groups, in analogy with crystalline gas hydrates [19,20]. Such ice-sheaths would lead to the masking of reactive groups. This theory involves difficulties on both thermodynamic and structural grounds. No direct evidence is available for the existence of stable, long-lived immobilized layers of water around macromolecules, as would be required for the permanent masking of groups. While exposed non-polar groups lead to ordering of water, as discussed above, the presence of large regions of this kind would lead to aggregation of the macromolecules [12], in analogy with the formation of micelles.

In the work of *Némethy* and *Scheraga* [14], attention was centered on interactions involving a limited number of amino acid side chains, such as "pairwise interactions" (Fig. 4). On the basis of hydrocarbon solubility and of the statistical thermodynamic theory developed for hydrocarbon solutions [13], lower and upper limits were estimated for ΔF°, ΔH°, and ΔS° of such interactions for all pairs of nonpolar amino acid side chains. Table 1 contains some representative examples for various types of side chains.

Table 1. Thermodynamic and structural parameters (calculated values) for the formation of pairwise hydrophobic bonds of maximum strength between selected amino acid side chains [a] at 25 °C.

Side chains	Thermodynamic parameters			Structural parameters [c]	
	$\Delta F^\circ_{H\varphi}$ kcal mol^{-1}	$\Delta H^\circ_{H\varphi}$ kcal mol^{-1}	$\Delta S^\circ_{H\varphi}$ e.u.	ΔY^s	Z_R
Ala-Ala [b]	−0.3	0.4	2.1	4	2
Ileu-Ileu	−1.5	1.8	11.1	10	5
Phe-Leu	−0.5	0.9	4.7	6	3
Phe-Phe	−1.4	0.8	7.5	12	6

[a] These values are approximately those for a hydrophobic bond of minimum strength between any two side chains.

[b] Ala = Alanine, Ileu = Isoleucine, Leu = Leucine, Phe = Phenylalanine.

[c] The meaning of ΔY^s and of Z_R is explained in the text.

The free energy of the hydrophobic bond $\Delta F^\circ_{H\varphi}$, is derived as a sum of several contributions: The free energy change (ΔF°_W) for the structural change in water, after which ΔY^s water molecules are no longer neighbors of previously exposed nonpolar groups; the difference of the van der Waals forces occuring between the nonpolar groups ($Z_R E_R$, where E_R is the attractive force for a pairwise contact, there being Z_R such pairs) and the forces occurring between the exposed nonpolar groups and the ΔY^s water molecules which were their neighbors ($\frac{1}{2}\,\Delta Y^s E_{RW}$); an entropy change due to the partial loss of flexibility of nonpolar side chains (on macromolecules) when the bond is formed ($\Sigma \Delta F_{rot}$), resulting in the expression

$$\Delta F^\circ_{H\varphi} = \Delta Y^s \Delta F^\circ_W + Z_R E_R - \tfrac{1}{2}\,\Delta Y^s E_{RW} + \Sigma \Delta F_{rot} \qquad (1)$$

The two energy parameters are $E_R = -0.15$ kcal/mole for aliphatic and −0.50 kcal/mole for aromatic groups, $\frac{1}{2}\,E_{RW} = -0.031$ kcal/mole for aliphatic and −0.16 kcal/mole for aromatic groups. ΔF_{rot} ranges from 0 to 0.3 kcal/mole for the amino acids occurring in proteins, depending on the size of the side chain.

[15] *H. J. Sage* and *S. J. Singer*, Biochem. *1*, 305 (1962).

[16] *H. A. Scheraga*, *G. Némethy*, and *I. Z. Steinberg*, J. biol. Chemistry *237*, 2506 (1962).

[17] *I. M. Klotz*, Brookhaven Symp. Biology *13*, 25 (1960).

[18] *I. M. Klotz*, Federat. Proc. *24*, Suppl. *15*, S-24 (1965).

[19] *M. v. Stackelberg* and *H. R. Müller*, Z. Elektrochem., Ber. Bunsenges. physik. Chem. *58*, 25 (1954).

[20] *R. McMullan* and *G. A. Jeffrey*, J. chem. Physics *31*, 1231 (1959).

ΔF_W° is temperature dependent. At 25 °, its value is −0.123 kcal/mole [13]. Typical values of ΔYs and of Z_R are given in Table 1.

This calculation was extended [14,21] to hydrophobic bonds involving nonpolar parts of side chains which are generally classified as polar, such as glutamic acid, glutamine, lysine, or tyrosine. It was shown [21] that such side chains can form hydrophobic bonds with other side chains or even with the peptide backbone, while their terminal polar group can be exposed to the solvent or to other polar groups. For example, in crystalline myoglobin side chains are found which lie parallel to the surface of the molecule [22].

The free energy of interactions involving more side chains was also calculated [14]. In particular, thermodynamic parameters were estimated for the transfer of nonpolar side chains from a completely aqueous environment into an existing nonpolar region [14]. Calculated values for this process are listed in columns 2–4 of Table 2, together, for comparison, with the

Table 2. Calculated thermodynamic parameters of transfer of amino acid side chains and of corresponding hydrocarbons from water into a nonpolar medium at 25 °C.

	Amino acid side chains [a]				Hydrocarbons	
	ΔF_{tr}° (kcal mol^{-1})	ΔH_{tr}° (kcal mol^{-1})	ΔS_{tr}° e.u.	Δf_t [d] (kcal mol^{-1})		ΔF_{tr}° (kcal mol^{-1})
Ala	−1.3	+1.5	+ 9.4	−0.73	Methane	−2.6
Val	−1.9	+2.2	+13.7	−1.69	Propane	−5.0
Leu	−1.9	+2.4	+14.3	−2.42	Butane	−5.8
Ileu	−1.9	+2.4	+14.5	−2.97		
Met	−2.0	+2.7	+16.0	−1.30		
Pro	−2.0	+2.2	+14.0	–		
Phe	−0.3 [b]	+2.7	+10.1	−2.65		
	−1.8 [c]	+1.0	+ 9.5	–	Toluene	−5.3
Contribution of a methyl group				−0.73		−0.8 [e]
Ref.	[14]	[14]	[14]	[23]		[13]

[a] Ala = Alanine, Ileu = Isoleucine, Leu = Leucine, Met = Methionine, Phe = Phenylalanine, Pro = Proline, Val = Valine.

[b] For transfer into aliphatic environment.

[c] For transfer into aromatic environment.

[d] Side chain contribution to the free energy of transfer of an amino acid from water into ethanol, calculated by *Tanford* [23].

[e] For CH_2 increment. From [13]. $\Delta H_{tr}^\circ = -0.23$ kcal/mole, $\Delta S_{tr}^\circ = +1.76$ e.u. for unbranched hydrocarbons.

free energy of transfer of hydrocarbons of similar size from water into a hydrocarbon solvent (column 6). In comparing the values for hydrocarbons and for amino acid side chains, one must bear in mind that the parameters for the transfer of a side chain from one medium to the other must always be smaller in magnitude than for the dissolution of the free hydrocarbon with the same number of carbon atoms. The steric bulk of the peptide backbone reduces the number of solvent molecules in contact with the exposed side chain.

Tanford [23–26] has applied a somewhat different approach to the estimation of the stabilization of protein conformations by hydrophobic bonding. He assumed [23] that the free energy of unfolding of a protein is given as

$$\Delta F = -T\Delta S_{conf} + \Sigma\Delta f_u \qquad (2)$$

where ΔS_{conf} is the change in conformational entropy of the polypeptide chain, and $\Sigma\Delta f_u$ is the free energy change for transfer of the small component groups of the protein molecule from their environment in the native form of the protein to their environment in the unfolded form (Fig. 5). He further assumed (a) that

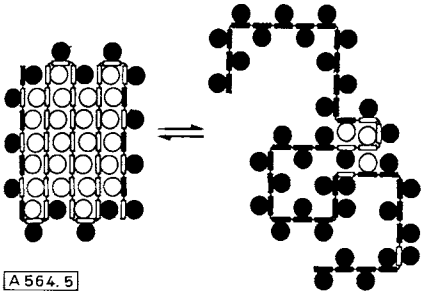


Fig. 5. Schematic diagrams of the native (left) and unfolded (right) states of a protein molecule, according to *Tanford* [25]. Rectangles represent peptide groups, circles indicate side chains. The symbols in black represent groups in contact with the solvent, symbols in white those shielded from the solvent. Reproduced, by permission of the American Chemical Society, from work by *Tanford* [25].

the major part of $\Sigma\Delta f_u$ arises from the exposure of formerly "buried" nonpolar groups to water, (b) that $\Sigma\Delta f_u$ can be calculated additively from the Δf_u values determined for the single amino acid side chains composing the protein, and (c) that Δf_u for the transfer of an amino acid side chain can be equated with Δf_t, the free energy change of the same side chain on transfer from ethanol solution to water. He calculated Δf_t for each amino acid side chain by subtracting the free energy of transfer of glycine from that of the amino acid. By determining the solubilities of the amino acids in mixed solvents, estimates of $\Sigma\Delta f_u$ were made [23,24] for solvent induced denaturation. *Tanford* describes a procedure for the numerical estimation of differences in conformational stability of proteins in various solvents, based on the comparison of Δf_u values for transfer between various solvents.

The Δf_t data determined experimentally by *Tanford* [23] for the ethanol-water transfer are listed in Table 2 for comparison with the calculated values [14]. The difference in the two sets of values may arise from two sources: where $|\Delta f_t| > |\Delta F_{tr}^\circ|$, this may reflect the difference between the free amino acid and the side chain in a bulky protein as discussed above. The nature of the solvent may also play a role. Thus the calculated values are for transfers from hydrocarbons into water, while *Tanford* and *Nozaki* used ethanol as

[21] *G. Némethy, I. Z. Steinberg,* and *H. A. Scheraga,* Biopolymers *1*, 43 (1963).

[22] *J. C. Kendrew,* Brookhaven Symp. Biology *15*, 216 (1962).

[23] *C. Tanford,* J. Amer. chem. Soc. *84*, 4240 (1962).

[24] *Y. Nozaki* and *C. Tanford,* J. biol. Chemistry *238*, 4074 (1963).

[25] *C. Tanford,* J. Amer. chem. Soc. *86*, 2050 (1964).

[26] *Y. Nozaki* and *C. Tanford,* J. biol. Chemistry *240*, 3568 (1965).

the organic medium. The polar OH group of the latter may account for the apparent discrepency.

While one ultimately hopes to be able to derive the free energy of stabilization of a protein conformation from the amino acid composition and the sum total of the possible interactions between the side chains, caution must be exercised in the application of eq. (2). In the native protein, not all amino acid side chains may be buried, and some nonpolar interactions presumably persist in the unfolded state [27a]. Both effects tend to diminish $\Sigma\Delta f_u$ from the value calculated purely from the Δf_t data and amino acid composition. The problem of additivity will be discussed later.

The effect of intramolecular hydrophobic bonding on the conformations of polyamino acid helices can also be studied by the methods of statistical mechanics [27]. Hydrophobic bonds can exist between sufficiently large side chains on adjacent turns of the α-helix [14], and even between a Cβ atom of an L-amino acid and the Cα atom of the fourth preceding residue along the chain in the right-handed α-helix [14]. These hydrophobic bonds can contribute to the stabilization of the α-helix [16]. The Lifson-Roig theory [28] for the helix-coil transition of polyglycine was modified [29] to include the Cβ-Cα hydrophobic bond which occurs in poly-L-alanine. For a chain length of 100 residues, the temperature of the helix-coil transition is increased by 175 °C as compared with a polyglycine of the same size. This result was based on the $\Delta F^{\circ}_{H\varphi}$ value given by *Némethy* and *Scheraga* [14]. Experimentally, it was found [29a] that a poly-L-alanine chain of about 175 residues retains the helical form at least up to 95 °C, while polyglycine (which is not water-soluble) forms no α-helix, even in nonaqueous solvents at room temperature.

In a more detailed treatment of noncovalent bonds in polyamino acids, *Poland* and *Scheraga* [27] have included hydrophobic bonding in the random coil. They showed that, while hydrophobic bonds in helical sequences can stabilize the helix greatly, the presence of such bonds in the random coil largely offsets this stabilization. The thermal transition curves in the absence of hydrophobic bonds and in the presence of such bonds in both helix and coil are very similar (Fig. 6). In the random coil, there is a relatively high probability of formation of hydrophobic bonds between side chains of adjacent residues: about 0.2 for Ala-Ala, 0.3 for Leu-Leu, 0.6 for Ileu-Ileu pairs (Table 3 in [27c]). The probability of formation of large loops in the random coil diminishes rapidly with size.

If t is the number of peptide units between the two interacting side chains, the probability becomes 0.03–0.04 for $t = 2$ and 0.02 for $t = 3$ [27c].

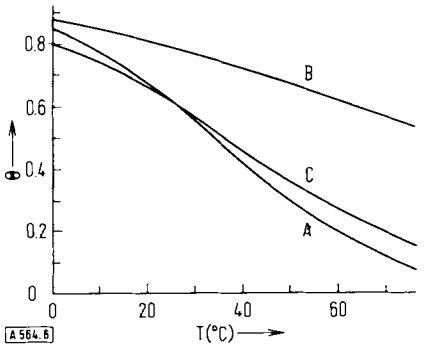


Fig. 6. Calculated helix-coil transition curves of a 20 amino-acid residue polypeptide chain (A) in the absence of hydrophobic bonds, (B) with hydrophobic bonds in the helix only, (C) with hydrophobic bonds in both the helix and the random coil. The ordinate represents the fraction of hydrogen bonds. Reproduced from work by *Poland* and *Scheraga* [27a].

Poland and *Scheraga* also showed that the helix is strongly stabilized if interhelical hydrophobic bonds are present; a sharp helix-coil transition can then occur [27b,c]. Short polyamino acid chains normally form a single, helical sequence but the probability of several shorter helices being formed is high if establishment of inter-helix side chain interactions is thereby permitted. For a particular choice of parameters, *Poland* and *Scheraga* calculated [27b] that at low temperatures (<40 °C) the most probable structure for a 20-residue poly-L-alanine chain has two parallel, interacting helices. The single chain and three interacting helices have lower probability. In the 40–80 ° range, the structure with three interacting helices is most stable, while above this temperature there is a transition to the random coil (Fig. 7). Similar results have been

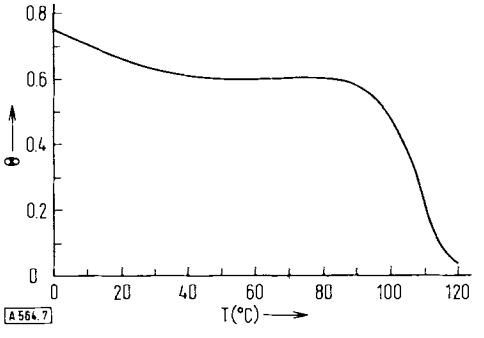


Fig. 7. Calculated helix-coil transition curve for a 20 amino-acid residue poly-L-alanine chain with interactions between helices. The ordinate represents the fraction of hydrogen bonds. Reproduced from work by *Poland* and *Scheraga* [27b].

calculated for longer helices [27c]. The calculated probabilities and transition temperatures are very sensitive to the choice of parameters.

These calculations are at present purely theoretical since no such transitions have been observed yet, possibly because they are beyond the power of present-day experimental techniques for polyamino acids. However, it was suggested by *Poland* and *Scheraga* [27c] that the triple thermal transition occurring in a copolymer of L-leucine and L-glutamic acid [30] may arise from some kind of interhelical interaction. It is notable that the calculated helix-coil thermal transition is sharpened

[27] *D. C. Poland* and *H. A. Scheraga*, Biopolymers *3*, (a) 283, (b) 305, (c) 335 (1965).

[28] *S. Lifson* and *A. Roig*, J. chem. Physics *34*, 1963 (1961).

[29] *M. Bixon, H. A. Scheraga*, and *S. Lifson*, Biopolymers, *1*, 419 (1963).

[29a] *W. B. Gratzer* and *P. Doty*, J. Amer. chem. Soc. *85*, 1193 (1963).

[30] *G. D. Fasman, C. Lindblow*, and *E. Bodenheimer*, Biochemistry *3*, 155 (1964).

considerably if interhelical interactions are assumed and that it then becomes similar to the type of transition curves observed in globular proteins [27b].

Experimental Studies on Model Compounds

The main purpose of solubility studies on model compounds is the determination of free energies of transfer of nonpolar groups (a) from water to a nonpolar solution, in order to estimate the free energy of placing nonpolar groups into hydrophobic regions of proteins, (b) from water to mixed solvents, in order to estimate the contribution of hydrophobic bonds to the stabilization of proteins towards solvent denaturation.

1. Solubilities of Hydrocarbons and the Effects of Heavy Water

Determinations of thermodynamic properties of hydrocarbons provide the most direct information on behavior of nonpolar groups. For this reason, solubility data from the literature were used as standards in developing the theory of water structure and hydrophobic bonding [13,14]. More recently, *Kresheck et al.* [31] have redetermined the solubilities of propane and butane between 0 and 60 °C by a gasometric technique and confirmed their earlier measurements (cited in [13]). They also determined the solubilities of these hydrocarbons in D_2O and found them to be very slightly higher than in H_2O. The free energy of transfer, ΔF_{tr}^{o}, for the process

$$\text{RH (in } H_2O) \rightleftharpoons \text{RH (in } D_2O)$$

is about -40 ± 10 cal/mole at 0 °C and decreases to near zero at 50 °C. On the other hand, solubility measurements for amino acids in D_2O and H_2O by the same authors [31] gave small positive values of Δf_t for the side chain contributions. Micelle critical concentration data in the two solvents [31] also indicate a slightly decreased solubility of nonpolar groups in D_2O. From this *Kresheck et al.* [31] have concluded that hydrophobic bonds are slightly stronger in D_2O. The ΔF_{tr}^{o} for argon [32] has the same sign as ΔF_{tr}^{o} for the hydrocarbons. Thus, either there is a perturbing effect of the polar group to which the amino acid side chains are attached, or there is some error in the observed data for non-polar substances. However, since the solubility differences in the two solvents are very small, no large difference is expected for the strengths of hydrophobic bonds in D_2O and H_2O.

Wetlaufer et al. [33] studied the solubility of several hydrocarbons in 7 M urea and 4.9 M guanidinium chloride solutions (Fig. 8). Except for methane and ethane at low temperatures, the free energy of transfer from water into these solutions is negative (*i.e.* the solubility increases). Its main component is a large positive entropy of transfer predominating over a positive enthalpy contribution. At 25 °C, ΔF_{tr}^{o} ranges from +60 cal/mole for methane to −770 cal/mole for skatole (the analogue of tryptophan). These data agree with the solubility determinations of amino acids by *Nozaki* and *Tanford* [24], discussed below. They indicate that urea and guanidinium chloride must weaken hydrophobic bonds [34].

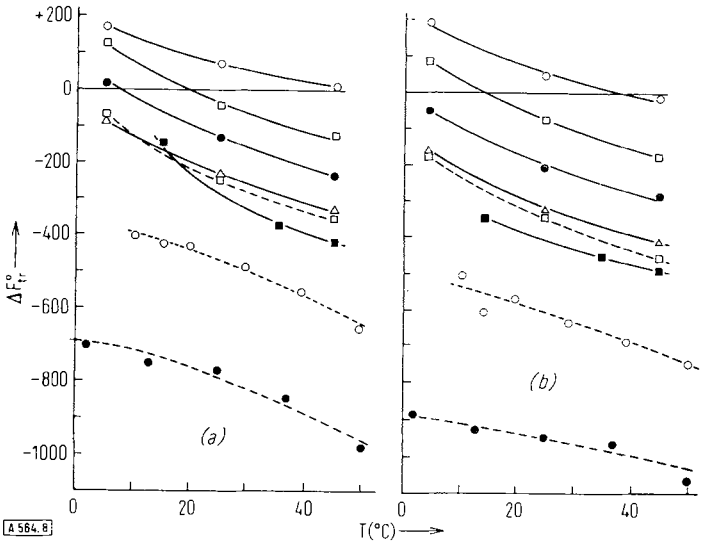


Fig. 8. The temperature dependence of the free energy (cal/mol) of transfer of hydrocarbons from water into (a) a 7 M solution of urea (based on concentrations in mole fractions) and (b) into a 4.9 M solution of guanidinium chloride. Reproduced, by permission of the American Chemical Society, from work by *Wetlaufer et al.* [33].

o—o Methane
□—□ Ethane
●—● Propane
Δ—Δ Isobutane
□—□ Butane
■—■ Neopentane
o—o Toluene
●—● Skatole

The use of hydrocarbons as model compounds has two drawbacks: (a) because of their low solubility in water, it is difficult to obtain sufficiently accurate data, and (b) their use may result in misleading conclusions if the polar substituents in proteins or other multifunctional solutes exert a perturbing effect, *i.e.* if there is no strict additivity of the interactions of various functional groups with water. For these two reasons, much of the work involving model compounds has been done with alcohols, amides, carboxylic acids, and amino acids.

2. Solubilities of Amino Acids

The use made by *Tanford* [23] of solubility data has been cited above. In later work, he and *Nozaki* [24,26] extended the measurements to aqueous urea and

[31] *G. C. Kresheck, H. Schneider,* and *H. A. Scheraga,* J. physic. Chem. *69,* 3132 (1965).

[32] *A. Ben-Naim,* J. chem. Physics *42,* 1512 (1965).

[33] *D. B. Wetlaufer, S. K. Malik, L. Stoller,* and *R. L. Coffin,* J. Amer. chem. Soc. *86,* 508 (1964).

[34] The denaturing effects of urea and of guanidinium chloride may not entirely be due to the weakening of hydrophobic interactions: *Robinson* and *Jencks* [35] have concluded, from a solubility study of *N*-acetyl tetraglycine ethyl ester, that the peptide group itself becomes more soluble in the presence of these two solutes.

[35] *D. R. Robinson* and *W. P. Jencks,* J. biol. Chemistry *238,* PC 1558 (1963).

ethylene glycol solutions. They found an increased solubility for most amino acids, indicating that urea and ethylene glycol tend to weaken hydrophobic bonds. Table 3 summarizes some of their data from which it is evident that urea is a much more effective denaturing agent than ethylene glycol.

Table 3. The measured contribution of side chains to the free energy of transfer of amino acids from water into urea and ethylene glycol at 25 °C. After *Nozaki* and *Tanford* [24,26].

Side chain	Δf_t, cal/mole		
	Urea		Ethylene glycol
	6 M	8 M	30 %
Ala [a]	+ 10	+ 10	+ 30
Leu	−225	−295	−130
Met	−325	−415	− 65
Phe	−470	−600	−215
Try	−730	−920	−515
Tyr	−580	−735	−305
Gln	−190	−230	+ 10

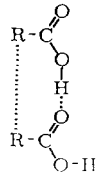
[a] Ala = Alanine, Gln = Glutamine, Leu = Leucine, Met = Methionine, Phe = Phenylalanine, Try = Tryptophan, Tyr = Tyrosine.

As pointed out by *Wetlaufer* [33], the amino acid solubility data are to be preferred to those of hydrocarbons if the additivity of functional group effects is violated by the presence of the peptide group. However, it may even be doubted whether free amino acids are fully adequate as models for the peptides of a protein chain, since the former contain near by charged NH_3^+ and COO^--groups.

3. Interactions Involving Other Low Molecular Weight Compounds

Solubility measurements provide information analogous to the transfer of nonpolar groups from aqueous medium to the protein interior where they are "buried". In estimating the stabilization of proteins by hydrophobic bonds, it is equally important to know the interactions between nonpolar groups which are not completely buried. These correspond to the "pairwise" hydrophobic bonds for which the theory was developed by *Némethy* and *Scheraga* [14].

It was shown by *Schrier*, *Pottle*, and *Scheraga* [36] that the increase in the dimerization constants of carboxylic acids with chain length (from formic through acetic, propionic, and butyric to phenylacetic acids) in water can be explained in terms of hydrophobic bond formation between the nonpolar side chains of the dimerized acids according to formula *(1)*.



(1)

A single hydrogen bond is formed between the carboxyl groups, whereas presumably a double hydrogen bond is formed between the dimers in the gas phase where the dimerization constant is independent of chain length. The increments in dimerization constants in aqueous solution are close to the values predicted from hydrophobic bonding theory [14].

In a similar study, the thermodynamic parameters were determined [37] for the adsorption of several carboxylic acids and alcohols from water onto a polystyrene interface. While there was approximate agreement between theoretical [14] and experimental values for the effects of the nonpolar tail groups in the acids, no such agreement was found for the alcohols. Interpretation of the observed data involves several uncertainties both because of pronounced head group effects in adsorption and because the nature of nonpolar interactions in the polystyrene-adsorbent system is not so well defined as in a solution system.

The dimerization of higher carboxylic acids in terms of the formation of hydrophobic bonds has also been analyzed by *Mukerjee* [38]. He points out that the hydrophobic contribution to dimerization seems to level out after a certain size ($C_{16}H_{31}COOH$), presumably due to the coiling of long side chains and concurrent changes in the degree of exposure of methylene groups to water (cf. [13]).

Eagland and *Franks* [39] have studied the hydrolysis of fatty acid soaps and shown that the chain length dependence of the rate of hydrolysis indicates association of fatty acid molecules into the form $HX{\cdot}X^-$; the thermodynamic parameters agree with hydrophobic bonding theory [14].

Micelles

The formation of micelles gives an excellent example of the stabilization of nonpolar aggregates by hydrophobic bonding. Micelle formation involves pronounced head-group effects, as evidenced by the large observed variety of critical micelle concentrations and their sizes and shapes in different systems. However, the interaction between the nonpolar groups was recognized as one of the decisive factors in the early theories of micelle formation [40,41]. In their treatment of nonionic micelle stability, *Poland* and *Scheraga* [42] have discussed micelles in terms of hydrophobic bonding: the free energy of the micelle is shown to be composed of terms relating to the micelle as a whole, to internal freedom of motion of hydrocarbon chains in the micelle, and to solvent contri-

[36] *E. E. Schrier*, *M. Pottle*, and *H. A. Scheraga*, J. Amer. chem. Soc. *86*, 3444 (1964).

[37] *H. Schneider*, *G. C. Kresheck*, and *H. A. Scheraga*, J. physic. Chem. *69*, 1310 (1965).

[38] *P. Mukerjee*, J. physic. Chem. *69*, 2821 (1965).

[39] *D. Eagland* and *F. Franks*, Trans. Faraday Soc. *61*, 2468 (1965).

[40] *P. Debye*, J. physic. Colloid Chem. *53*, 1 (1949).

[41] *E. D. Goddard*, *C. A. J. Hoeve*, and *G. C. Benson*, J. physic. Chem. *61*, 593 (1957).

[42] *D. C. Poland* and *H. A. Scheraga*, J. physic. Chem. *69*, 2431 (1965).

butions. The latter were treated in terms of the theory of hydrophobic bonding [14], which accounts well for the dependence of micelle size on concentration and temperature [43].

Micelles can also serve as models in the study of the effect of solvent additives on hydrophobic bonding. In particular, the effect of urea on micelles has been studied by several workers [45,46]. Urea raises the critical micelle concentration, indicating a weakening of hydrophobic bonds (cf. the solubility data discussed above). Studies on the association of dye molecules give similar results [47].

Proteins

1. Interactions with Nonpolar Solutes

One of the means of studying hydrophobic bonding in proteins is the investigation of their interactions with low molecular weight non-polar solutes. Binding of nonpolar solutes to nonpolar regions of proteins can have two effects: (a) the solubility of the solute can be increased, either by adsorption on the surface of the protein or by incorporation into hydrophobic regions, or (b) the solute can induce conformational changes in the protein in that the hydrophobic regions are disrupted because of the formation of stronger solute-nonpolar group hydrophobic interactions.

An example of the first effect is seen in the work of *Wishnia* [48]. He measured the solubility of ethane, propane, and butane in solutions of bovine serum albumin, hemoglobin, and lysozyme. The solubilities in the protein solutions increase several fold over those in water. The ratio of the solubilities in water and in the protein solutions is almost constant over a temperature range of 25 °C, indicating that the enthalpy of binding is small and that the solubilization is entropy-driven. A similar effect was observed for the solubilization of these hydrocarbons in micellar dodecyl sulfate solutions [49].

Wishnia and *Pinder* [50] have shown that the F-form of bovine serum albumin, stable at pH < 4, binds hydrocarbons to a much smaller extent than the N-form: the ratio of binding is 1:4 for butane and 1:5 for pentane. For the transfer of butane from water to the protein solution, $\Delta S^\circ = 17$ e.u. and ΔH° is near zero. Both values are close to those for the transfer of a hydrocarbon from water to a nonpolar solution [13]. The results were interpreted [50] as indications that the hydrocarbon binding sites are in hydrophobic regions of the protein molecule, and that the sites are altered during the conformational change because of disruption of the hydrophobic regions. From similar studies on β-lactoglobulins A and B, *Wishnia* and *Pinder* concluded [51] that in these proteins, only hydrophobic regions of limited size can incorporate hydrocarbons.

In proteins of marginal conformational stability, the binding of a nonpolar solute may induce a conformational change. *Wetlaufer* and *Lovrien* [52] have observed rapidly reversible changes in the viscosity, titration behavior, optical rotation, and ultraviolet spectrum of bovine serum albumin at alkaline pH values and of β-lactoglobulin in the neutral pH range, on addition of various hydrocarbons.

Conversely, hydrophobic bonding of small molecules on the surface of a protein molecule may protect the protein from unfolding. For example, sodium dodecyl sulfate protects bovine serum albumin from denaturation [53,54]. The protective effect requires the simultaneous binding of the anionic head group to cationic groups on the protein surface [54]. Thus the detergent acts as a bifunctional binding reagent. Presumably, this is the reason for the difference between its effect and that of the hydrocarbons.

A systematic study of the effect of nonpolar compounds on protein denaturation was undertaken by *Schrier* and *Scheraga* [55,56]. The addition of alcohols to aqueous solutions of ribonuclease lowers the temperature of thermal transition, T_{tr}. The change in T_{tr} is proportional to the alcohol concentration (up to several molar) and increases with the chain length of the alcohol (Fig. 9 and Table 4). The lowering of T_{tr} can be calculated from hydrophobic bonding theory by estimating a binding constant of the alcohol to the

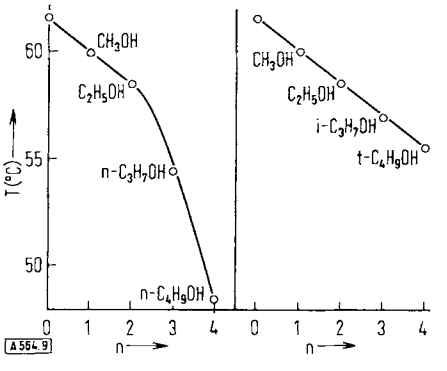


Fig. 9. The temperature of thermal denaturation of ribonuclease in 1 M alcohol solutions: (a) straight-chain, (b) branched chain (n is the number of C atoms in the alkyl chain of the alcohol). Reproduced by permission of the American Chemical Society, from work by *Schrier, Ingwall*, and *Scheraga* [56].

[43] The theory could also be extended to account for the behavior of micelles whose molecules carry charges [44].

[44] *D. C. Poland* and *H. A. Scheraga*, J. Colloid Sci. *21*, 273 (1966).

[45] *W. Bruning* and *A. Holtzer*, J. Amer. chem. Soc. *83*, 4865 (1961).

[46] *P. Mukerjee* and *A. Ray*, J. physic. Chem. *67*, 190 (1963).

[47] *P. Mukerjee* and *A. K. Ghosh*, J. physic. Chem. *67*, 193 (1963).

[48] *A. Wishnia*, Proc. nat. Acad. Sci. USA *48*, 2200 (1962).

[49] *A. Wishnia*, J. physic. Chem. *67*, 2079 (1963).

[50] *A. Wishnia* and *T. Pinder*, Biochemistry *3*, 1377 (1964).

[51] *A. Wishnia* and *T. W. Pinder, jr.*, Biochemistry *5*, 1534 (1966).

[52] *D. B. Wetlaufer* and *R. Lovrien*, J. biol. Chemistry *239*, 596 (1964).

[53] *R. Lovrien*, J. Amer. chem. Soc. *85*, 3677 (1963).

[54] *G. Markus, R. L. Love*, and *F. C. Wissler*, J. biol. Chemistry *239*, 3687 (1964).

[55] *E. E. Schrier* and *H. A. Scheraga*, Biochim. biophysica Acta *64*, 406 (1962).

[56] *E. E. Schrier, R.T. Ingwall*, and *H. A. Scheraga*, J. physic. Chem. *69*, 298 (1965).

Table 4. The lowering of the temperature T_{tr} of the thermal denaturation of ribonuclease in aqueous solution by various alcohols (concentration: 1 M).

Alcohol	$\Delta F^{\circ}_{H\varphi}$ [a], [56] kcal/mole	ΔT_{tr} (°K) [b] Calculated [56]	Observed [56] [c]	Observed [57]
CH_3OH	−0.80	− 1.9	− 1.6	−1.4
CH_3CH_2OH	−1.15	− 3.3	− 3.1	−3.0
$CH_3CH_2CH_2OH$	−1.55	− 6.0	− 7.1	−7.5
$CH_3CH_2CH_2CH_2OH$	−1.95	−11.0	−13.1	

[a] Free energy of hydrophobic bond formation between the non-polar part of the alcohol and a nonpolar region of similar size on the ribonuclease. Calculated for 62 °C.

[b] T_{tr} = 61.5 °C at pH 6.7 in the absence of alcohols [55].

[c] Cf. Fig. 11.

protein from the free energy $\Delta F^{\circ}_{H\varphi}$ of such bonds and from the entropy loss on association [56] (Table 4). Interestingly, the lowering of the transition temperature by branched-chain alcohols (*e.g.* iso-propanol) is closer in magnitude to that caused by the next lower straight-chain homologue (ethanol) than to the corresponding normal alcohol (n-propanol) [55]. Apparently, the nonpolar binding sites are limited in size or shape so that not all of the nonpolar tail of the branched alcohols can bind to them. One must treat the alcohols in terms of an "effective chain length", corresponding to the unbranched part of the molecule.

In a study of the effect of various solutes on the thermal transition of ribonuclease, *von Hippel* and *Wong* [57] obtained similar results for various tetraalkylammonium salts and for alcohols. The lowering of the transition temperature increases with chain length. The effective chain length differs from that of alcohols: for example, isopropanol and tetra-n-propyl ammonium salts produce nearly the same temperature change. The magnitudes of the change in T_{tr} for 1 M solutions in alcohol which were observed in the two studies are in close agreement (Table 4). *Von Hippel* and *Wong* interpret their results, not in terms of direct binding of the solute to nonpolar groups, but rather as a diminution in the availability of water molecules for "iceberg formation" about exposed nonpolar chains as a result of competition by the added solute. The model based on direct interaction between solute molecules and nonpolar groups [56] would fit *von Hippel* and *Wong*'s data better: if the action were due to the decreased availability of water, tetra-n-propyl ammonium bromide would be at least four times as effective as ethanol, since it has four, longer hydrocarbon chains.

While the effects cited can clearly be assigned to hydrophobic interactions, it is not always easy to determine the exact nature of the interaction causing denaturation for multifunctional additives, or even to predict which function of a compound will be the most important stabilizing or destabilizing factor. *Jencks et al.* [58,59] have discussed the effect of various denaturing agents for proteins and DNA, and found that denaturing strength is not correlated in all cases with the hydrophobic character of the reagent.

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2. Other effects

Association of protein subunits can be stabilized by hydrophobic bonding. The polymerization of tobacco virus protein [60] is an endothermic process. It is also accompanied by the release of large amounts of tightly bound water, and an increase in partial molal volume. The association could be caused either by the formation of intermolecular ion pairs, with the release of water bound to the ions, or by the formation of intermolecular hydrophobic bonds.

Although conformational changes of enzymes, related to the effects of substrates, activators, or inhibitors, are often interpreted in terms of hydrophobic bonding, many recent papers have omitted a quantitative evaluation of the data.

The effect of hydrophobic bonding on the binding of substrates or inhibitors to enzymes has been treated quantitatively in only a few cases. An example is provided in a paper by *Anderson et al.* [61] who have studied the inhibition of yeast alcohol dehydrogenase by 1-alkyl-3-aminocarbonylpyridium chlorides, as a function of the alkyl chain length over the range C_1 to C_{11}. The effectiveness of the inhibitors, as measured by the binding constant for inhibition, increases linearly with chain length from C_3 to C_{11}. The increment in the free energy of binding is −0.37 kcal/mole per CH_2 group which is in good agreement with theoretically calculated values (Table 4, column 2).

Zahn [62] has called attention to the role of hydrophobic bonding in fibrous proteins. The results of various experiments on wool keratin and collagen, *e.g.* the weakening of the tensile strength of wool keratin fibers and the lowering of the shrinkage temperature of collagen by alcohols [62,63] parallel closely those for globular proteins. The observed chain length dependence is similar to that in the ribonuclease transition [55,56], even to the need for the use of the concept of "effective chain length". The reactivity of SH-groups in wool is enhanced by the addition of alcohols, but reduced by sodium dodecyl sulfate (cf. effects on bovine serum albumin).

3. Conformational Stability of Polyamino Acids

Hydrophobic bonds can be expected to play a role in the stabilzation of both α-helical and β-structures of polyamino acids [14] (Figs. 10 and 11). *Fasman et al.* [30] found an increase in helix content (as measured

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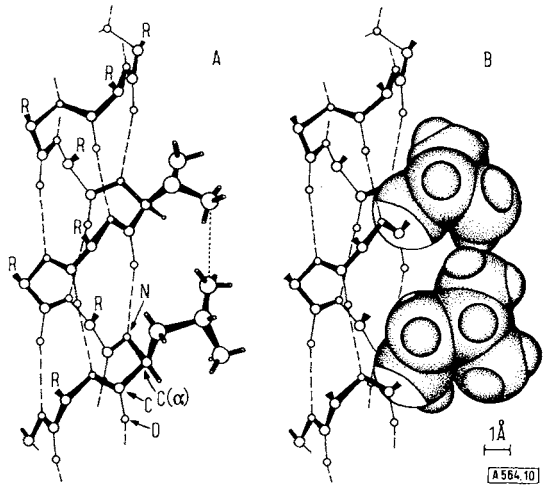


Fig. 10. Hydrophobic bond between an L-leucyl and an L-valyl side chain on adjacent turns of a right-handed α-helix. The dashed lines represent peptide hydrogen bonds. (A) Skeletal drawing showing the position of the atoms. The dotted line indicates the methyl groups in contact. (B) Space-filling model of the side chains, drawn to scale [14].

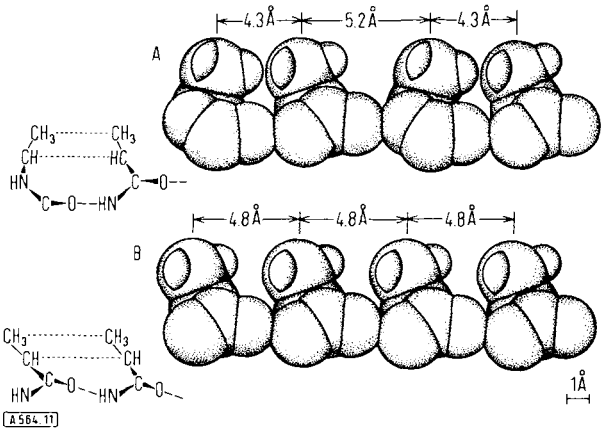


Fig. 11. Hydrophobic bonds between neighboring peptide chains in pleated sheet structures; (A) chain running antiparallel and (B) running parallel [14]. The van der Waals radii are drawn to scale. The peptide chains run perpendicularly to the plane of the drawing. The side chains are represented as alanines. On the right are shown space-filling models corresponding to the structural formulae on the left. The distances shown between the β-CH_3 groups are corrected values [14a].

by b_0 of the Moffitt equation) with increasing temperature for both poly-L-glutamic acid and a copolymer of L-glutamic acid and L-leucine over a limited temperature range. This inversion of thermal stability has been attributed to hydrophobic bonding [27c, 30].

Gratzer and *Doty* [64] have shown that a poly-L-alanine helix of 175 residues is very stable in water. The result can also be explained easily in terms of hydrophobic bonds [16, 27a, b, 29]. According to the theoretical treatment [27a, 29], shorter poly-L-alanine sequences should have thermal transitions in a lower temperature range; this has been qualitatively confirmed [65]. In these studies, the nonpolar polyamino acid was rendered water-soluble by flanking it at both ends with blocks of randomly coiled poly-D,L-glutamic acid or poly-D,L-lysine. *Auer* and *Doty* [66] showed that poly-L-leucine and poly-L-phenylalanine α-helices are less stable than the poly-L-alanine α-helix in chloroform solution, presumably because of steric interference of the bulky chains. Conversely, the order of stability to the helices in water is poly-L-leucine > poly-L-phenylalanine > poly-L-alanine. This can be ascribed of hydrophobic bonding between the side chains.

The Effect of Urea

At one time, the denaturing action of urea was thought to be due to its ability to compete with intramolecular peptide hydrogen bonding. However, evidence has accumulated recently which shows that urea also weakens hydrophobic bonding. Measurements of solubilities [24, 33] and of micelle stability [45, 46] indicate that nonpolar groups are more soluble in aqueous urea solutions than in water. The same effect has been observed with azo dyes for which thermodynamic data are available [67]. In a calorimetric study [68] of amino acids and peptides with nonpolar side chains, a high partial molal heat capacity C_{p2} was obtained for these solutes in water, this being in agreement with the theoretical postulate [13] of more ordered water structure around them. However, C_{p2} is lower in solutions of urea. Very likely, protein denaturation by urea involves the breaking of hydrophobic regions. In some cases there is a poor correlation between the expected effects of urea, based on the model compounds, and observed effects in proteins. Example of such discrepancies are found in the thermodynamics of denaturation of chymotrypsinogen [69], or the difference in the heat capacity of ovalbumin [68] in aqueous and urea solutions. *Tanford* [25] has made theoretical estimates of the free energy of unfolding for proteins in urea, based on the studies of model compounds [24]. While no equilibrium constant for the unfolding could be calculated *a priori*, the comparison of experimental and calculated data suggested that the unfolding may occur in several steps [25].

As yet, the mechanism of the action of urea has not been interpreted quantitatively in terms of effects on water structure or on the water-hydrocarbon interactions. *Frank* and *Franks* [70] suggest that the effect may be explained in terms of changes in the relative amounts of ordered and disordered water when urea is added. For reason of geometry, urea can mix into the disordered water regions only. In so doing it lowers the chemical potential of disordered water causing some clusters to melt in order to reestablish the equilibrium. A detailed theoretical treatment has not yet been published so that the explanation of the effect of urea on hydrophobic interactions and hence on protein denaturation remains one of the important unsolved questions in this field of research.

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Experimental Studies on other Macromolecules

Very little work has been done on hydrophobic interactions in macromolecules other than proteins and polyamino acids.

It can be expected that stacking in polynucleotides and in nucleic acids involves hydrophobic interactions because of the large, partially nonpolar areas of the bases which come into contact with each other. *Fasman et al.*[71] have studied the optical rotatory dispersion of single-stranded polycytidylic acid and found that, in aqueous solution at pH 7.0, the molecule appears highly ordered. Since the order is destroyed by the addition of methanol or of ethylene glycol, evidence exists for the importance of hydrophobic interactions in stacking. On the other hand, studies on trinucleotides[72] and on polyadenylic acid[73] indicate that, for these compounds, the predominating factor in neighbor-neighbor stacking interaction is not the hydrophobic bond, although it, too, can make an important contribution.

Sinanoğlu[74] has treated the denaturation of DNA in terms of hydrophobic interactions. However, in his theory, the free energy of placing a nonpolar group into solution is interpreted in terms of the energy requirement for the creation of a solvent cavity around the group, and is correlated with the surface tension. This replaces a structural description with a discussion in terms of a macroscopic property of the liquid.

Studies of synthetic polymers in aqueous solution are rare, owing to problems of solubility. *Eliassaf*[75] has attributed the difference in some thermodynamic properties of polyacrylic acid and polymethacrylic acid solutions to the possibility of hydrophobic bond formation in the former but not in the latter.

Methods for the Detection of Hydrophobic Interactions

Most of the conclusions about the effect of nonpolar solutes on water structure, and about hydrophobic interactions in macromolecules are based on indirect evidence, primarily thermodynamic data, since no methods are available for the direct measurement of hydrophobic interactions.

It would be desirable to be able to detect the increase in water structure around nonpolar solutes directly, both in order to obtain proof for the structural theories of aqueous solutions, and to develop a tool for the detection of the formation and breaking of hydrophobic bonds. Nuclear magnetic resonance techniques have a potential for such work, since they provide information about the correlation and relative motions of neighboring molecules. Measurements of changes in the hydrogen chemical shift have produced ambiguous results which are difficult to interpret (see, for example, the discussion by *Clifford* and *Pethica*[76]). On the other hand, relaxation times of water are increased in the neighborhood of dissolved nonpolar substances by a factor of about two compared with pure water[77,78], indicating an increase in the ordering of water in the solution. On the basis of his nuclear magnetic resonance measurements[77], *Hertz* has developed a new theory[79] of aqueous solutions to explain structural changes. He gives a qualitative description, so that no full evaluation of the scope of the theory is possible yet.

The presence of hydrophobic regions inside or on the surface of a protein molecule has often been inferred from the binding of small molecules (*e.g.*[48,53,61]) or from changes in the reactivity of certain functional groups (*e.g.*[52,62]). Similarly, alterations of the UV spectra of chromophoric groups in macromolecules can be interpreted in terms of these groups being buried inside nonpolar regions of the protein, and thus becoming inaccessible to water[80,81]. The groups whose spectra are studied can occur naturally in the macromolecule, such as tyrosine or tryptophan in proteins[80], or they can be introduced artificially, whereby one obtains an easily interpretable spectrum or one can label specific sites of the molecule[82].

The fluorescence of certain dyes depends strongly on the nature of their solvent environment. The use of fluorescent dyes which can be adsorbed into nonpolar regions has been suggested[83,84] as a tool for probing hydrophobic regions of proteins. *McClure* and *Edelman*[84] have initiated a study of this effect in various solvent environments.

Conclusions

Hydrophobic interactions occur widely in aqueous solutions of both biological macromolecules and materials of low molecular weight. While the principles governing their occurrence are well understood, and it is possible to calculate their strength from theory, there are also several open problems relating to their detection and to the interpretation of their effects.

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In experimental work, reliable and accurate means of the detection and measurement of hydrophobic bonding are lacking. In the interpretation of the effect of noncovalent interactions upon the thermodynamic behavior of solutes in general and upon the conformation of macromolecules in particular, the so far unsolved question of additivity must be raised: Is the total contribution of various types of noncovalent interactions the sum of the individual contributions of each of them, as determined by composition and spatial arrangement and according to parameters derived from simple model compounds, or do the various interactions perturb each other? The question has been discussed by *Némethy et al.* [21], *Tanford* [23], and *Wetlaufer et al.* [33]. It seems that the effects of various functional groups are approximately additive. However in exact quantitative treatments deviations from additivity will have to be considered explicitly.

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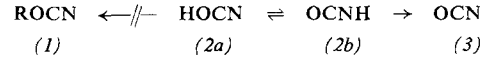
New Methods of Preparative Organic Chemistry VI[**]

Synthesis and Reactions of Cyanic Esters

BY E. GRIGAT AND R. PÜTTER [*]

In 1963, it was found that sterically unhindered esters of cyanic acid, which had previously been considered unobtainable, could be easily prepared from phenols and cyanogen halides. Another synthesis, involving the thermolysis of thiatriazole derivatives, was discovered in 1964. The aryl cyanates in particular have since been found to have many uses as starting materials for the preparation of numerous new classes of compounds [e.g. derivatives of esters of imidocarbonic acid (esters, amides, imides, hydrazides, hydroxylamides, sulfamides, sulfhydrazides, semicarbazides); esters of imidocarboxylic acids; s-triazines, pyrimidines, tetrazoles, triazoles, triazolones, oxadiazoles, thiadiazoles, benzoxazinones, etc.], mainly by addition of nucleophilic or 1,3-dipolar reactants, or as aids e.g. in the elimination of H_2O or H_2S or in the transfer of CN groups.

The preparation of true esters *(1)* of cyanic acid, *i.e.* those in which the organic group is bonded to the oxygen, was a problem that remained unsolved for a very long time. Since cyanic acid always reacted in the iso form *(2b)* to give isocyanates *(3)* [1], attempts were made as early as the second half of the 19th century to



(1) *(2a)* *(2b)* *(3)*

synthesize the molecule *(1)* by combination of a component RO– with a component –CN. However, cyanates could not be obtained either by the reaction of esters of hypochlorous acid with cyanides [2, 3] or by the reaction of phenoxides (or alkoxides) with cyanogen halides [4–10].

In 1895 it was reported by *Nef* [9] and by *Hantzsch* and *Mai* [10] that the reaction of phenoxides (alkoxides) with cyanogen halides leads only to imidocarbonates *(4)* and cyanurates *(5)*. Though *Nef* regarded *(6)* as an intermediate in the formation of *(4)*, and considered *(5)* to result from the decomposition of *(4)* with elimination of phenol [9], it seems reasonable to assume that the products *(4)* and *(5)* are in fact formed by further reaction of an initially formed cyanate.

An exception is the reaction of sterically hindered *o*-substituted phenols with cyanogen chloride, which according to *Stroh* and *Gerber* [11] represents the first preparation of true cyanate esters. The expected

[*] Dr. E. Grigat and Dr. R. Pütter
Wissenschaftliches Laboratorium der Zwischenproduktenabteilung der Farbenfabriken Bayer AG.
509 Leverkusen-Bayerwerk (Germany)

[**] The articles of the previous five series have been published in five volumes by Verlag Chemie, Weinheim/Bergstr. English edition: Academic Press, New York-London. The present article, with the addition of procedures, will be published in Vol. VI of this series.

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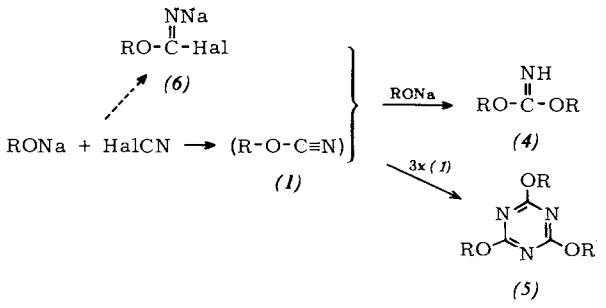
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further reaction of *(1)* to form *(4)* or *(5)* does not take place because of steric hindrance by the *ortho* substituents. The cyanate structure was recognized from the IR spectra [12] and from the formation of carbamates on hydrolysis.

1. Synthesis of Cyanates

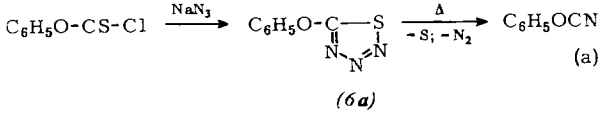
Early in 1963, we discovered a simple synthesis of cyanates by reaction of phenols with cyanogen halides (avoiding an excess of phenoxide) [13–15]. This method is successful with mono- and polyphenols as well as with a number of aliphatic hydroxy compounds, and can be easily carried out on an industrial scale. Most aryl cyanates are surprisingly stable; they are formed

$$ArOH + ClCN \xrightarrow[-\text{Base}\cdot HCl]{+\text{Base}} ArOCN \qquad (1)$$

in excellent yields, and in many cases almost quantitatively.

About a year later, but before the publication of our first patent application [13], *D. Martin*, Berlin [16], and *K. A. Jensen* and *A. Holm*, Copenhagen [17], simultaneously reported the formation of phenyl and ethyl cyanates on thermolysis of phenoxy- *(6a)* and ethoxy-1,2,3,4-thiatriazole *(6b)*.

Martin obtained phenyl cyanate in accordance with equation (a). He used this method for the preparation

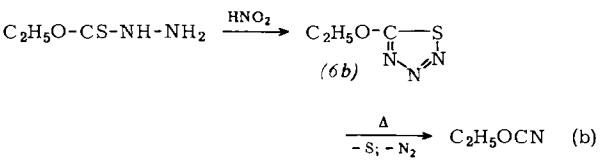


(a)

(6a)

of a number of aryl cyanates [18], and later for alkyl cyanates [20].

Jensen and *Holm* obtained ethyl cyanate in accordance with equation (b), and subsequently also obtained other alkyl cyanates [19]. The yields of aryl cyanates produced by this method are generally lower than



(b)

(6b)

when phenol and cyanogen chloride are used. Alkyl cyanates are obtained in yields of only 60 % by equation (a) and 75–80 % equation (b).

Jensen and *Holm* also obtained cyanates by the elimination of H_2S from thiocarbamates with heavy metal oxides (yields: 40–57 %) [24]. Attempted syntheses using this method had hitherto proved unsuccesful [21–23].

Finally, *Kauer* and *Henderson* [25] reported the preparation of three aliphatic cyanates (cf. Table, p. 217) by the reaction of sterically hindered alkoxides or "bridgehead" alcohols with cyanogen chloride. *Hedayatullah* and *Denivelle* prepared a few cyanates by the methods known at the time (cf. Table, p. 216) [26].

2. Reactions of the Cyanates

Alkyl cyanates *(1)* readily undergo exothermic rearrangement to form alkyl isocyanates *(3)* [17,19,20,25]; the tendency toward isomerization decreases with increasing chain length of the alkyl group. The rearrangement of cyanates of bicyclic alcohols having the OH group in the bridgehead position proceeds only when catalysed by Lewis acids [25]. Cyanates of secondary alcohols (*e.g.* isopropanol) decompose into olefin and HOCN [19]. Thus alkyl cyanates behave in the same manner as the alkyl thiocyanates, which also rearrange readily to form alkyl isothiocyanates.

Because of this tendency toward isomerization, the alkyl cyanates have not yet assumed preparative importance. To verify their constitution they have been converted into known secondary products by the addition of H_2S [17,19] or alcohol [20,25], and apart from this they have been used in preparative reactions in two cases only (cf. Sections 2.1.8. and 2.2.1) [79,82].

Aryl cyanates, on the other hand, like the aryl thiocyanates, do not rearrange to form aryl isocyanates They can be used for many further reactions which will be discussed in the following survey.

Cyanates of acidic alcohols,particularly the halogeno alcohols such as β,β,β-trichloroethyl alcohol [14,15], are very similar in stability and reactivity to the aryl cyanates.

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2.1. Addition of Nucleophiles to Aryl Cyanates

The carbon atom of the OCN group is strongly electrophilic because of its two electronegative neighbors. Therefore, nucleophilic reagents can react with these substances under mild conditions. The addition is catalysed by both acids (activation of the OCN group by protonation) and bases (increase in the nucleophilic strength of the other reactant by proton abstraction). The addition of nucleophiles is the most important reaction in the preparative chemistry of cyanates.

2.1.1. Nucleophiles having One Mobile Hydrogen on the O, S, or N Atom

Reagents *(7)* with a nucleophilic O, S, or N atom carrying one mobile hydrogen atom add to the CN group of the aryl cyanates under mild conditions to give adducts *(8)* that cannot be obtained in any other way. When heated, or with alkali, the adducts *(8)* generally undergo cleavage as in equation (c), with formation of the phenol from which the aryl cyanate is derived. Thus the cyanates can act as cyanide donors.

$$\underset{(1)}{ArOCN} + \underset{(7)}{HX} \longrightarrow \underset{(8)}{ArO\text{-}\overset{\overset{NH}{\|}}{C}\text{-}X} \longrightarrow \underset{(9)}{ArOH} + NC\text{-}X \quad (c)$$

X = OR, SR, NRR'

The reactions indicated by equation (c) are illustrated by the following examples:

Phenols (HX = HOAr) add smoothly to aryl cyanates in the presence of bases to give symmetrical or unsymmetrical bisaryl imidocarbonates [26–28], generally *via* both possible routes. When the substituents Ar and Ar′ are different, the decomposition of *(10)* leads to the formation of the more acidic phenol [28].

$$\begin{array}{l} ArOCN + Ar'OH \\ \qquad\qquad \searrow \\ \qquad\qquad\quad ArO\text{-}\overset{\overset{NH}{\|}}{C}\text{-}OAr' \longrightarrow ArOH + (Ar'OCN) \\ \qquad\qquad \nearrow \qquad\qquad\quad \downarrow \\ ArOH + Ar'OCN \qquad\quad (10) \qquad\qquad (Ar'OCN)_3 \end{array}$$

$$pK_{ArOH} < pK_{Ar'OH}$$

Aryl cyanates do not react with alcohols (HX = HOAlk) in the absence of catalysts. In the presence of bases and acids, the reaction yields alkyl aryl imidocarbonates *(11)*, the hydrochlorides of which are stabilized by loss of alkyl halide to form carbamates *(12)* [28–30].

$$\begin{array}{l} \qquad\qquad\qquad\qquad\qquad\qquad\quad \overset{\overset{O}{\|}}{ArOC\text{-}NH_2} + AlkCl \\ \qquad\qquad\qquad\qquad\quad \overset{\overset{NH}{\|}}{} \quad HCl \nearrow \quad (12) \\ \underset{(1)}{ArOCN} + HOAlk \longrightarrow \underset{(11)}{ArO\text{-}\overset{\overset{NH}{\|}}{C}\text{-}OAlk} \\ \qquad\qquad\qquad\qquad\qquad\quad Base \searrow \\ \qquad\qquad\qquad\qquad\qquad\qquad\quad ArOH + (NCO\text{-}Alk) \end{array}$$

An excess of alkoxide leads to decomposition of *(11)* according to the general equation (c). Loss of phenol results in the formation of alkyl cyanate which trimerizes to give cyanurate or adds alkoxide to form a symmetrical dialkyl imidocarbonate [28]. The decomposition of unsymmetrical dialkyl imidocarbonates proceeds similarly [25]. In an excess of alcohol with acid catalysis, *(1)* gives moderate yields of orthocarbonate [30].

In the reaction of aryl cyanates with mercaptans (HX = HSR) or thiophenols, the cyanide group is transferred from the oxygen to the sulfur [32] *via* the thioimidocarbonate *(13)* [31]. The transfer proceeds particularly smoothly in the case of electronegatively

$$\underset{(1)}{ArOCN} + R'SH \longrightarrow \underset{(13)}{ArO\text{-}\overset{\overset{NH}{\|}}{C}\text{-}SR'} \longrightarrow ArOH + R'\text{-}SCN$$

substituted cyanates. In many cases, the thioimidocarbonates *(13)* can be isolated as crystalline substances [32]; they were not previously available by any other route. Thus this method can be used for the introduction of a thiocyanate group under mild conditions [33].

Secondary amines (HX = HNRR′) add to *(1)* to give isoureas *(14)* [34–37].

$$ArOCN + HN\begin{matrix} R \\ R' \end{matrix} \longrightarrow \underset{(14)}{ArO\text{-}\overset{\overset{NH}{\|}}{C}\text{-}N\begin{matrix} R \\ R' \end{matrix}} \xrightarrow[Base]{\Delta} ArOH + NC\text{-}N\begin{matrix} R \\ R' \end{matrix}$$

Whereas the *O*-arylisoureas *(14)* are decomposed by heat or by alkali into phenols and cyanamides, their salts (*e.g.* hydrochlorides, sulfates) are very stable even toward heat [36]. The imino group of *(14)* can be acylated by acyl and sulfonyl halides, cyanogen halides, or even isocyanates, or alkylated with alkylating agents [36].

$$(14) + XR^2 \rightarrow ArO\text{–}C(=NR^2)\text{–}NRR' + HX$$

X = Halogen; $R^2 = COR^3, SO_2R^3, CN$

$$(14) + R^2\text{–}N{=}C{=}O \rightarrow ArO\text{–}C(=N\text{–}CO\text{–}NHR^2)\text{–}NRR'$$

$$(14) + O(C_2H_5)_3{}^{\oplus}BF_4{}^{\ominus} \xrightarrow{-O(C_2H_5)_2;\ -HBF_4} ArO\text{–}C(=N\text{–}C_2H_5)\text{–}NRR$$

[26] *M. Hedayatullah* and *L. Denivelle*, C. R. hebd. Séances Acad. Sci. *256*, 4029 (1963); *258*, 606 (1964); *260*, 2839 (1965); *260*, 3985 (1965).

[27] *E. Grigat* and *R. Pütter*, German Pat. 1178421, Farbenfabriken Bayer AG. (March 2nd, 1963).

[28] *E. Grigat* and *R. Pütter*, Chem. Ber. *97*, 3018 (1964).

[29] *E. Grigat* and *R. Pütter*, Publ. German Pat. Appl. 1233853, Farbenfabriken Bayer AG. (Nov. 23rd, 1963).

[30] *D. Martin*, *H.-J. Herrmann*, *S. Rackow*, and *K. Nadolski*, Angew. Chem. *77*, 96 (1965); Angew. Chem. internat. Edit. *4*, 73 (1965).

[31] *E. Grigat* and *R. Pütter*, German Pat. Appl. 1212519, Farbenfabriken Bayer AG. (Sept. 12th, 1963).

[32] *E. Grigat* and *R. Pütter*, Chem. Ber. *97*, 3022 (1964).

[33] *E. Grigat* and *R. Pütter*, German Pat. Appl. F 41619 IVb/12o, Farbenfabriken Bayer AG. (Dec. 23rd, 1963).

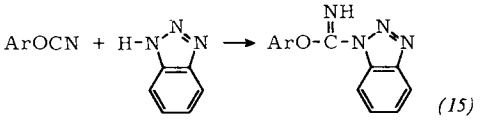
[34] *E. Grigat* and *E. Pütter*, German Pat. Appl. F 40006 IVb/12o, Farbenfabriken Bayer AG. (June 19th, 1963); corresponding Belg. Pat. 649488 (Dec. 21st, 1964).

[35] *E. Grigat* and *R. Pütter*, German Pat. Appl. F 40717 IVb/12o, Farbenfabriken Bayer AG. (Sept. 10th, 1963).

[36] *E. Grigat* and *R. Pütter*, Chem. Ber. *97*, 3027 (1964).

[37] Regarding the two isoureas in [30], cf. also [38] and [39].

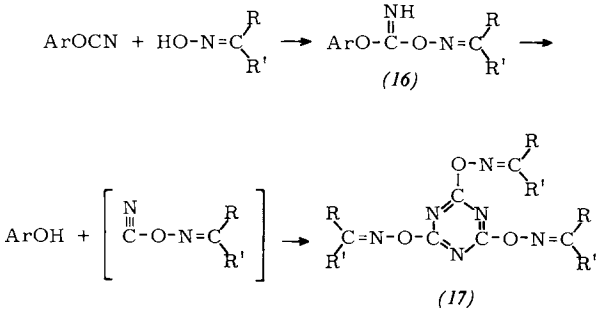
Aromatic-heterocyclic compounds containing an NH grouping also add to cyanates smoothly [34–36], *e.g.* to give the benzo[*d*][1,2,3]triazole derivative *(15)*.



(15)

Unlike the isoureas *(14)*, benzotriazoles such as *(15)* are thermally very stable (up to about 180 °C).

Cyanates react with ketoximes (HX=HON=CRR') to give initially the adducts *(16)* [40,41], which lose phenol more or less readily and trimerize to form



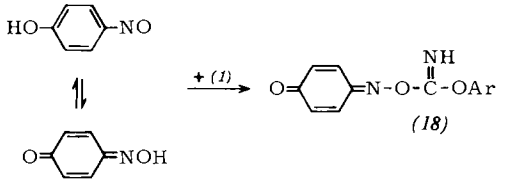
(16)

(17)

triazine derivatives *(17)*. On acidification, the oxime derivatives *(16)* undergo Beckmann rearrangement [41] according to equation (d).

$$(16) \xrightarrow{HCl} ArO{-}CO{-}NH_2 + R{-}CO{-}NHR' \qquad (d)$$

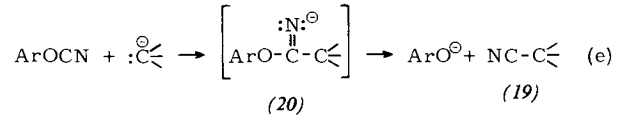
p-Nitrosophenols (= quinone monoximes) and quinone dioximes react with *(1)* in the same way as ketoximes, *e.g.* to form *(18)* [40,41].



(18)

2.1.2. Reagents having a Nucleophilic Carbon Atom

The reactions (e) of cyanates with compounds containing a nucleophilic carbon atom can be formally included in the reaction scheme (c). However,whereas the reactions in equation (c) lead to derivatives of carbonic acid, the reactions (e) result in the formation



(20) *(19)* (e)

[38] *E. Grigat* and *R. Pütter*, Angew. Chem. *77*, 452 (1965); Angew. Chem. internat. Edit. *4*, 430 (1965).

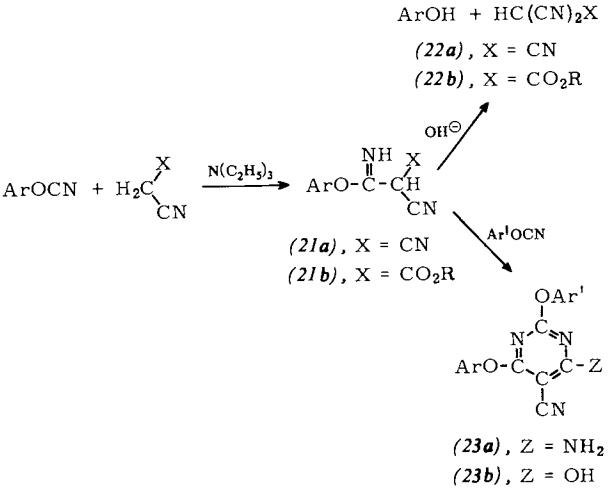
[39] *D. Martin*, Chem. Ber. *98*, 3286 (1965).

[40] *E. Grigat* and *R. Pütter*, German Pat. Appl. F 46044 IVb/12o, Farbenfabriken Bayer AG. (May 11th, 1965).

[41] *E. Grigat* and *R. Pütter*, Chem. Ber. *99*, 2361 (1966).

of a C–C bond, and hence give carboxylic acid derivatives (nitriles) *(19)*, often with direct transfer of the cyanide group, so that *(20)* cannot be isolated.

Aryl cyanates *(1)* react smoothly with CH acids in the presence of triethylamine to give esters of imidocarboxylic acids [*], *e.g.* *(21a)* and *(21b)* [42,43]. The imidocarboxylate ester group loses phenol under the action of alkalis, with formation of a nitrile group [see *e.g.* *(22a)*, *(22b)*] which is formed directly when the reaction is carried out in alkaline solution [43–45]. The 1:1 adducts with malononitrile or ethyl cyanoacetate, *(21a)* and *(21b)*, can be converted by an excess of aryl cyanate into amino- and hydroxypyrimidines *(23a)* and *(23b)* [43,46–48].

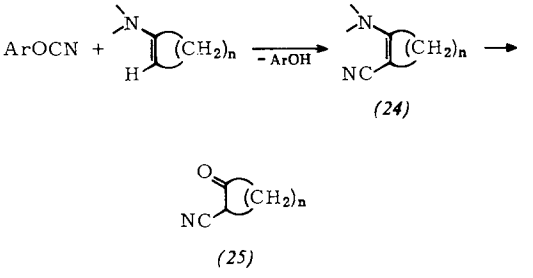


(22a), X = CN
(22b), X = CO_2R

(21a), X = CN
(21b), X = CO_2R

(23a), Z = NH_2
(23b), Z = OH

The reaction of aryl cyanates *(1)* with enamines leads to the introduction of a nitrile group into the enamines; no intermediate *(20)* could be isolated [43,44] The cyano enamines *(24)* are readily hydrolysed to α-cyano ketones *(25)* [45].



(24)

(25)

[*] *Martin* has recently found that compounds of this type having at least one CN group [*e.g.* *(21a)* and *(21b)*] exist at room temperature in the tautomeric aminoethylene form [*D. Martin, K.-H. Schwarz, S. Rackow, P. Reich*, and *E. Gründemann*, Chem. Ber. *99*, 2302 (1966)].

[42] *E. Grigat* and *R. Pütter*, German Pat. Appl. F 46002 IVb/12o, Farbenfabriken Bayer AG. (May 7th, 1965).

[43] *E. Grigat, R. Pütter*, and *E. Mühlbauer*, Chem. Ber. *98*, 3777 (1965).

[44] *E. Grigat* and *R. Pütter*, German Pat. 1215153, Farbenfabriken Bayer AG. (Dec. 24th, 1963).

[45] *D. Martin* and *S. Rackow*, Chem. Ber. *98*, 3662 (1965).

[46] *E. Grigat* and *R. Pütter*, German Pat. Appl. F 46739 IVd/12p, Farbenfabriken Bayer AG. (July 27th, 1965).

[47] *E.Grigat* and *R. Pütter*, German Pat.Appl. F 46709 IVd/12p, Farbenfabriken Bayer AG. (July 23rd, 1965).

[48] *E. Grigat* and *R. Pütter*, Angew. Chem. *77*, 913 (1965); Angew. Chem. internat. Edit. *4*, 877 (1965).

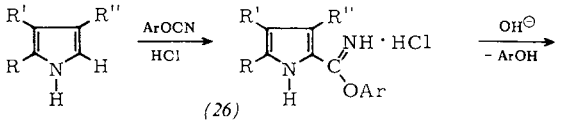
In the reaction of aryl cyanates *(1)* with Grignard compounds, no intermediate *(20)* could be isolated, the nitriles being formed directly [43–45]. An excess of Grignard compound reacts with the nitriles in the usual manner to form ketones [45].

$$RMgBr + ArOCN \longrightarrow (ArO\text{-}\overset{\overset{NMgBr}{\|}}{C}\text{-}R) \xrightarrow{-\,ArOMgBr}$$

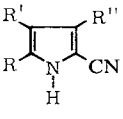
$$RCN \xrightarrow[2)\ H_2O]{1)\ RMgBr} R\text{-}CO\text{-}R$$

R = C_6H_5, C_2H_5, C_6H_5-C≡C

Pyrroles which are not substituted in the 2-position react with *(1)* in the presence of HCl only [45]. The reaction gives first the hydrochlorides of the adducts *(26)*, which then react with alkali to form 2-cyanopyrroles *(27)* [45].

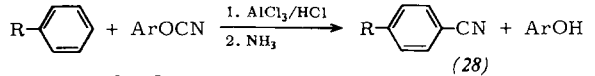


(26)



(27)

The still less nucleophilic aromatic compounds anisole and toluene only react with *(1)* on additional activation by Lewis acids. In the presence of $AlCl_3$ and HCl at 0–5 °C, the corresponding nitriles were obtained in yields of about 30 % on neutralization of the reaction solution with NH_3 [45]. No intermediates were isolated.



R = CH_3, CH_3O

(28)

Reaction of *(1)* with hydrogen cyanide in water/acetone [45,49] leads to loss of phenol and formation of dicyanogen. Depending on the reaction conditions, the product is either phenoxide [45] or iminocarbonate [45,49], the latter resulting from the reaction of the phenoxide with further aryl cyanate *(1)*; *(29)* was not isolated.

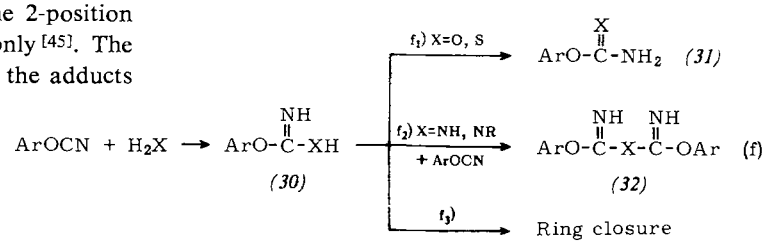
$$ArOCN + HCN \longrightarrow \left[ArO\text{-}\overset{\overset{NH}{\|}}{C}\text{-}CN\right] \longrightarrow ArOH + (CN)_2$$

(29)

[49] *E. Grigat* and *R. Pütter*, Chem. Ber. *99*, 958 (1966).

2.1.3. Nucleophiles having Two Mobile Hydrogen Atoms on the O, S, or N Atom

The reactions of aryl cyanates with nucleophiles having two mobile H aroms on the O, S, or N atom can lead to various products. The reaction may stop at stage *(30)* after the addition of one molecule of *(1)*. Where X = O or S, the 1:1 adduct is stabilized by route (f_1) with formation of the isomeric (thio)carbamate *(31)*. Where X = NH or NR, *(30)* may react with a further molecule of *(1)* to form bis(imidocarbonate)imides *(32)* (route f_2). Finally, *(30)* can also be stabilized by ring closure (route f_3).



X = O, S, NH, NR

The addition of water to aryl cyanates proceeds rapidly and almost quantitatively, even in weakly acidic solution, with formation of carbamates *(33)* (route f_1) [11,16,18,26,28].

$$ArOCN + H_2X \xrightarrow{H\oplus} ArO\text{–}CX\text{–}NH_2 \qquad \begin{matrix}(33)\ X = O\\(34),\ X = S\end{matrix}$$

The reaction with hydrogen sulfide ($H_2X = H_2S$) leads equally smoothly to thiocarbamates *(34)* [50,32]. However, *(34)* can be more readily prepared from *(1)* and thiosulfates [43].

$$ArOCN + H_2S_2O_3 \xrightarrow{H_2O} ArO\text{–}CS\text{–}NH_2 + H_2SO_4$$

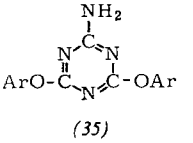
(34)

The reactions of aryl cyanates with ammonia, primary amines, hydroxylamine, and semicarbazides proceed by route f_2.

In the reaction of aryl cyanates with ammonia in anhydrous ether, the components immediately react in a molar ratio of 2:1 to form bis(imidocarbonate)-imides *(32a)* [36,51]. 1:1 adducts *(30)* could not be

$$2\ ArOCN + NH_3 \longrightarrow ArO\text{-}\overset{\overset{NH}{\|}}{C}\text{-}NH\text{-}\overset{\overset{NH}{\|}}{C}\text{-}OAr \xrightarrow[-\,ArOH]{ArOCN}$$

(32a)



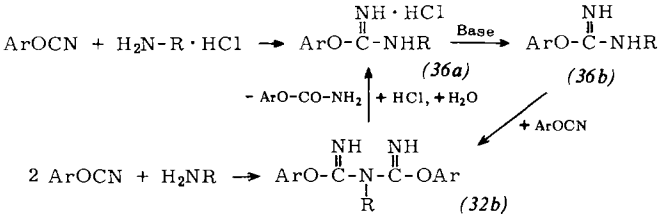
(35)

[50] *E. Grigat* and *R. Pütter*, German Pat. Appl. F 41443 IVb/12o, Farbenfabriken Bayer AG. (Nov. 30th, 1963).

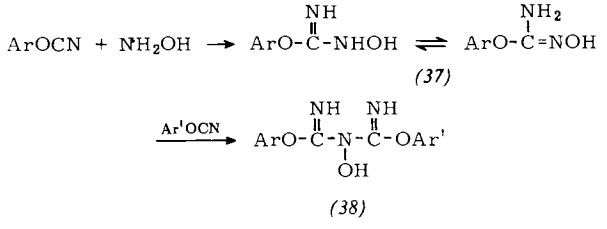
[51] *E. Grigat* and *R. Pütter*, German Pat. 1212521, Farbenfabriken Bayer AG. (Dec. 17th, 1963).

isolated. Under certain conditions (in aqueous solution with ammonium salts of weak acids) the reaction does not stop at the formation of *(32a)*, but a third molecule of aryl cyanate is added, with loss of phenol, to form the *s*-triazine derivative *(35)* [36,52].

In the reaction with primary amines ($H_2X = H_2N-R$), the initially formed *O*-arylisourea *(36b)* often reacts immediately with a second molecule of aryl cyanate to form a bis(imidocarbonate)imide *(32b)* [36,38,51]; the salts *(36a)* do not react with ArOCN. *(32b)* can be cleaved into *(36a)* and carbamate by treatment with hydrochloric acid [38].



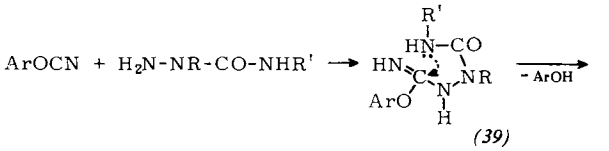
Hydroxylamine adds smoothly to aryl cyanate to form hydroxyamides of imidocarbonates *(37)* [53,54], which react with a second molecule of ArOCN on addition of alkali to form *(38)* [55]. *(37)* can be acylated at the

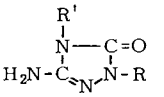


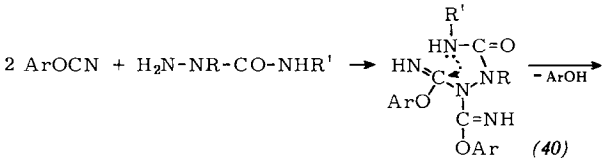
oxygen of the oxime group by the action of acyl or sulfonyl halides. The reaction of *(37)* with isothiocyanates leads to loss of phenol and formation of 5-amino-3-oxo-2,3-dihydro-1,2,4-thiadiazoles [53,56]. In the presence of alkali, *(37)* enters into a two-step reaction with chloroformates to give 3-aryloxy-5-oxo-2,5-dihydro-1,2,4-oxadiazole [53,57].

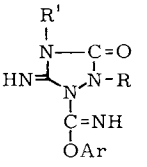
The semicarbazides ($H_2X = H_2N-NR-CO-NHR'$) formally belong to the class of compounds discussed in Section 2.1.4. However, since all the primary reactions take place on the NH_2 group, the semicarbazides will be discussed in the present section. The reactions yield two types of products, depending on substitution and reaction conditions. Reaction with 1 mole of aryl cyanate *(1)* yields *(39)* while two moles of *(1)* give the compound *(40)*.

Both *(38)* and *(40)* can lose phenol to form 1,2,4-triazole derivatives [58–60].



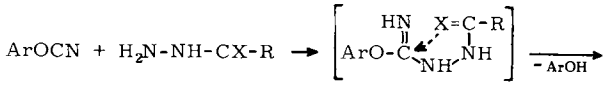


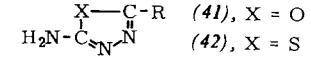




The reactions of *(1)* with hydrazides of carboxylic and thiocarboxylic acids are examples of the stabilization of compounds of the type *(30)* by ring closure.

Hydrazides of carboxylic acids ($H_2X = H_2N-NH-CO-R$) react with aryl cyanates, even at room temperature, to form 2-amino-1,3,4-oxadiazoles *(41)* [61]. Hydrazides





of thiocarboxylic acids react similarly to give 2-amino-1,3,4-thiadiazoles *(42)* [62].

Despite the presence of two mobile H atoms, a series of compounds H_2X add only one molecule of aryl cyanate to form stable 1:1 adducts of the type *(30)*.

The reaction of aryl- or alkylhydrazines ($H_2X = H_2N-NRR'(H)$) with aryl cyanates yields hydrazides of imidocarbonates *(43)*, which are much more stable to heat and to alkalis than the corresponding *O*-arylisoureas. They can again be readily alkylated and acylated [61,63]. Hydrazones react in the same manner as hydrazines [43,61].

[52] *E. Grigat* and *R. Pütter*, German Pat. 1201847, Farbenfabriken Bayer AG. (Feb. 29th, 1964).

[53] *E. Grigat, R. Pütter*, and *C. König*, Chem. Ber. *98*, 144 (1965).

[54] *E. Grigat* and *R. Pütter*, German Pat. 1212520, German Pat. 1217369, Farbenfabriken Bayer AG. (Dec. 4th, 1963 and Sept. 1st, 1964).

[55] *E. Grigat* and *R. Pütter*, German Pat. Appl. F 46569 IVb/12o, Farbenfabriken Bayer AG. (July 10th, 1965).

[56] *C. König, E. Grigat*, and *R. Pütter*, German Pat. Appl. F 42271 IVd/12p, Farbenfabriken Bayer AG. (March 11th, 1964).

[57] *C. König, E. Grigat*, and *R. Pütter*, German Pat. Appl. F 42212 IVd/12 p, Farbenfabriken Bayer AG. (March 5th, 1964).

[58] *E. Grigat* and *R. Pütter*, Chem. Ber. *98*, 2619 (1965).

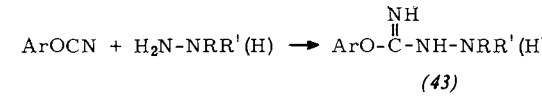
[59] *E. Grigat* and *R. Pütter*, German Pat. 1213835, 1220846, German Publ. Pat. Appl. 1228243, Farbenfabriken Bayer AG. (April 29th, 1964, Dec. 3rd, 1964 and Dec. 8th, 1964).

[60] The 1:1 adduct of semicarbazide and 4-CH_3–C_6H_4–OCN; see also [30].

[61] *E. Grigat* and *R. Pütter*, Chem. Ber. *97*, 3560 (1964).

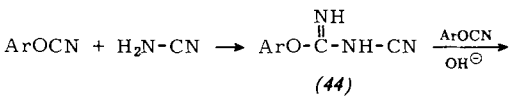
[62] *E. Grigat* and *R. Pütter*, Chem. Ber. *98*, 1359 (1965).

[63] *E. Grigat* and *R. Pütter*, German Pat. 1212522, Farbenfabriken Bayer AG. (Jan. 17th, 1964).

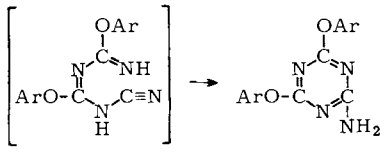


(43)

Cyanamides (H_2X = H_2N–CN, HRN–CN) also add only one molecule of aryl cyanate to the amino group to form *(44)*. Further reaction with a second molecule of ArOCN takes place in strongly alkaline media, with formation of aminobisaryloxy-*s*-triazine *(45)* [58,64].



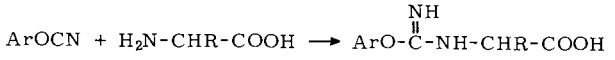
(44)



(45)

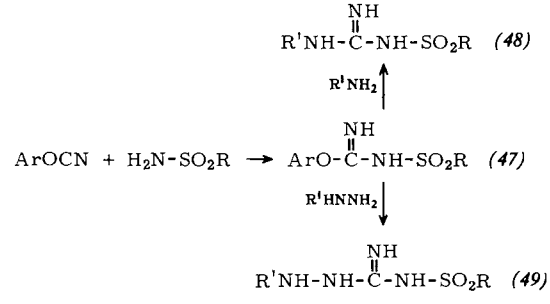
The secondary reaction *(44)* → *(45)* was not observed in the case of monosubstituted cyanamides.

Amidocarboxylic and amidosulfonic acids also add only one molecule of aryl cyanate *(1)*, with formation of *O*-arylisourea derivatives *(46)* [34,36].



(46)

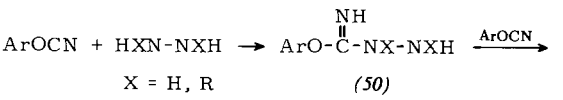
In the presence of bases, sulfonamides (H_2X = H_2N–SO_2R) add one molecule of aryl cyanate to form *(47)*. The aryloxy group in *(47)* can be readily replaced by an amino group to form *(48)* or by a hydrazino group to form *(49)* [49].



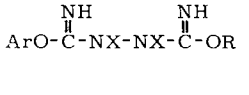
(48) *(47)* *(49)*

2.1.4. Reactants having a Second NH_2 or NH Group in Addition to an NH_2 or NH Group

In substances having a second NH_2 or NH group in addition to an amino or imino group, the first molecule of aryl cyanate *(1)* adds to one of the amino or imino groups, and a second molecule of *(1)* generally adds to the other. The reaction of semicarbazides H_2N–NR–CO–NHR′ is exception; cf. Section 2.1.3). The 1:1 adduct cannot always be isolated.

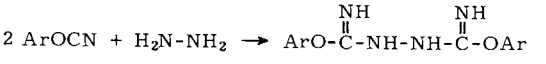


(50)



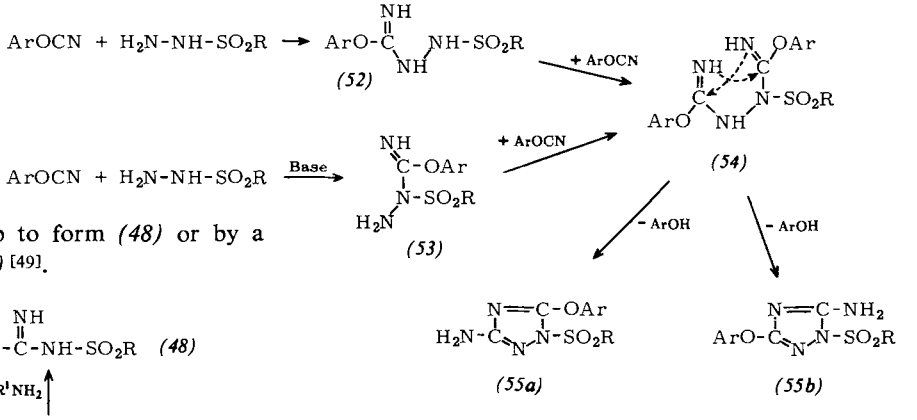
X = H, R

Hydrazine and its salts react immediately with two molecules of aryl cyanate, even when the hydrazine is present in excess, to give 1,2-bis(aryloxycarbonimidoyl)hydrazines *(51)* [61,65], which form dihydrochlorides that are only sparingly soluble in water.



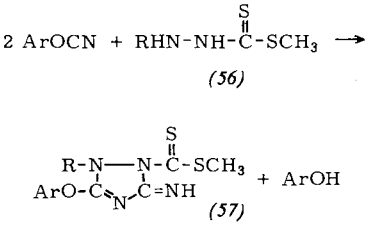
(51)

In the case of sulfonylhydrazines (H_2N–NHX = H_2N–NH–SO_2R), aryl cyanate adds on to the β-N atom in acidic and neutral media to give *O*-aryl-1-arylsulfonylisosemicarbazide *(52)*, while in alkaline media it adds on to the α-N atom to form the *O*-aryl-2-arylsulfonylisosemicarbazide *(53)*. A second molecule of ArOCN adds to the unsubstituted N atom of *(52)* or *(53)* to give *(54)* [49].



(52) *(53)* *(54)* *(55a)* *(55b)*

Ring closure of *(54)* with elimination of ArOH has been observed. This reaction yields the isomeric 3,5-disubstituted triazoles *(55a)* and *(55b)* [49].



(56) *(57)*

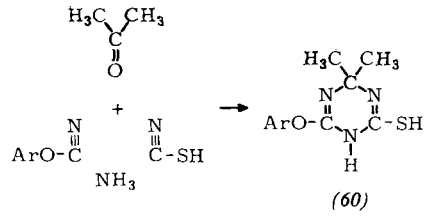
[64] *E. Grigat* and *R. Pütter*, German Pat. Appl. F 44635 IVb/12o, Farbenfabriken Bayer AG. (Dec. 5th, 1964).

[65] *E. Grigat* and *R. Pütter*, German Publ. Pat. Appl. 1225631, Farbenfabriken Bayer AG. (Jan. 10th, 1964).

Both N atoms in the hydrazides of dithiocarbonates *(56)*, react immediately with two molecules of aryl cyanate causing ring closure to form the triazole *(57)* [43,66].

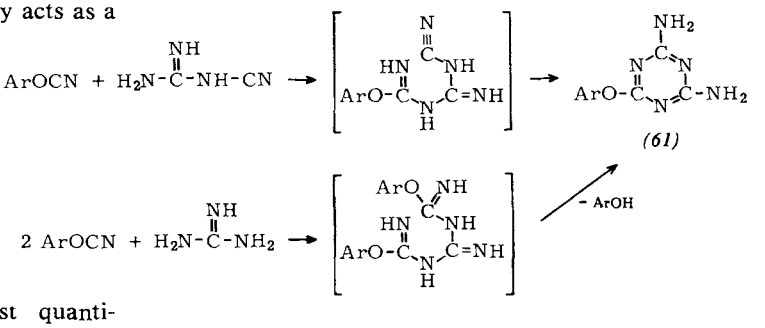
2.1.5. Direct Ring Closure to Form *s*-Triazines

A number of reactions of aryl cyanates lead to direct ring closure and formation of *s*-triazine derivatives. These reactions will be grouped here according to the final products, irrespective of the course of the reaction. In these ring closures, one ArOCN molecule is incorporated in the ring; another frequently acts as a source of cyanide groups.



(60)

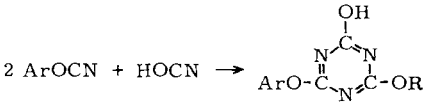
Diaminoaryloxy-*s*-triazines *(61)* are formed by the reaction of aryl cyanates with either dicyanodiamide or guanidine [70,71]; no intermediates have been isolated.



(61)

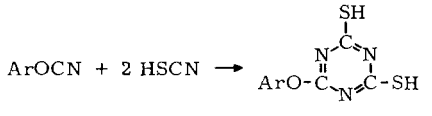
Trisaryloxy-*s*-triazines are formed almost quantitatively by trimerization of aryl cyanates [15,18,67]. The trimerization is promoted by acids, Lewis acids, and bases, as well as by the addition of phenol to the aryl cyanate.

Cyanic acid cotrimerizes with aryl cyanates to give mainly diaryl cyanurate *(58b)* together with a little monoaryl cyanurate *(58a)* [49].



(58a), R = H
(58b), R = Ar

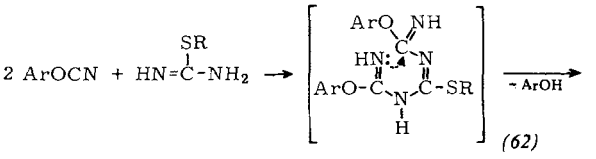
ArOCN reacts uniformly and smoothly with thiocyanic acid, which is liberated from its salts in the reaction solution by the addition of mineral acid. The reaction gives excellent yields of aryloxydimercapto-*s*-triazines *(59)* [49,68], the SH groups of which can be alkylated or acylated, and can react with isocyanates and cyanates.



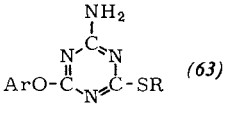
(59)

2-Aryloxy-6-mercapto-4,4-dimethyl-1,4-dihydro-*s*-triazine *(60)* has been obtained by the reaction of NH_4SCN with ArOCN in acetone [49,69].

The reaction of aryl cyanates with isothioureas gives aminoaryl(alkyl)thioaryloxy-*s*-triazines *(63)* in good yields; the intermediate *(62)* again could not be isolated [70,72].



(62)



(63)

2.1.6. Elimination of H_2O by Aryl Cyanates

Aryl cyanates can act as agents for the elimination of H_2O; in so doing they are converted into carbamates. Intramolecular dehydration takes place after the addition of the nucleophile to form the imidocarbonate derivative [*e.g. (64)*], from which the carbamate is liberated. In the intermolecular elimination of water, the very reactive primary adducts [*e.g. (68)*], which have not been isolated, act as acylating agents.

Aldoximes and aryl cyanates undergo addition reactions to form *O*-(aryloxycarbonimidoyl)aldoximes *(64)*, which break down into nitrile and carbamate when heated [41]. If the Ar residues carry strongly electron-donating groups, isonitrile is formed as well as nitrile [41,73]. At higher temperatures, (above about

[66] *E. Grigat* and *R. Pütter*, German Pat. 1219031, Farbenfabriken Bayer AG. (March 13th, 1965).

[67] *E. Grigat* and *R. Pütter*, German Pat. 1183507, Farbenfabriken Bayer AG. (May 2nd, 1963).

[68] *E. Grigat* and *R. Pütter*, German Pat. 1217965, Farbenfabriken Bayer AG. (Feb. 11th, 1965).

[69] *E. Grigat* and *R. Pütter*, German Pat. 1219939, Farbenfabriken Bayer AG. (June 5th, 1965).

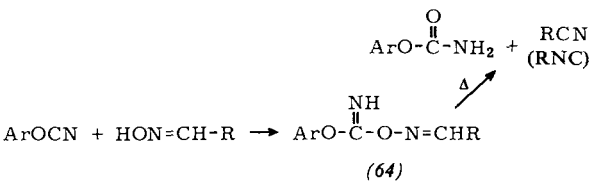
[70] *E. Grigat* and *R. Pütter*, Chem. Ber. *98*, 1168 (1965).

[71] *E. Grigat* and *R. Pütter*, German Pat. 1213415, Farbenfabriken Bayer AG. (July 18th, 1964).

[72] *E. Grigat* and *R. Pütter*, German Pat. 1220860, Farbenfabriken Bayer AG. (Sept. 27th, 1964).

[73] *E. Müller* and *B. Narr*, Z. Naturforsch. *16b*, 845 (1961).

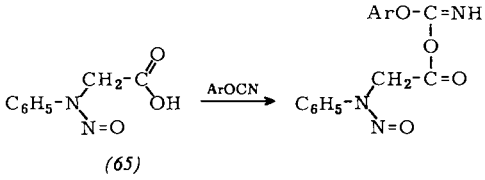
80 °C), *(64)* can no longer be isolated, and the nitrile is formed directly [39, 74].



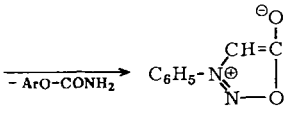
(64)

Amides are also converted into nitriles at high temperatures only [39].

N-Nitroso-*N*-phenylglycine *(65)* can be converted into *N*-phenylsydnone *(66)* in good yields at about 100 °C [39].

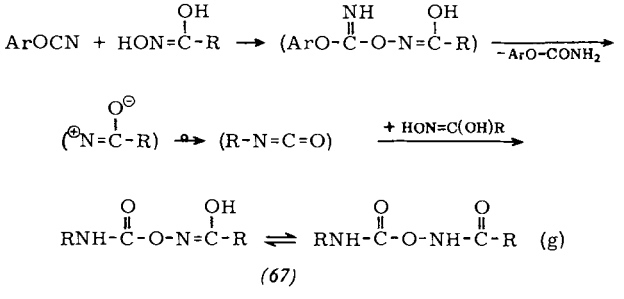


(65)



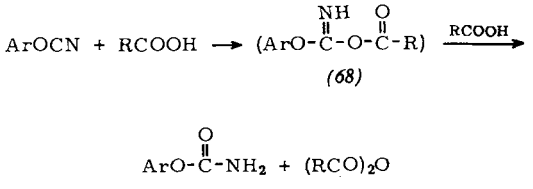
(66)

Hydroxamic acids are converted directly into *O*-carbamoylhydroxamic acids *(67)* by aryl cyanates, according to scheme (g) [62, 75].

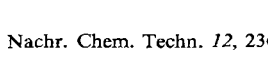


(67)

Carboxylic acids [30, 39, 62], sulfonic acids [39, 40], and monoesters of phosphoric acid [30, 39] undergo intermolecular dehydration with formation of the anhydrides. The reaction probably proceeds *via* the mixed anhydride of *e.g.* the carboxylic acid and the monoaryl imidocarbonate, which has not been isolated and which acts as a strong acylating agent, acylating a second molecule of the acid.



(68)

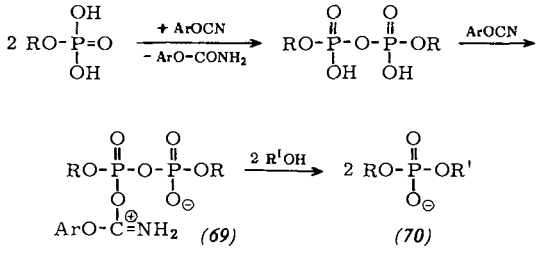


[74] *E. Grigat*, Nachr. Chem. Techn. *12*, 236 (1965).

[75] *C. D. Hurd* and *L. Bauer*, J. Amer. chem. Soc. *76*, 2791 (1954).

The reaction of some carboxylic acids (*e.g.* benzoic acid, chloroacetic acid) with aryl cyanates in the presence of alcohol yields esters of the carboxylic acids. It is not certain whether the alcohol is acylated by *(68)* or by the anhydride of the carboxylic acid [30, 39].

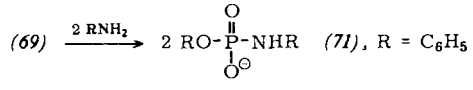
Whereas sulfonic acids solely catalyse the addition of aryl cyanates to alcohols to form the alkyl aryl imidocarbonate *(11)* [39], monoesters of phosphoric acid are further esterified to the diesters *(70)* in an excess of alcohol with *(1)*, presumably *via* an initially formed pyrophosphate [39].



(69) *(70)*

With aryl cyanate in the presence of triethylamine, orthophosphoric acid and benzyl alcohol gave only moderate yields of the monoester (35 %) and diester (14 %) [39].

In the reaction of carboxylic acids or sulfonic acids with cyanates in the presence of amines, the addition of the amine to the cyanate to form isoureas is much faster than amide formation [30, 39, 62], whereas monophenyl phosphate, aniline, and phenyl cyanate give the phosphoramidate *(71)* *via* adducts such as *(69)* [30, 39].



2.1.7. Elimination of H_2S by Aryl Cyanates

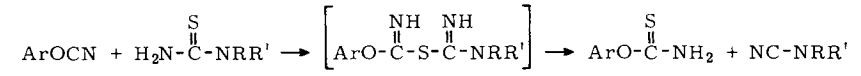
Aryl cyanates eliminate hydrogen sulfide from organic compounds even more readily than water, the hydrogen sulfide adding to the cyanates to form thiocarbamates. The elimination of H_2S can also take place intramolecularly or intermolecularly, and like the elimination of water, proceeds *via* primary adducts of the cyanate to the S atom of the other reactant.

The reaction of thioureas with aryl cyanates leads to cyanamides or carbodiimides, depending on the substitution of the thiourea [70, 76]; intermediates such as *(72)* or *(73)* have not been isolated [70].

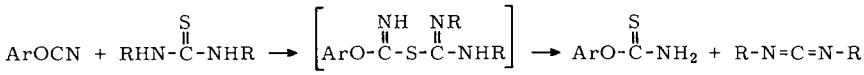
The elimination of H_2S from amides of thiocarboxylic acids proceeds smoothly, with almost quantitative formation of nitriles and thiocarbamates [62, 76].

Aryl cyanates also remove hydrogen sulfide from dithiocarbamates. In the case of dithiocarbamates of primary amines, a molecule of amine takes the place of the molecule of thiocarbamic acid *(75b)* eliminated

[76] *E. Grigat* and *R. Pütter*, German Pat. Appl. F 43500 IVb/12o, Farbenfabriken Bayer AG. (July 18th, 1964).

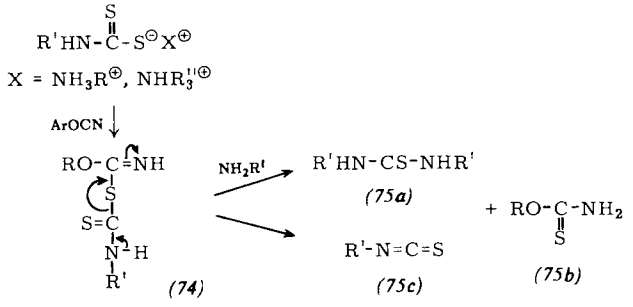


(72)

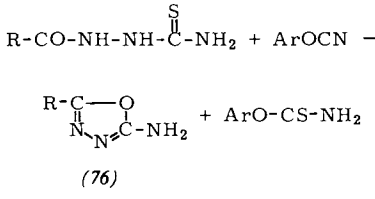


(73)

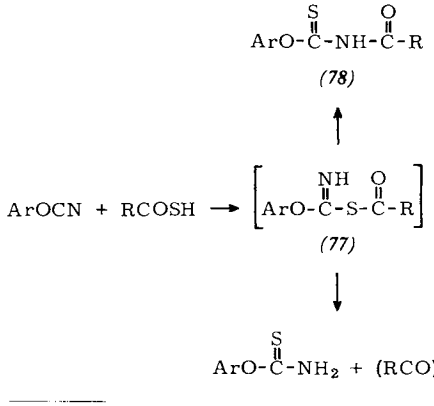
from the primary adduct *(74)* (which has not been isolated), with formation of a thiourea *(75a)*. In the reaction of dithiocarbamates of tertiary amines with *(1)*, the second proton required for the formation of *(75b)* can only come from the amido group of *(74)*, and isothiocyanates *(75c)* are formed [39].



After the elimination of H_2S from 1-acylthiosemicarbazides with aryl cyanates, the residue is stabilized by ring closure to form the 2-amino-5-alkyl-1,3,4-oxadiazole *(76)* [77].

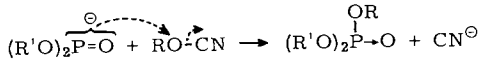


Thiocarboxylic acids [30,39,62,76] or xanthic acids, RO–CS–SH [62,76] are converted into the anhydrides under even milder conditions than are required for carboxylic acids. The primary products *(77)* [*], which cannot be isolated, again act as strong acylating agents. A transacylation *(77)* → *(78)* has been observed in one case [62]. The reaction of thiocarbonates with aryl cyanates in the presence of alcohol gives esters of carboxylic acids and thiocarbamates [39]. Unlike carboxylic and sulfonic acids (cf. Section 2.1.6.), thiocarboxylic acids react with amines and cyanates to give the amides of the carboxylic acids in good yield [39].



2.1.8. Nucleophilic Additions to the Oxygen Atom of Aryl Cyanates

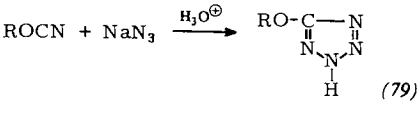
In all cases described so far, the addition of nucleophiles to aryl cyanates takes place on the C atom of the OCN group. However, two groups of investigators [78,79] found that when a reaction analogous to that of trialkyl phosphites with thiocyanates [79] is carried out with cyanates, nucleophilic attack also takes place on the O atom of the OCN group. When dialkyl phosphites are used, the attack occurs exclusively on the oxygen [79]; triesters of phosphoric acid are formed in yields of up to 83 %.



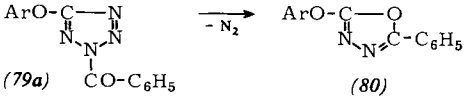
2.2. 1,3-Dipolar Additions [80]

The cyanates have been found much more reactive than nitriles in additions to 1,3-dipolar compounds.

Aryl cyanates react smoothly with sodium azide to form 5-aryloxytetrazoles *(79)* [30,43,81,82]. Alkyl cyanates also undergo this reaction, but the yields are much lower (13 to 36 %) [30,82].



The 5-aryloxytetrazoles can be acylated in the 2-position; when the 2-benzoyl derivative *(79a)* was heated in dimethylformamide, it was converted into the oxadiazole *(80)*, with liberation of nitrogen [82].



[77] *E. Grigat* and *R. Pütter*, German Pat. Appl. F 49281 IVd/12p, Farbenfabriken Bayer AG. (May 25th, 1966).

[*] *(78)* can be ruled out as the primary product, since it can be prepared by another route and does not undergo the secondary reactions under the above conditions.

[78] *K. Pilgram* and *F. Korte*, Tetrahedron Letters *1966*, 881.

[79] *D. Martin* and *A. Weise*, Chem. Ber. *99*, 976 (1965).

[80] *R. Huisgen*, Proc. chem. Soc. (London) *1961*, 357; Angew. Chem. *75*, 604, 742 (1963).

[81] *E. Mühlbauer*, *E. Grigat*, and *R. Pütter*, German Pat. 1216880, Farbenfabriken Bayer AG. (July 4th, 1964).

[82] *D. Martin* and *A. Weise*, Chem. Ber. *99*, 317 (1966).

Table 1. Synthesized aryl cyanates.

Ar	M.p. (°C)	B.p. (°C/mm)	Yield (%) from phenol and cyanogen halide [a]	Yield (%) from aryloxy-1,2,3,4-thiatriazole [b]
Phenyl		82—83/16	94	
		74—75/10		85
2-Methylphenyl		87—90/10	92	
3-Methylphenyl		70—71/0.8	89	
		90—91/10		60
4-Methylphenyl		68/2—3	98.5	
		90—91/10		84
2,4-Dimethylphenyl		75—77/2	98	
3,5-Dimethylphenyl		81—83/2	90	
2,6-Dimethylphenyl	38	70/0.5	97.5	
2,6-Diethylphenyl		86—90/2—3	85	
2-Isopropylphenyl		100—102/6	75	
3-Isopropylphenyl		75/0.4	81	
2-t-Butylphenyl		75/0.9	95	
4-t-Butylphenyl		80/0.5	86	
2,6-Di-t-butylphenyl	52	142/20	80 [11]	
2-Isopropyl-6-t-butylphenyl		139/10	— [11]	
4-Methyl-2,6-di-t-butylphenyl	72		— [11]	
4-Allyl-2,6-di-t-butylphenyl	58	172/10	— [11]	
2,4,6-Tri-t-butylphenyl	156.5		— [11]	
4-(1,3,3-Trimethylpentyl)phenyl		140/2	92	
4-(n-Nonyl)phenyl		134—137/0.8	84	
4-Isododecylphenyl		160/0.2	65	
4-Vinylphenyl	rearranges		80	
4-Cyclohexylphenyl		134—137/0.5	91	
3-Trifluoromethylphenyl		55/1.5	61	
4-Biphenylyl	62		81	— [26]
2,6-Diphenylphenyl	83		— [26]	
2,4,6-Triphenylphenyl	110		— [26]	
2-Chlorophenyl		64—67/0.5	91.5	
		68—70/0.1		71
3-Chlorophenyl		82—84/2	89	
		99—100/10		80
4-Chlorophenyl	42	56/0.2	95	
		100—101/10		85
2,4-Dichlorophenyl	66—67		92	
		79—81/0.03		83
2,4,6-Tribromophenyl	89—92	120—121/0.05		90
3-Chloro-2-methylphenyl	54—55		97	
4-Chloro-2-methylphenyl	61—62		88	
4-Chloro-3-methylphenyl	38		95	
5-Chloro-2-methylphenyl	63		69	
6-Chloro-2-methylphenyl		88—91/2	82	
6-Chloro-3-methylphenyl	55		71	
4-Chloro-2,6-di-t-butylphenyl	67	158/10	— [11]	
4-Cyano-2,6-di-t-butylphenyl	80		— [11]	
3-Nitrophenyl	63		78	
4-Nitrophenyl	75—76		76	70
4-Nitro-3-methylphenyl	57		65	
2-Methoxyphenyl		93/2.3	94	
		121—122/10		86
3-Methoxyphenyl		74/0.7	94	
4-Methoxyphenyl	33—34	118—119/10	82	85
4-Allyl-2-methoxyphenyl		104—108/0.5	78	
3-Acetyloxyphenyl		115—122/1.8	44	
4-Methacryloyloxyphenyl	61		95	
4-Methylthiophenyl		103/0.8	79	
2,4-Bis(methylthio)-3-methylphenyl	81		95	
4-Methylsulfonyl-3,5-dimethylphenyl	134—135		78	
3,4-(—SO_2—CH_2—O—)phenyl	177		72	
2-Acetylphenyl		110/0.6	82	
4-Acetylphenyl	65		92.5	
4-Formylphenyl	54		95	
4-Dimethylaminophenyl	51—52		44	
4-Dimethylamino-3-methylphenyl		100/10	62	
4-(*N*-Methyl-*N*-formylamino)phenyl	60		85	
4-Acetylaminophenyl	123—125		50	
4-Acryloylaminophenyl	rearranges		90	
4-Methacryloylaminophenyl	85—86		93	
4-Methacryloylamino-2-methylphenyl	73		92	
3-Methacryloylamino-6-methylphenyl	93—94		86	
4-Methoxycarbonylphenyl	46		70	
2-Methoxycarbonylphenyl	61—62		91	
2-Ethoxycarbonylphenyl		98—100/2.5	70	
2-Isobutoxycarbonylphenyl		102—106/0.4	76	
2-Phenoxycarbonylphenyl	56—58		98	
2-(β-Naphthoxycarbonyl)phenyl	88—90		70 [94]	
2-(2-Chlorophenoxycarbonyl)phenyl	63—64		90 [94]	
2-(2,4-Dichlorophenoxycarbonyl)phenyl	115—118		40 [94]	
2-(2,6-Dichlorophenoxycarbonyl)phenyl	77—80		71 [94]	
2-Methoxycarbonyl-6-methylphenyl	38—39	115/0.3	78	
2-Ethoxycarbonyl-4-chlorophenyl	53		88	
2-(2,6-Dichlorophenoxycarbonyl)-4-chlorophenyl	98—100		66 [94]	
2-(2,6-Dichlorophenoxycarbonyl)-4-chloro-6-methylphenyl	91—93		80 [94]	
2,4-Di-(methoxycarbonyl)phenyl	92—93		70	
2-Morpholinylcarbonylphenyl	99—101		34 [94]	
1-Naphthyl	36	161/11	96	
2-Naphthyl	rearranges	131/1.5	97	
2-Methoxycarbonylnaphth-1-yl	86		87	
3-Methoxycarbonylnaphth-2-yl	97		96	
2-Phenoxycarbonylnaphth-1-yl	94—96		54 [94]	
3-Phenoxycarbonylnaphth-2-yl	110—111		70 [94]	
2-Morpholinylcarbonyinaphth-1-yl	130—131		78 [94]	
3-Morpholinylcarbonylnaphth-2-yl	148—150		54 [94]	
3-(Diethylaminocarbonyl)naphth-2-yl	85—87.5		63 [94]	
Anthraquinon-1-yl	155—157		70	
4-Hydroxyanthraquinon-1-yl	157—159		86	
5-Quinolyl	101		81	
3-Carbazyl	124		65	
2-Methoxycarbonylcarbaz-3-yl	158—159		85	

[a] Where no reference is given, the data are taken from [13—15, 83].

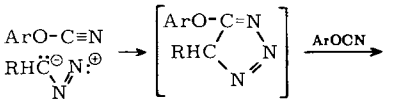
[b] Where no reference is given, the data are taken from [16, 18, 93].

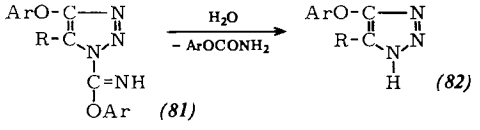
"Rearranges" signifies that the substance rearranges on heating (tri- or polymerizes).

Table 2. Synthesized alkyl cyanates ROCN.

	B.p. (°C/mm) or m.p. (°C)	Yield (%) from thermolysis of alkoxy-1,2,3,4-thiatriazoles [20]	[19]	from thiocarbamate + HgO [24]	from alcohol + cyanogen halide [15,25]
Methylcyanate			17	—	—
Ethylcyanate		60	91		—
n-Propylcyanate			82	40 to 57	—
Isopropylcyanate		—	77		—
n-Butylcyanate	57—58/12 [20]	—	78		—
Isobutylcyanate		—	73	—	—
s-Butylcyanate		—	77	—	—
β,β,β-Trichloroethylcyanate	70—71/5 [15]	—	—	—	93 [15]
β,β,β-Tribromoethylcyanate	73/2.5 [15]	—	—	—	85 [15]
β,β,β-Trifluoroethylcyanate	32/2 [15]	—	—	—	80 [15]
β,β-Dichloroethylcyanate	45—48/1 [15]	—	—	—	55 [15]
Neopentylcyanate	123/185 [25]	—	—	—	4.4 [25]
1,4-Dicyanatobicyclo[2.2.2]octane	(155—156) [25]	—	—	—	41 [25]
1-Cyanato-3-ethoxy-2,2,4,4-tetramethylcyclobutane	63/0.1 [25]	—	—	—	30 [25]

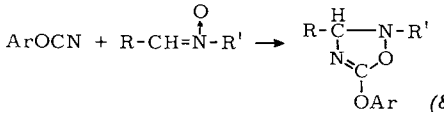
Diazomethane reacts with aryl cyanates in a molar ratio of 1:2, in ethereal solution at room temperature, to form *(81)*, which yields an aryloxytriazole *(82)* on hydrolysis [82]. Diazoacetic ester (R = $CO_2C_2H_5$) reacts in the same manner [82].



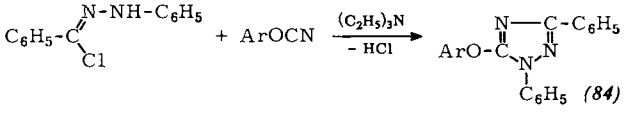


R = H, $CO_2C_2H_5$

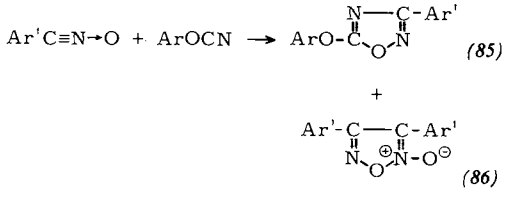
Nitrones and aryl cyanates undergo an exothermic reaction at room temperature to form Δ^4-1,2,4-oxadiazolines *(83)* [43].



Aryl cyanates react with nitrilimines produced *in situ* to form 5-aryloxy-1,3-diphenyl-1,2,4-triazoles *(84)* [82].



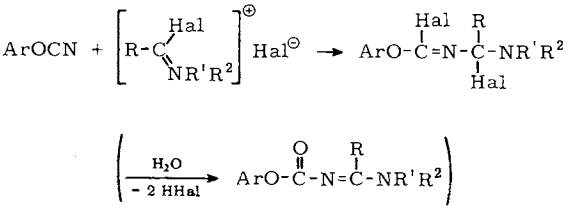
Nitrile oxides, produced *in situ* from hydroxamyl chlorides or nitroalkanes, react with aryl cyanates to form 3-aryl-5-aryloxy-1,2,4-oxadiazoles *(85)* and 3,4-diaryl-1,2,5-oxadiazole-2-oxides *(86)* (dimerization products of the nitrile oxides) [30,82].



2.3. Electrophilic Addition

Electrophilic addition to the OCN group of the aryl cyanates proceeds less readily than addition to the corresponding nitriles. No reaction occurred in attempted alkylations with alkyl halides, sulfonates, and dialkyl sulfates [83]; in only one case, with triethyloxonium fluoroborate, a little phenetole was formed [84] from phenyl cyanate.

Attempted syntheses with aryl cyanates, acylating agents, and diazonium salts have also proved unsuccessful. Only two reactions with electrophilic reagents proceed smoothly. The addition of *N*-phenylnitrilium salts leads to quinazolines [84], while the addition of amide chlorides yields *N*-aminohalogenoalkylmethylimidocarbonate chlorides [85].



2.4. 2-Substituted 4*H*-1,3-Benzoxazin-4-ones

In esters of arylcarboxylic acids having a cyanato group in the *ortho* position, *e.g. (87)*, the addition of a nucleophile to the OCN group to form *(88)* is frequently (sometimes spontaneously, and sometimes on heating) followed by ring closure with the COOR group to form 2-substituted 4*H*-1,3-benzoxazin-4-ones *(89)*, which were hitherto largely unknown [86]. A second route to *(89)*, based on the ease of replacement of the

[83] *E. Grigat*, unpublished.

[84] *D. Martin*, Angew. Chem. *77*, 1033 (1965); Angew. Chem. internat. Edit. *4*, 985 (1965).

[85] *J. Zirner, E. Grigat*, and *R. Pütter*, German Pat. Appl. F 48469 IVb/12o, Farbenfabriken Bayer AG. (Feb. 18th, 1966).

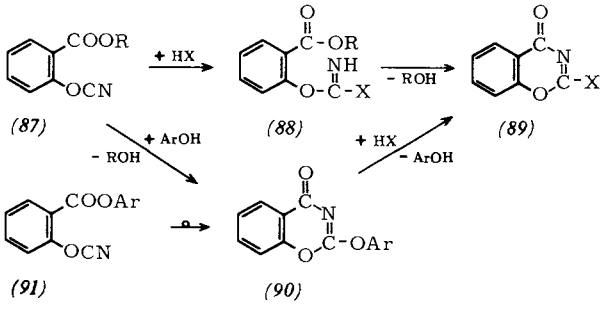
[86] *E. Grigat, R. Pütter, K. Schneider*, and *K. F. Wedemeyer*, Chem. Ber. *97*, 3036 (1964).

Table 3. Cyanates of bi- and trifunctional phenols synthesized from cyanogen halides.

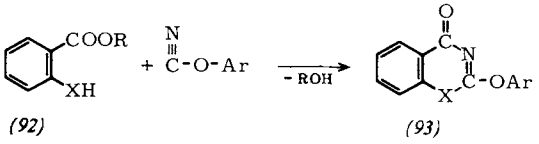
Cyanate	M.p. (°C)	Yield (%) [a]
1,3-Dicyanatobenzene	80	96
1,4-Dicyanatobenzene	115—116	94
		30 [b] [18]
1,3-Dicyanato-5-methylbenzene	72—84	57
1,3-Dicyanato-4-acetylbenzene	78—80	40
1,3,5-Tricyanatobenzene	102	71
1,5-Dicyanatonaphthalene	rearranges	92
1,4-Dicyanatoanthraquinone	rearranges	93
4,4'-Dicyanatobiphenyl	131	85
2,2'-Dicyanato-1,1'-binaphthyl	149	41
2,2-Bis(4-cyanatophenyl)propane	82	98
4,4'-Dicyanato-diphenylsulfone	169—170	90
4,4'-Dicyanato-3,3'-dimethoxy-carbonyldiphenylmethane	100—101	62 [94]
2,2'-Dicyanato-3,5,3',5'-tetramethy-dibenzylether	107—108	55
[o-NCO-C_6H_4-O-CH_2-Si$(CH_3)_2$-]$_2$O	(decomp.oil)	60
1,4-Dicyanato-2,5-di-t-butyl-benzol	130	— [26]
4,4'-Dicyanato-3,5,3',5'-tetra-t-butyl-diphenylmethane	206	— [11]
4,4'-Dicyanato-3,5,3',5'-tetra-t-butyl-biphenyl	263	80 [26]

[a] Where no reference is given, the data are taken from [13—15, 83].
[b] The starting material was an aryloxy-1,2,3,4-thiatriazole [18] in this case only.

aryloxy group by nucleophilic reagents, is *via* the 2-aryloxy-4*H*-1,3-benzoxazin-4-ones *(90)*, which can be obtained either by rearrangement of the aryl *o*-cyanatoarylcarboxylate *(91)* or by addition of phenols to an ester of *o*-cyanatoarylcarboxylic acid *(87)* [86,87].



X = NH_2, NHR, NRR' [86,88,89], NH—NHR, NH—NRR' [61, 88,89], HN—NH—COR [61], NHOH, NROH [53,91], NH—C(SR)=NH [70], HN—NR—CO—NHR' [58], NH—NR—CS—NHR' [74], HN—CN, NR—CN [58], SH, SR [43, 62,70,86,90], O—N=CRR' [41], NH—SO_2R, NH—NHSO_2R [49], and HX = CH acids [43].



1,3-Benzoxazinones *(93)*, X = O, -thiazinones *(93)*, X = S, and quinazolones *(93)*, X = NH, can also be prepared from esters of *o*-hydroxy-, *o*-mercapto-, or *o*-aminoarylcarboxylic acids *(92)* and aryl cyanates [86,92].

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Translated by Express Translation Service, London

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[91] *E. Grigat* and *R. Pütter*, German Pat. Appl. F 41953 IVd/12p, Farbenfabriken Bayer AG. (Feb. 7th, 1964).

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Structures and Syntheses of Carboranes

BY R. KÖSTER AND M. A. GRASSBERGER [*]

Following a discussion of bonding, the structures of the known carboranes of the clovo type and of the incompletely condensed types are described; the recently discovered carboranes with high carbon contents, such as tetracarbahexaborane ("boracarbane") are also discussed. The preparation of carboranes from polyboranes and the possibility of obtaining organo carboranes from organoboranes are then described. Some rearrangements which take place within the carborane skeleton are also mentioned.

1. Introduction

For a long time our knowledge of compounds containing boron-carbon bonds was confined to the thermally and chemically very stable boron carbide $(CB_4)_x$ [1], and to the simple, very reactive alkyl- and arylboranes containing the grouping BC_3 [2] and similar compounds.

It was possible to foresee that carbon and boron could

[*] Dr. R. Köster and Dr. M. A. Grassberger
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1
433 Mülheim/Ruhr (Germany)

[1] *F. Wöhler* and *H. Sainte-Claire Deville*, Ann. Chimie [3] *52*, 63 (1858); *A. Joly*, C.R. hebd. Séances Acad. Sci. *97*, 456 (1883); *H. Moissan*, ibid. *118*, 556 (1894); *O. Mühlhaeuser*, Z. anorg. allg. Chem. *5*, 92 (1894).

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also form substances intermediate between these two classes of substances; however, it was only recently that the necessary foundations (the isolation and characterization of the boron hydrides [3] and a knowledge of the bonding in such compounds [4]) had been laid for the discovery of these new BC systems, which are nowadays known as carboranes [5,6]. The existence of new systems was almost simultaneously postulated by theorists [7] and recognized by experimental chemists [8–10]. It is impossible to decide how theory and practice influenced each other in this work; but it may be said that the first observations on carboranes were reported as early as 1953 [11] whereas these systems have been discussed theoretically since 1954 [12–14].

Carborane research gained momentum when decaborane [3] became available in large quantities [15,16]. The investigation of this substance led to the synthesis of a compound that was isoelectronic with the $B_{12}H_{12}^{2\ominus}$ ion [17], and whose skeleton consists of an icosahedral arrangement of two carbon atoms and ten boron atoms [18]. This compound was dicarbaclovododecaborane(12) (cf. Section 3.1.1.).

Organocarboranes [19] containing from two to five boron atoms are now readily available by several routes from organoboranes [6,20,21]. The following discussions are mainly concerned with carboranes having less than ten boron atoms, since reviews [22–24a] dealing with both the preparation and the reactions of the C_2B_{10} system have already been published.

[3] *A. Stock* and *C. Massenez*, Chem. Ber. *45*, 3529 (1912); *A. Stock*: Hydrides of Boron and Silicon. Cornell University Press, Ithaca, N.Y. 1933.

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[18] Cf. Chem. Engng. News *41*, No. 49, p. 62 (1963).

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2. Structures of Carboranes

2.1. Characterization of the Type of Compound

2.1.1. Position of the Carboranes in Relation to the Polyboranes and Aromatic Hydrocarbons

The carboranes occupy a position intermediate between the polyboranes and the aromatic hydrocarbons. If the carbon atoms of an aromatic hydrocarbon (*e.g.* benzene) are successively replaced by boron atoms, which carry a smaller number of electrons, the decrease in the number of bonding electrons leads to a progressively closer packing of the skeletal atoms, and three-dimensional structures are formed. Thus in the series $C_{6-n}B_nH_6$ ($n = 0, 2, 4$), we pass from the planar benzene, with 18 bonding electrons in the C-skeleton, *via* the pentagonal-pyramidal tetracarbahexaborane(6) $C_4B_2H_6$ (16 bonding electrons) [6], to the close-packed tetragonal-bipyramidal dicarbaclovohexaborane(6) $C_2B_4H_6$ (14 bonding electrons) [25] (cf. Fig. 1). Hexahydrohexaborate(2-), which is isoelectronic with $C_2B_4H_6$, also has the same structure [26]. As in

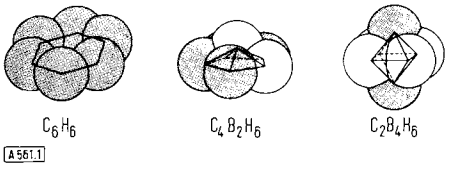


Fig. 1. Arrangement of the atoms in the series $C_{6-n}B_nH_6$ for $n = 0, 2, 4$.

the crystal lattice of the borides of bivalent metals [27], the boron atoms occupy the apices of an octahedron. LCAO–MO calculations [7,13,28] have shown that all the bonding orbitals in $C_2B_4H_6$ are filled. The completely closed and highly symmetrical three-dimensional structure, together with the particularly saturated electronic configuration, makes compounds of this type chemically and physically stable.

Between the fully condensed carboranes $C_2B_nH_{n+2}$ and the BCH compounds with polyhedral structures, which are not carboranes, there are many intermediate types; thus, the "dihydrocarboranes" $C_2B_nH_{n+4}$ [29], which contain BH_bB groups [*] on "open" sides of the BC skeleton, are a link with the polyboranes. The pentagonal-pyramidal tetracarbahexaboranes(6) [6], which are very close to the hydrocarbons, are relatively far removed from the condensed carboranes. The progressive substitution of the BH_b groups by carbon leads *e.g.* from hexaborane(10) *(1)* *via* the neutral compounds 2-carbahexaborane(9) *(2)*, 2,3-dicarbahexaborane(8) *(3)* and 2,3,4-tri-carbahexaborane(7) *(5)* to tetracarbahexaborane(6) (diborahexacarbane) *(4)*.

[25] *I. Shapiro*, *B. Keilin*, *R. E. Williams*, and *C. D. Good*, J. Amer. chem. Soc. *85*, 3167 (1963).

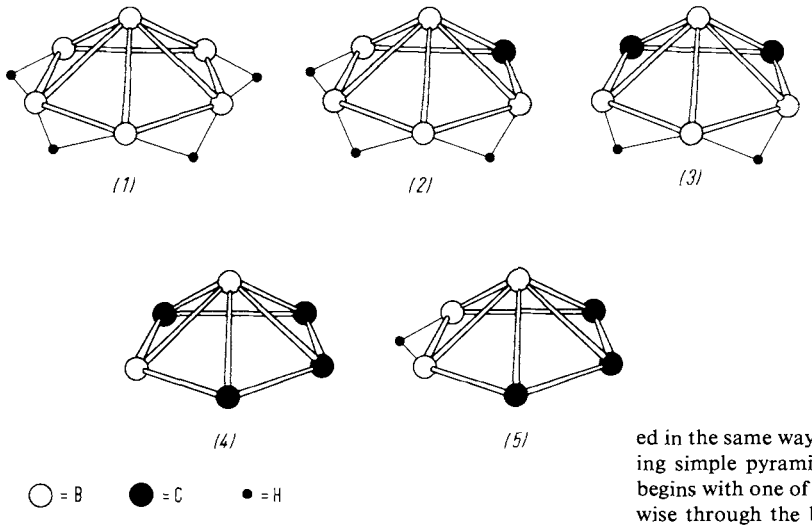
[26] *J. L. Boone*, J. Amer. chem. Soc. *86*, 5036 (1964).

[27] *M. v. Stackelberg* and *F. Neumann*, Z. physik. Chem., Abt. *B 19*, 314 (1932).

[28] *R. Hoffmann* and *W. N. Lipscomb*, J. chem. Physics *36*, 3489 (1962).

[29] *T. P. Onak*, *R. E. Williams*, and *H. G. Weiss*, J. Amer. chem. Soc. *84*, 2830 (1962).

[*] BH_bB denotes two boron atoms with a common hydrogen atom (bridge hydrogen atom).



2.1.2. Nomenclature

There is as yet no uniform and generally obligatory system of nomenclature for the carboranes. Consequently, trivial names (*e.g.* "dihydrocarborane"[29]) are used side by side with semisystematic and systematic designations.

2.1.2.1. *Systematic Names*

A system that is widely used is that proposed by the Nomenclature Committee of the American Chemical Society[5]; this system, which is derived from the system used for the polyboranes, is particularly commendable for three-dimensional BC structures with high boron contents. The carbon of a carborane is regarded as a hetero atom and the compound $C_2B_3H_5$, for example, is known as dicarbapentaborane(5).

As in the case of the polyboranes, the number of hydrogen atoms attached to the carbon and boron atoms is given in brackets after the name. To emphasize the three-dimensional structure, "clovo" (from the Greek κλωβός = cage) is inserted between "carba" and "borane" in the names of carboranes of the fully condensed type $C_2B_nH_{n+2}$: *e.g.* dicarbaclovopentaborane(5). The number of hydrogen atoms need not be indicated for the clovo types. The skeletal atoms are numbered in the same way as in the polyboranes. In compounds having simple pyramidal or bipyramidal structures, numbering begins with one of the apices of the pyramids, proceeds clockwise through the base atoms as viewed from above and, in the case of a bipyramid, ends at the other apex (for exception see Section 2.3.2.1.). Thus the carborane $C_2B_3H_5$ *(6)* in Figure 2 is a 1,5-dicarbaclovopentaborane(5). It is not always possible to distinguish clearly between the apex and base atoms, as in the icosahedral dicarbaclovododecaboranes(12) *(7)*. In such cases numbering begins with a carbon atom and continues clockwise round the ring. In numbering systems containing more than one ring, the lowest index of the second ring should be among the lowest indices of the first ring. Hetero atoms (*e.g.* carbon atoms) should have the lowest indices possible.

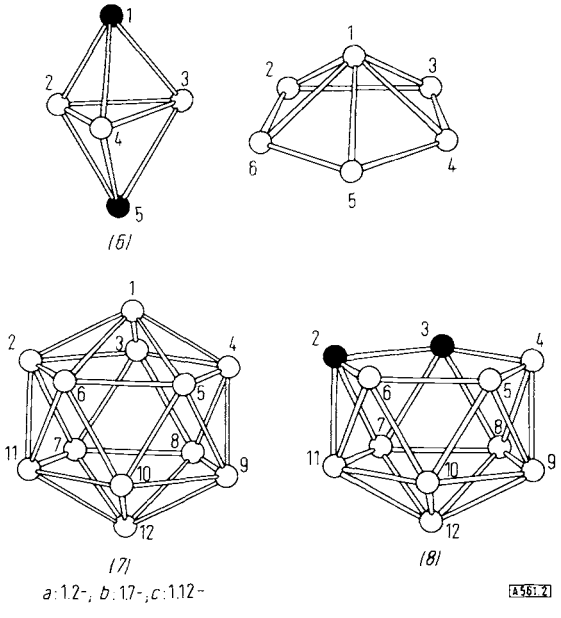


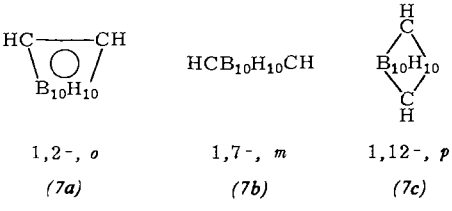
Fig. 2. Numbering of the skeletal atoms in carboranes.

Though this nomenclature can in principle also be used for three-dimensional BC structures having high carbon contents, it seems rather pointless *e.g.* to call the system $C_4B_2H_6$ *(4)* "tetracarbahexaborane(6)" since the skeleton contains more carbon atoms than boron atoms. In this case it is better to regard the boron atoms as hetero atoms, and to call the system "diborahexacarbane(6)"[6].

The anionic BC compounds with polyhedral structures are known as borates. The number of ligands outside the skeleton is given first, then the position and number of the carbon atoms in the skeleton, and finally the total number of skeletal atoms. Negative charges are given as a figure in brackets following the name. Thus the $C_2B_4H_7^{1\ominus}$ ion[29a] is a heptahydro-2,3-dicarbahexaborate(1-) ion.

2.1.2.2. *Trivial Names*

The word "carborane" itself, which was originally derived from "car(ba)borane" for the compounds $C_2B_nH_{n+2}$[8], has acquired more than one meaning. The widest meaning is now a BCH compound with carbon atoms in the skeleton and having a closed or almost closed polyhedral structure. However, the name "carborane" is often used specifically for the systems $C_2B_{10}H_{12}$ [dicarbaclovododecaboranes(12)] having an icosahedral structure, the three stereoisomers with the carbon atoms in the 1,2-position (adjacent), the 1,7-position (separated by one boron atom), and the 1,12-position (opposite apices) being distinguished as *ortho-*, *meta-*, and *para*-carboranes[5] [cf. *(7)*]. Corresponding to the hexagonal symbol for the benzene ring, the three isomers can be denoted by the formulae *(7a)–(7c)*.



1,2-, *o* (*7a*) | 1,7-, *m* (*7b*) | 1,12-, *p* (*7c*)

[29a] *T. P. Onak* and *G. B. Dunks*, Inorg. Chem. 5, 439 (1966).

Other trivial names are "barene" [30] (used only in Russian literature) for 1,2-dicarbaclovododecaborane(12), "neocarborane" [31] for 1,7-dicarbaclovododecaborane(12), and "dihydrocarborane" [29] for 2,3-dicarbahexaborane(8) *(3)*.

An advantageous combination of trivial names and systematic nomenclature provides *e.g.* the name "dicarbollide" (Spanish olla = jar or kettle) for the $C_2B_9H_{11}^{2\ominus}$ residue [32], in which the carbon and boron atoms occupy eleven corners of an icosahedron. Taking into account the vacant twelfth corner, the skeletal atoms are numbered in the same manner as the icosahedra $C_2B_{10}H_{12}$ systems, the number of the vacant position being given in brackets before the name. *(8)* in Figure 2 would be called (1)-2,3-dicarbollide.

2.2 Bonding

2.2.1. Nature of Bonding and Coordination Numbers

The skeletal atoms of the carboranes, like those of the polyboranes, generally have higher coordination numbers than the maximum valence with covalent two-center bonds. The lines drawn between the atoms of the carborane nucleus in this article are simply geometrical aids intended to show the polyhedral arrangement of the atoms. The bonds present result from the delocalization of the bonding electrons in multi-center orbitals over a large area of the molecule. The bonds in the carboranes are intermediate between covalent and metallic bonds.

The tendency to assume high coordination numbers, which is also evident in other boron compounds such as boron carbide [33,34], and particularly in elementary boron [35–37], is due to the electronic configuration of boron. A boron atom has four available orbitals, but only three bonding electrons. For example, comparison of the electronic energies in multi-center orbitals as found from LCAO calculations shows that the participation of an unoccupied atomic orbital is always accompanied by a gain in energy. The bonding energy of the three-center bond formed by the combination of three atomic orbitals is lower, *e.g.* than that of the two-center bond.

If three covalent bonds were formed, one orbital and one electron being donated to each by each of the bonded atoms, one orbital of boron would remain unoccupied. Thus in boron compounds in which there are no additional electrons available for bonding, arrangements involving close packing of the atoms are energetically favored. Such arrangements permit multiple interaction of all four orbitals of boron, and hence the formation of stable multi-center bonds.

If the "electron deficiency" of boron is compensated by the uptake of an extra electron, as in the borate ion, or by partial delocalization of a lone pair of electrons *via* a π bond (back-donation), as in compounds with elements of groups V to VII, the tendency to form multi-center bonds is lost.

2.2.2. The Three-Center Bond Theory and its Application to Carboranes [4]

The description of the π-electron system of the aromatic compounds by means of covalent bonds can also be applied to bond systems of polyboranes or carboranes if, in addition to localized two-center bonds, one also allows corresponding bonds between three atoms [12]. The simple line notation is retained. It is possible in this way, not only to represent clearly the bond systems of known boron compounds (see *e.g.* Fig. 3.), but also to make a choice on the basis of empirical rules, (cf. Sections 2.2.2.2. and 2.2.2.3.)

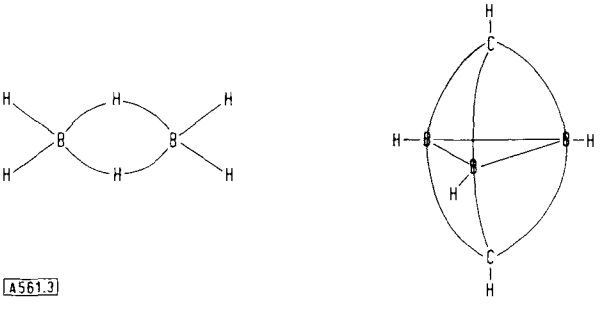


Fig. 3. Two- and three-center bonds in diborane (left) and in 1,5-dicarbaclovopentaborane(5) (right).

between several possible spatial arrangements of the atoms in compounds whose structures are unknown. Moreover, the use of the line notation also provides certain quantitative information for the estimation of charge distributions and bond orders [4]. A simple, clear representation is possible for all compounds other than those containing particularly large numbers of atoms and where the symmetry is unfavorable.

2.2.2.1. *The Three-Center Bond*

When two orbitals of two atoms interact, a bonding and an antibonding orbital are formed. The bonding orbital can accommodate two electrons, which thus constitute a covalent two-center bond. Similarly three orbitals of three atoms can also interact. The result in this case is two antibonding orbitals and one bonding orbital which can again accommodate two electrons. According to *Lipscomb* [4,12], the resulting three-center bonds exist in an open and a central (or symmetrical) type. Thus one atomic orbital may interact with an orbital of each of two other atoms (open type), or three atomic orbitals may interact with one another in the same manner (central type) (Fig. 4).

In the open type the electron distribution, to a first approximation, is $1e^-$ on the central atom and $^1/_2e^-$ on each of the outer atoms. The bond order p_{lk}, which is defined by

$$p_{lk} = 2\, c_l c_k \qquad c_l, c_k = \text{atomic orbital coefficients}$$

is $^1/_2$. In the central type the charge distribution is $^2/_3e^-$ on each of the three atoms and the bond order p_{lk} is $^2/_3$.

[30] *L. I. Zakharkin, V. I. Stanko, V. A. Brattsev, Yu. A. Chapowskii,* and *O. Yu. Ochlobystin,* Izvest. Akad. Nauk SSSR Ser. chim. *1963*, 2238; Chem. Abstr. *60*, 9301f (1964).

[31] *D. Grafstein* and *J. Dvorak,* Inorg. Chem. *2*, 1128 (1963).

[32] *M. F. Hawthorne* and *R. L. Pilling,* J. Amer. chem. Soc. *87*, 3987 (1965).

[33] *G. S. Zhdanov* and *N. G. Sevast'yanov,* Doklady Akad. Nauk SSSR *32*, 432 (1941); Chem. Abstr. *37*, 1911[1] (1943).

[34] *H. K. Clark* and *J. L. Hoard,* J. Amer. chem. Soc. *65*, 2115 (1943).

[35] *B. F. Becker* and *J. S. Kasper,* Acta crystallogr. *12*, 503 (1959).

[36] *J. L. Hoard, S. Geller,* and *R. E. Hughes,* J. Amer. chem. Soc. *73*, 1892 (1951).

[37] *R. E. Hughes, C. H. L. Kennard, D. B. Sullenger, H. A. Weakliem, D. E. Sands,* and *J. L. Hoard,* J. Amer. chem. Soc. *85*, 361 (1963).

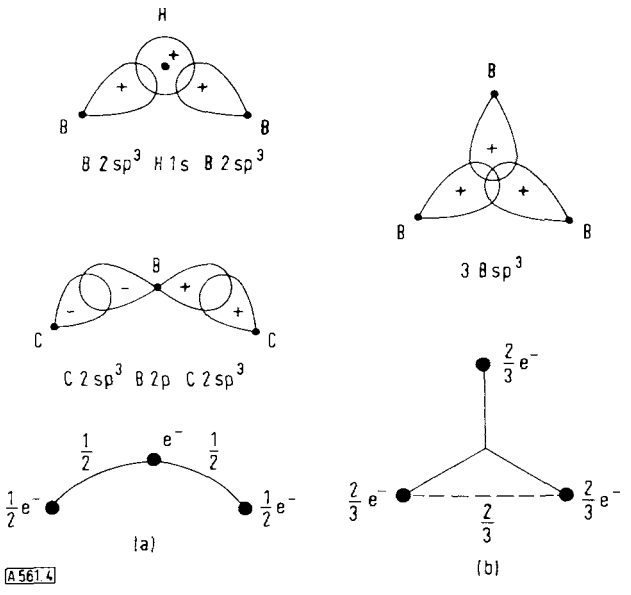


Fig. 4. Three-center bonds (a) open, (b) central. The two bottom diagrams show the electron distributions and the bond orders.

2.2.2.2. *Number of Two- and Three-Center Bonds in Carboranes*

Two electrons and three orbitals are required for a three-center bond. Since each boron atom in neutral boron compounds has one "extra" orbital available, the number of possible three-center bonds in carboranes is equal to the number of boron atoms present. Neglecting the outward-directed B–H and C–H two-center bonds, the number of electrons accommodated in the three-center bonds is equal to the number supplied by the boron atoms for bonding in the carborane skeleton. The number of two-center bonds is therefore determined by the number of C atoms and bridge H atoms. In general, for a carborane having x C atoms, y bridge H atoms, and z B atoms:

the number of three-center bonds $= z$
the number of two-center bonds $= {}^1/_2\,(3\,x + y)$.

2.2.2.3. *Resonance* [4, 38]

Owing to the localization of the electrons in bonds that extend over two or three atoms only, there are generally several possible arrangements of the calculated numbers of two- and three-center bonds. According to *Hoffmann* and *Lipscomb* [38], it is possible to distinguish between "resonance structures" and "equivalent structures". Resonance structures are arrangements that can be converted into one another by the application of symmetry operations (of the symmetry group of the molecule) Fig. 5a).

Equivalent structures are fundamentally different arrangements of the bonds and cannot be converted into one another by symmetry operations (Fig. 5b) [*]. All the resonance structures corresponding to each equivalent structure must be considered in giving complete description of a system. The number of resonance structures depends on the size and symmetry of the bond system; this number can be reduced by the following limiting conditions a–c with no appreciable decrease in its (overall) information value [38]:

a) Two atoms cannot be joined together by both a two-center and a three-center bond.

b) Two atoms cannot be joined together by both an open and a central three-center bond.

c) Two open three-center bonds cannot cross each other.

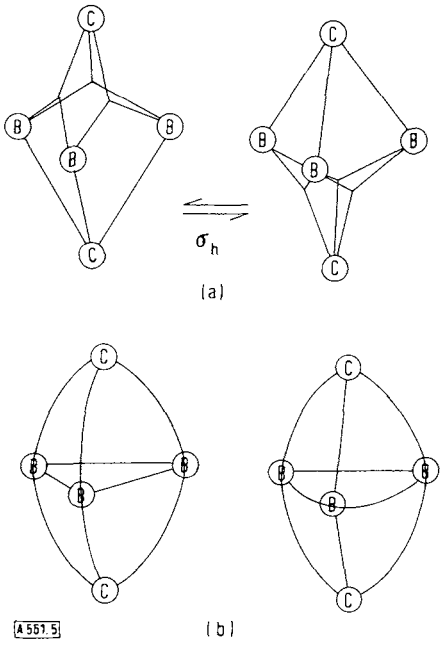


Fig. 5. Resonance structures (a) and equivalent structures (b) for the trigonal-bipyramidal 1,5-dicarbaclovopentaborane(5) *(6)*.

2.2.2.4. *Net Charges and Bond Orders* [4,38]

The net charges q_k and the bond orders p_{lk} can be estimated from the values indicated for the two three-center bonds by summation over all N resonance structures. Assuming that all the resonance structures have the same statistical weight in the combination [38]:

$$q_k = \frac{1}{N}\sum_{i=1}^{N} q_k^i \quad \text{and} \quad p_{lk} = \frac{1}{N}\sum_{i=1}^{N} p_{lk}^i$$

where q_k^i is the net charge on the atom k and p_{lk}^i is the bond order of the bond between the atoms k and l in the i-th resonance structure.

2.2.2.5. *Example*

For the isomeric dicarbaclovododecaboranes(12) *(7)*, there are three two-center and ten three-center bonds ($x=2$, $y=0$, and $z=10$). Using conditions a–c, and assuming that a two-center bond is localized between the two carbon atoms in *ortho*-carborane and that each carbon atom in *meta*- and *para*-carboranes forms one two-center bond, a total of 37 resonance structures are found for *ortho*-carborane, 93 for *meta*-carborane, and 121 for *para*-carborane [4, 28]. The charge distributions calculated from the three-center bond theory by taking into account all these structures show good qualitative agreement with those obtained from LCAO calculations [4, 28].

[38] *R. Hoffmann* and *W. N. Lipscomb*, J. chem. Physics *37*, 2872 (1962).

[*] The word "equivalent" should not be interpreted too literally here, since the structures are by no means always energetically equivalent.

2.2.3. LCAO–MO Calculations

A more accurate picture of the bond system of the carboranes can be obtained by the application of quantum-mechanical approximation methods. The extended Hückel method used by *Lipscomb* and *Hoffmann* has proved particularly successful for this purpose [28, 39–41].

2.2.3.1. *The Method* [4, 28, 39–41]

The wave functions of carboranes like those of π orbitals of aromatic systems, can be represented as linear combinations of atomic orbitals:

$$\Psi = \sum_n c_n \varphi_n$$

The coefficients of the linear combination can be calculated by the scheme of the Hückel method, taking into account the interactions, not merely between the nearest neighbors, but between all the atoms of the molecule.

In addition to the 1s orbitals of the hydrogen atoms, the combination must include four atomic orbitals per boron or carbon atom; consequently for a carborane having the general composition $C_xB_zH_{x+z}$, the combination contains a total of $5(x+z)$ terms. The coefficients c_n satisfy secular equations of the general form

$$(\alpha_n - ES_{nn})c_n + \sum_m{}' (\beta_{nm} - ES_{nm})c_m = 0$$

On introduction of the approximation

$$\beta_{nm} = KS_{nm}$$

and of the normalization condition

$$S_{nn} = 1$$

the secular equations simplify to

$$(\alpha_n - E)c_n + \sum_m{}' (K - E)S_{nm}c_m = 0$$

where

$\alpha_n = \int \varphi_n H \varphi_n \, d\tau$ (Coulomb integral)

$\beta_{nm} = \int \varphi_n H \varphi_m \, d\tau$ (resonance integral)

$S_{nm} = \int \varphi_n \varphi_m \, d\tau$ (overlap integral)

K = const.

The solutions of the secular determinants give the energy eigenvalues and the coefficients of the linear combinations for the individual molecular orbitals. With the aid of the coefficients it is possible, according to *Mulliken* [42], to estimate the electron-density distributions $n(k,l)$ between the atoms and $N(k)$ on the atoms:

$$n(k, l) = \sum_i \sum_r \sum_s n(i, r_k, s_l)$$

$$n(i, r_k, s_l) = 2\, N(i) c_{r_k i} S_{r_k, s_l} c_{s_l i}$$

and

$$N(k) = \sum_i \sum_r N(i, r_k)$$

$$N(i, r_k) = N(i) c_{r_k i} \sum_l \sum_s S_{r_k, s_l} c_{s_l i}$$

In these equations, c_{rki} and c_{sli} are the coefficients of the atomic orbitals r and s on the atoms k and l in the molecular orbital i, $S_{rk,sl}$ is the corresponding overlap integral, and $N(i)$ is the occupation number of the i-th molecular orbital.

2.2.3.2. *Application of the Series $C_2B_nH_{n+2}$ to Carboranes*

The calculation of the electron systems of the carboranes $C_2B_3H_5$ (trigonal bipyramid), $C_2B_4H_6$ (octahedron), $C_2B_5H_7$ (pentagonal bipyramid), and $C_2B_{10}H_{12}$ (icosahedron) gives a closed electronic structure in every case, all the bonding orbitals just being filled [28]. This explains the extraordinary stability of these compounds. Comparative calculations for polyhydropolyborates(2-) $B_nH_n^{2\ominus}$, which are isoelectronic with the carboranes, showed [39] that the order of the molecular orbitals with respect to energy is not affected when the 1s atomic orbitals of hydrogen and the hybrid orbitals directed outward from the B and C atoms toward the hydrogens are omitted from the linear combination. The only differences resulting from this omission are in the calculated electronic transition energies. Thus the BH and CH bonds may be treated as normal covalent bonds. Other simplifications, excluding the factorization associated with the symmetry properties of the bond systems, have been found to be either inadmissible or admissible to a limited extent only [39].

Experimental data for comparison are at present available for the dicarbaclovododecaboranes(12) only *(7)*, and in particular for "*ortho*-carborane" *(7a)*. In this case good agreement is found between experiment and theory [43–47a].

2.2.4. Aromaticity of the Carboranes

The nature of the bonding in the carboranes and their surprising stability suggest a comparison with aromatic systems. If we take the degree of delocalization of the bonding electrons as a measure of the aromaticity, and so regard the metallic phase as a "superaromatic" system, then at least some carboranes, *e.g.* the dicarbaclovododecaboranes(12) possess aromatic character. However, few data are available at present for comparison. Above all, checks should be carried out to see whether the predicted directing influence of sub-

[39] *R. Hoffmann* and *W. N. Lipscomb*, J. chem. Physics *36*, 2179 (1962).

[40] *R. Hoffmann*, J. chem. Physics *39*, 1397 (1963).

[41] *E. B. Moore jr.*, *L. L. Lohr jr.*, and *W. N. Lipscomb*, J. chem. Physics *35*, 1329 (1961).

[42] Cf. *R. S. Mulliken*, J. chem. Physics *23*, 1833, 1841, 2338, 2343 (1955).

[43] *H. Schroeder*, *T. L. Heying*, and *J. R. Reiner*, Inorg. Chem. *2*, 1092 (1963).

[44] *L. I. Zakharkin*, *V. I. Stanko*, *V. A. Brattsev*, and *Yu. A. Chapovskii*, Doklady Akad. Nauk SSSR *157*, 1149 (1964); Proc. Acad. Sci. USSR *157*, 773 (1964); Chem. Abstr. *61*, 14043g (1964).

[45] *M. F. Hawthorne*, *T. E. Berry*, and *P. A. Wegner*, J. Amer. chem. Soc. *87*, 4746 (1965).

[46] *L. I. Zakharkin* and *V. N. Kalinin*, Izvest. Akad. Nauk SSSR Ser. chim. *1965*, 1311; Chem. Abstr. *63*, 13302d (1965).

[47] *T. V. Potapova*, *R. A. Svitsyn*, *A. F. Zhigach*, *V. T. Laptev*, *I. V. Persianova*, and *P. Z. Sorokin*, Z. neorg. Chim. *10*, 2080 (1965); Chem. Abstr. *63*, 17862e (1965).

[47a] *J. A. Potenza*, *W. N. Lipscomb*, *G. D. Vickers*, and *H. Schroeder*, J. Amer. chem. Soc. *88*, 628 (1966).

stituents in reactions on the carborane nucleus does in fact occur. In all these comparisons, however, it should be remembered that the carboranes have "electron-deficient" bond systems, whereas an "excess of electrons" in aromatic systems leads to the formation of an additional stabilizing π-bond system.

2.3. Structural Analysis of Carboranes

2.3.1. Characteristics of the Structure Determination

The elucidation of the spatial structure of carboranes has so far been based mainly on the interpretation of ^1H and ^{11}B nuclear magnetic resonance spectra and of IR and Raman spectra. X-ray analysis could be carried out in only a few cases, since the necessary crystalline material is not available. Where such measurements have been possible, as in the cases of 2,3-dicarbahexaborane(8) *(3)* [48,49] and "*o*-carborane" *(7a)* [50–52] the results confirmed the structural formulae postulated on the basis of the NMR spectra. Fragments of the structures have also been characterized by chemical degradation [53–56] and synthesis [21].

2.3.2. Carboranes with Two Carbon Atoms in the Skeleton

2.3.2.1. *The Clovo Type $C_2B_nH_{n+2}$ ($n = 3$ to 10)*

In the fully condensed carboranes $C_2B_nH_{n+2}$, the boron and carbon atoms occupy the apices of generally highly symmetrical polyhedra, the faces of which in most cases are equilateral or almost equilateral triangles. All the structures can be traced back to trigonal, tetragonal, and pentagonal pyramids as the basic shapes. According to an empirical rule [57], compounds in which the carbon atoms have a coordination number of 5 (apex of a tetragonal pyramid) and in which the boron atoms have a coordination number of 6 (apex of a pentagonal pyramid) are particularly stable.

The formal first member of the series $C_2B_nH_{n+2}$ would be boracyclopropene C_2BH_3, which has not yet been definitely detected [58]. However, because of its planar structure and the 2 π-electron system corresponding to the Hückel rule (Fig. 6), this compound would resemble the aromatic hydrocarbons rather than the carboranes.

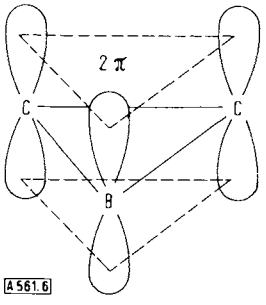


Fig. 6. π-Electron system of the unknown boracyclopropene.

The smallest known molecule of the series $C_2B_nH_{n+2}$ contains three boron atoms. According to NMR [59–61], IR [60,61], and Raman spectra [62], the two dicarbaclovopentaboranes(5) $C_2B_3H_5$ have the trigonal-bipyramidal structure predicted for the isoelectronic, hypothetical $B_5H_5^{2-}$ ion [41]. Of the three possible isomers of this structure, the 1,5- and the 1,2-isomers have been described [see Fig. 2, formula *(6)*].

In the more stable of these two isomers [1,5-dicarbaclovopentaborane(5)], the carbon atoms form the apices of the bipyramid. A quartet and a singlet can be distinguished in the ^1H-NMR spectrum of *(6)*, while the ^{11}B-NMR spectrum shows only a single sharp doublet ($^{11}B/^1H$ coupling) [60]. The ^{11}B-NMR spectra of the fully alkylated derivatives known at present [21,62] accordingly contain only a singlet. The ^1H-NMR spectrum of the 1,5-dimethyl-2,3,4-triethyl derivative [62] consists of two sharp signals having an intensity ratio of 6:15; these are assigned to the six protons of the *C*-methyl groups and to the 15-protons of the *B*-ethyl groups (Fig. 7). It is interesting to note that the methyl and methylene protons of the ethyl groups give only one signal, even at a measuring frequency of 100 MHz. The Raman spectra of the compounds give the symmetry D_{3h} [62].

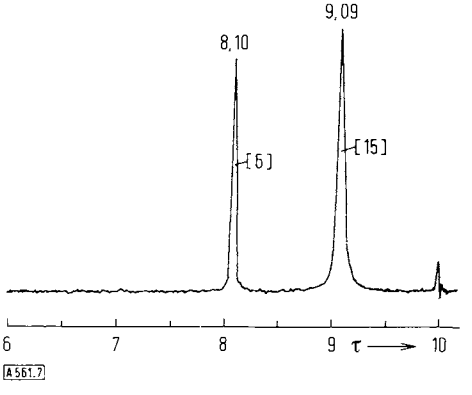


Fig. 7. ^1H-NMR spectrum of 1,5-dimethyl-2,3,4-triethyl-1,5-dicarbaclovopentaborane(5) [62,64].

[48] *W. E. Streib, F. P. Boer,* and *W. N. Lipscomb,* J. Amer. chem. Soc. *85,* 2331 (1963).

[49] *F. P. Boer, W. E. Streib,* and *W. N. Lipscomb,* Inorg. Chem. *3,* 1666 (1964).

[50] *J. A. Potenza* and *W. N. Lipscomb,* J. Amer. chem. Soc. *86,* 1874 (1964).

[51] *J. A. Potenza* and *W. N. Lipscomb,* Inorg. Chem. *3,* 1673 (1964).

[52] *D. Voet* and *W. N. Lipscomb,* Inorg. Chem. *3,* 1679 (1964).

[53] *C. Tsai* and *W. E. Streib,* J. Amer. chem. Soc. *88,* 4513 (1966).

[54] *F. Tebbe, P. M. Garret,* and *M. F. Hawthorne,* J. Amer. chem. Soc. *86,* 4222 (1964).

[54a] *T. E. Berry, F. N. Trebbe,* and *M. F. Hawthorne,* Tetrahedron Letters *1965,* 715.

[55] *R. Köster, M. A. Grassberger, E. G. Hoffmann,* and *G. W. Rotermund,* Tetrahedron Letters *1966,* 905.

[56] *L. I. Zakharkin,* Ž. obšč. Chim. *34,* 4121 (1964); Chem. Abstr. *62,* 9160h (1965).

[57] *R. E. Williams* and *F. J. Gerhart,* J. Amer. chem. Soc. *87,* 3513 (1965).

[58] *J. J. Eisch* and *L. J. Gonsior,* II. Internat. Sympos. organometallic Chem., Madison, Wisc. (USA), Sept. 1965, Abstr. of Proc. p. 47.

[59] *C. D. Good* and *R. E. Williams,* US-Pat. 3030289 (1959), Olin Mathieson Chem. Corp.; Chem. Abstr. *57,* 12534b (1962).

[60] *I. Shapiro, C. D. Good,* and *R. E. Williams,* J. Amer. chem. Soc. *84,* 3837 (1962).

[61] *R. N. Grimes,* J. Amer. chem. Soc. *88,* 1070 (1966).

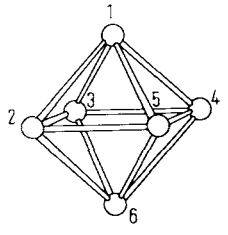
[62] *R. Köster* and *G. W. Rotermund,* Tetrahedron Letters *1964,* 1667.

[63] *R. N. Grimes,* J. Amer. chem. Soc. *88,* 1895 (1966).

[64] *E. G. Hoffmann,* Mülheim/Ruhr, ^1H- and ^{11}B-NMR-measurements.

The second isomeric $C_2B_3H_5$ [1,2-dicarbaclovopentaborane(5), cf. *(6)*] is at present known only as a dimethyl derivative [61,63]. One of the methyl groups is attached to B-3 and the other to one of the C atoms. The ^{11}B-NMR spectrum of the compound shows two clearly separated doublets ($^{11}B/^1H$ coupling) and a singlet having an intensity ratio 1:1:1. In the ^1H-NMR spectrum, the intensity ratio of the signals due to the methyl protons and to the hydrogen atom attached to the carborane carbon is 6:1. The two methyl groups give a broad signal, with only weak splitting.

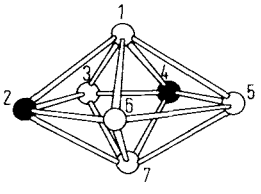
Conclusive evidence of the structures of the two known isomers of the next higher BH homologue $C_2B_4H_6$ is also lacking. However, the data available at present indicate that the predicted octahedral or tetragonal bipyramidal structure *(9)* [7] (with the C atoms in the 1,2 or 1,6 position) is fairly certain.



(9)
a:1,2-; *b*:1,6-

Mass-spectrometric analysis of the partially deuterated isomers have shown that they must be clovo compounds, in which each boron atom is associated with one hydrogen atom [25]. The IR spectra do not contain the characteristic absorption bands for the BH_bB grouping [25]. The ^1H- and ^{11}B-NMR spectra of the 1,6-isomer *(9b)* show four equivalent boron atoms and two equivalent carbon atoms [25,65]; on the other hand, the ^{11}B-NMR spectrum of the asymmetric form *(9a)* with the carbon atoms in the 1,2 position, clearly points to two non-equivalent pairs of boron atoms [25].

2,4-Dicarbaclovoheptaborane(7) $C_2B_5H_7$ *(10)* has a pentagonal-bipyramidal structure [65–66].



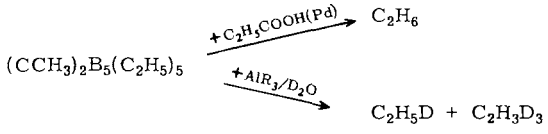
(10)

According to LCAO–MO calculations [28], *(10)* has a lower energy than any of the other three isomers having pentagonal bipyramidal structures.

The structure proposed on the basis of the IR and NMR spectra [65] was verified by analysis of the microwave spectrum [66]. The values found for the distances between the boron and carbon atoms in the base (atoms 2 to 6) are as follows:

$r_{B(5)-B(6)} = 1.650 \pm 0.005$ Å, $r_{B(3)-C(4)} = 1.606 \pm 0.1$ Å, $r_{B(5)-C(4)} = 1.502 \pm 0.1$ Å. Thus they roughly correspond to the lengths of BB and CB single bonds. The values for the BH and CH bonds of the base atoms are: $r_{B-H} = 1.250 \quad 0.06$ Å and $r_{C-H} = 1.09 \quad 0.05$ Å.

A fully alkylated and a partly alkylated dicarbaclovoheptaborane(7) could also be identified as 2,4-isomers by the ^1H- and ^{11}B-NMR spectra (cf. Figs. 8 and 9) in conjunction with chemical methods (cf. Section 3.2.2.1.) [55].



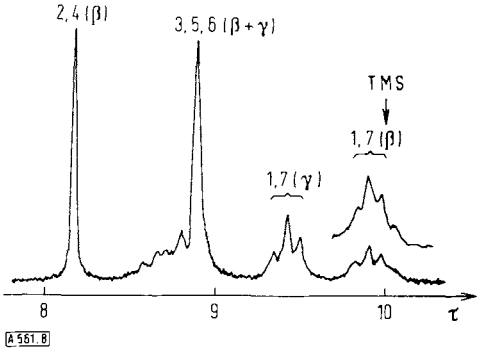


Fig. 8. ^1H-NMR spectrum of 2,4-dimethyl-1,3,5,6,7-pentaethyl-2,4-dicarbaclovoheptaborane(7) [55]. Numbering of the skeletal atoms as in *(10)*; H-atoms of the ligands: $\overset{\alpha}{-H}$, $\overset{\beta}{-CH_3}$, $\overset{\beta}{-CH_2}-\overset{\gamma}{CH_3}$.

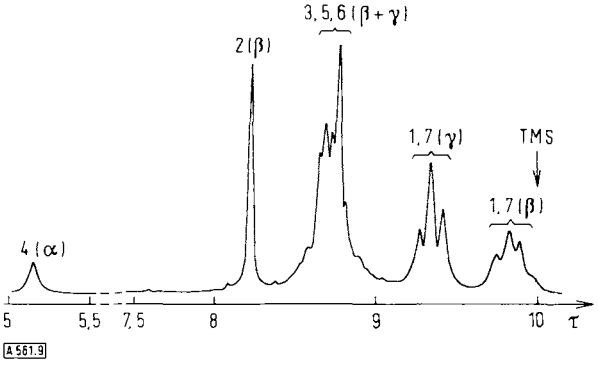
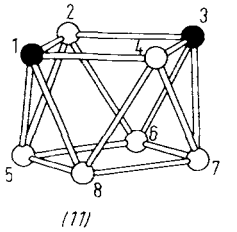


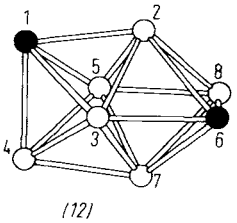
Fig. 9. ^1H-NMR spectrum of 2-methyl-1,3,5,6,7-pentaethyl-2,4-dicarbaclovoheptaborane(7) [55]. Numbering of the skeletal atoms as in *(10)*; H-atoms of the ligands: $\overset{\alpha}{-H}$, $\overset{\beta}{-CH_3}$, $\overset{\beta}{-CH_2}-\overset{\gamma}{CH_3}$.

Two structures are proposed for dicarbaclovooctaborane(8) $C_2B_6H_8$. The latest results [67] favor the Archimedian antiprism *(11)* rather than the bis-disphenoid *(12)* suggested earlier [57].

The one singlet in the ^1H-NMR spectrum of the C,C'-dimethylated compound indicates that the two carbon atoms



(11)



(12)

[65] *T. P. Onak, F. J. Gerhart,* and *R. E. Williams,* J. Amer. chem. Soc. *85*, 3378 (1963).

[65a] *T. Onak, G. B. Dunks, R. A. Beaudet,* and *R. L. Poynter,* J. Amer. chem. Soc. *88*, 4622 (1966).

[66] *R. A. Beaudet* and *R. L. Poynter,* J. Amer. chem. Soc. *86*, 1258 (1964).

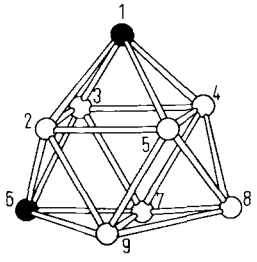
[67] *F. N. Tebbe, P. M. Garret, D. C. Young,* and *M. F. Hawthorne,* J. Amer. chem. Soc. *88*, 609 (1966).

occupy geometrically equivalent positions[57]. Only two doublets having an intensity ratio of 4:2 can be distinguished in the ^{11}B-NMR spectrum at 19.3 MHz[67]. Thus the structure is probably an Archimedian antiprism with the carbon atoms in the 1,3-position. Dicarbaclovooctaborane(8) would therefore be the only exception to the rule[57] that carboranes of the type $C_2B_nH_{n+2}$ have polyhedral structures built up entirely from triangles. If, in agreement with the earlier proposal, the boron and carbon atoms were arranged to form a bis-disphenoid, with the carbon atoms in the 1,6-position, the three pairs of equivalent boron atoms should give three doublets having an intensity ratio of 2:2:2 in the ^{11}B-NMR spectrum. However, the ratio of 4:2 observed at a measuring frequency of 19.3 MHz could be explained if two of the signals coincided. Another possibility that has recently been proposed[68] is that there are two isomeric bis-disphenoid structures with fast interconversion between the two.

For a final decision on the structure, it will be necessary to record a high-resolution ^{11}B-NMR spectrum or to carry out an X-ray analysis.

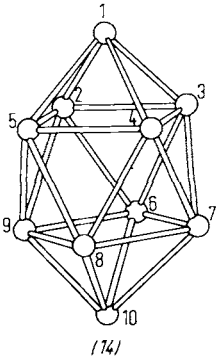
Dicarbaclovononaborane(9) $C_2B_7H_9$ *(13)*, which was reported only recently[67], probably has the structure of a tricapped trigonal prism.

The ^{11}B-NMR spectrum of the *C,C'*-dimethyl derivative indicates the presence of three types of boron atoms in the ratio 1:2:4. As is shown by the sharp signal in the ^{1}H-NMR spectrum, the two C-methyl groups are equivalent. Thus the two C atoms occupy the apices of two of the three pyramids, and have a coordination number of five.



(13)

Two *C,C'*-dimethylated skeletal isomers of the next higher BH homologue $C_2B_8H_{10}$ *(14)*[67] are known. On the basis of the ^{1}H-NMR spectra and by analogy with the isoelectronic $B_{10}H_{10}^{2\ominus}$ ion[69], these are assumed to have the structure of a bicapped Archimedean antiprism[67]. The C atoms in the more stable isomer are situated in the 1,10 positions. The less stable isomer is assigned the skeleton having the carbon atoms in positions 1 and 6.



(14)

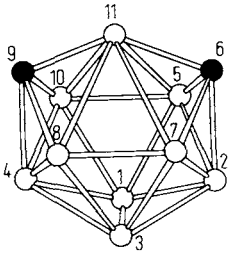
[68] *W. N. Lipscomb*, Science (Washington) *153*, 373 (1966).

[69] *R. D. Dobrott* and *W. N. Lipscomb*, J. chem. Physics *37*, 1779 (1962).

The protons of the *C*–CH_3 groups in the 1,10-isomer give one sharp signal in the ^{1}H-NMR spectrum; the boron atoms give only one doublet in the ^{11}B-NMR spectrum. Since the most favorable coordination numbers are 5 for carbon and 6 for boron, this compound should be the most stable of the condensed carboranes.

The ^{1}H-NMR spectrum of the 1,6-isomer consists of two separate sharp lines of equal intensity for the two CH_3 groups, clearly showing that the carbon atoms are not equivalent. The ^{11}B-NMR spectrum contains a single doublet for the apex boron atom, together with three overlapping doublets having an intensity ratio of 1:7. However, these data do not entirely rule out a structure with the C atoms in positions 1 and 2.

X-ray analysis of the *C,C'*-dimethyl derivative of dicarbaclovoundecaborane(11) $C_2B_9H_{11}$ *(15)*[53] confirmed the structure proposed earlier[54,54a], *i.e.* a C_2B_{10} icosahedron in which one edge has been replaced by a single boron atom.



(15)

The distance between atoms 6 and 9[*] (3.09 Å) is much shorter than *e.g.* in bis(acetonitrile)decaborane(12) (3.32 Å) or in decaborane(14) (3.55 Å). Other distances between adjacent atoms are $r_{B(11)-B(5)}$ = 2.05 Å and $r_{B(11)-C(6)}$ = 1.68 Å.

After the structure of the isoelectronic $B_{12}H_{12}^{2\ominus}$ ion, which had previously been deduced from theoretical considerations[12,14], had been confirmed[70], it was to be expected that dicarbaclovododecaborane(12) $C_2B_{10}H_{12}$ *(7)* would also prove to have the icosahedral structure. Contrary to earlier reports[72], three-dimensional X-ray studies on the derivatives $C_2H_2B_{10}Cl_8H_2$[50,51] and $C_2(CH_2Br)_2B_{10}H_{10}$[52] of *o*-carborane (C atoms in positions 1 and 2) and of bis-(*o*-carboranyl)[71] showed that the carbon and boron atoms are arranged in the form of an almost regular icosahedron. There is a slight asymmetry due to the difference in the covalent radii of the boron and carbon atoms.

The mean BC distances are between 1.71 and 1.72 Å, while the mean BB distances are 1.77 to 1.78 Å. The CC distance [1.67 Å in $C_2H_2B_{10}Cl_8H_2$ and 1.64 Å in $C_2(CH_2Br)_2B_{10}H_{10}$] is relatively large, indicating that the two carbon atoms are also joined by multicenter bonds. The dipole moment of unsubstituted *o*-carborane is 4.53 D[73]. The ^{11}B-NMR spectrum of *o*-carborane *(7a)* recorded at a frequency of 64.2

[*] The numbering of the atoms here is based on that used for decaborane(14).

[70] *J. A. Wunderlich* and *W. N. Lipscomb*, J. Amer. chem. Soc. *82*, 4427 (1960).

[71] *L. H. Hall, A. Perloff, F. A. Mauer*, and *S. Block*, J. chem. Physics *43*, 3911 (1965).

[72] *L. I. Zakharkin, V. I. Stanko, V. A. Brattsev, Yu. A. Chapovskii*, and *Yu. T. Strukhkov*, Izvest. Akad. Nauk SSSR Ser. chim. *1963*, 2069; Chem. Abstr. *60*, 5531f (1964).

[73] *A. W. Laubengayer* and *W. R. Rysz*, Inorg. Chem. *4*, 1513 (1965).

MHz[74] consists of four doublets in an intensity ratio of 2:2:4:2, corresponding to the four groups of geometrically equivalent boron atoms (positions 3 and 6; 8 and 10; 4, 5, 7, and 11; 9 and 12).

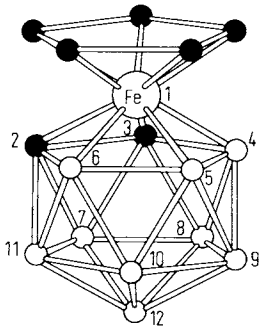
The ^{11}B-NMR spectrum of *m*-carborane (C atoms in positions 1 and 7) shows the presence of four types of equivalent boron atoms in the ratio 2:2:4:2, the signals being split into four doublets at 64.2 MHz[75]. The dipole moment of the compound is only 2.85 D[73].

The ^{11}B-NMR spectrum of *p*-carborane (C atoms in positions 1 and 12), which contains ten equivalent boron atoms, consists of only a single doublet[76]. Because of its molecular symmetry, the compound has no dipole moment[73].

2.3.2.2. *Compounds with π Bonds between Carborane and Metal*

The dicarbollide ion $C_2B_9H_{11}^{2\ominus}$ *(8)* forms a series of compounds with transition metals, which in their composition and structure correspond to the π-cyclopentadienylmetal compounds[32,77–79].

X-ray analysis shows that π-cyclopentadienyliron – π-(1)-2,3-dicarbollide has a ferrocene-like "sandwich" structure *(16)*[80]; in contrast to the ferrocene crystal[80a], however, the two five-membered rings are eclipsed.



(16)

The distances from the iron atom to the cyclopentadienyl ring (r_{FeC} = 2.07 Å) and to the C_2B_3 ring of the carborane residue (r_{FeB} = 2.09 Å and r_{FeC} = 2.04 Å) are surprisingly similar. The CC distance in the carbollide is 1.58 Å; the mean values for the BC and BB distances have been determined as 1.68 Å and 1.75 Å respectively[80].

2.3.2.3. *The Carboranes $C_2B_nH_{n+4}$*

Dicarbahexaborane(8) $C_2B_4H_8$ *(3)* ("dihydrocarborane") is one of the few carboranes for which an X-ray study has been carried out[48,49]. The apex of the pentagonal pyramid is occupied by a boron atom, while the base is formed by three boron atoms joined together by H bridges and two adjacent carbon atoms.

The following values have been found for the BB and BC distances[49]

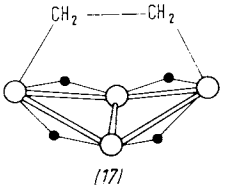
B(1)–B(5) = 1.779 Å, B(1)–B(6) = 1.779 Å, B(1)–B(4) = 1.765 Å, B(5)–B(6) = 1.783 Å, B(4)–B(5) = 1.798 Å, B(1)–C(2) = 1.784 Å, B(1)–C(3) = 1.751 Å, B(6)–C(2) = 1.509 Å, B(4)–C(3) = 1.489 Å. The C(2)–C(3) distance is 1.418 Å.

The C–C–C bond angle of 121 ° in the *C,C'*-dimethyl derivative[49] and the coupling constant $J_{^{13}CH}$ of 160 Hz in the ^{13}C-labeled carborane *(3)*[81] indicate substantial sp^2 hybridization of the carbon atoms in the carborane skeleton. The short CC distance also suggests that the CC bond has considerable double-bond character[82].

Dicarbaundecaborane(13) $C_2B_9H_{13}$ has not, as yet, been extensively studied[83]. A weak band at 1960 cm^{-1} in the IR spectrum points to a BH_bB grouping. Like the dicarbollide ion, this is presumably an icosahedral fragment, with the two carbon atoms adjacent to each other (*ortho*) or separated by a boron atom (*meta*) on an "open" pentagonal face.

2.3.2.4. *Compounds Having Special Structural Elements*

"Dimethylenetetraborane" $C_2B_4H_{12}$ *(17)* and dicarbanonaborane(13) *(17a)* occupy a position intermediate between the organoboranes and the carboranes. In contrast to the carboranes, each carbon atom in "dimethylenetetraborane"[84,85] is directly joined to only one boron atom; moreover, since the carbon atoms also carry two H atoms, they cannot contribute orbitals for the formation of multicenter bonds. Consequently, this compound does not exhibit the stabilization that characterizes the carboranes[84].



(17)

The structure of dicarbanonaborane(13) $C_2B_7H_{13}$[86] has been shown, by X-ray analysis[86a] of its C–C-derivative, to be an icosahedral fragment with two methylene groups separated from each other in the borane skeleton *(17a)*[*].

[74] *R. L. Pilling, F. N. Tebbe, M. F. Hawthorne,* and *E. A. Pier,* Proc. chem. Soc. (London) *1964*, 402.

[75] *G. D. Vickers, H. Agahigian, E. A. Pier,* and *H. Schroeder,* Inorg. Chem. *5*, 693 (1966).

[76] *S. Papetti* and *T. L. Heying,* J. Amer. chem. Soc. *86*, 2295 (1964).

[77] *M. F. Hawthorne, D. C. Young,* and *P. A. Wegner,* J. Amer. chem. Soc. *87*, 1818 (1965).

[78] *M. F. Hawthorne* and *T. D. Andrews,* J. Amer. chem. Soc. *87*, 2496 (1965).

[79] *M. F. Hawthorne* and *T. D. Andrews,* Chem. Commun. *1965*, 443.

[80] *A. Zalkin, D. H. Templeton,* and *T. E. Hopkins,* J. Amer. chem. Soc. *87*, 3988 (1965).

[80a] *J. D. Dunitz, L. E. Orgel,* and *A. Rich,* Acta crystallogr. *9*, 373 (1956).

[81] *T. P. Onak, R. P. Drake,* and *G. B. Dunks,* Inorg. Chem. *3*, 1686 (1964).

[82] *L. Pauling, L. O. Brockway,* and *J. Y. Beach,* J. Amer. chem. Soc. *57*, 2705 (1935); *L. Pauling* and *L. O. Brockway,* ibid. *59*, 1223 (1937).

[83] *R. A. Wiesboeck* and *M. F. Hawthorne,* J. Amer. chem. Soc. *86*, 1642 (1964).

[84] *B. C. Harrison, L. J. Solomon, R. D. Hites,* and *M. J. Klein,* J. inorg. nuclear Chem. *14*, 195 (1960).

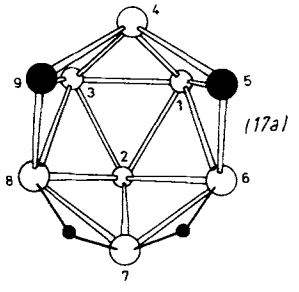
[85] *I. Shapiro, R. E. Williams,* and *S. G. Gibbins,* J. physic. Chem. *65*, 1061 (1961).

[86] *F. N. Tebbe, P. M. Garret,* and *M. F. Hawthorne,* J. Amer. chem. Soc. *88*, 607 (1966).

[86a] *D. Voet* and *W. N. Lipscomb,* Inorg. Chem. *6*, 113 (1967).

[*] On account of the peculiar structure of *(17a)* the numbering of the atoms [86a] corresponds only partly to the rules given in Section 2.1.2.1.

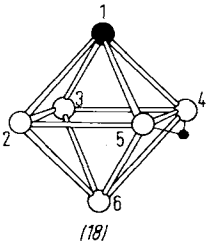
The structure *(17a)* had previously been suggested on the basis of the ^{1}H-NMR spectrum (two isolated CH_2 groups), the ^{11}B-NMR spectrum (five doublets having an intensity ratio 1:2:2:1:1), and the IR spectrum (ν_{BH_bB} = 2020 cm^{-1}) [86].



(17a)

2.3.3. Monocarbaboranes $C_1B_xH_y$

Carbahexaborane(7) CB_5H_7 *(18)* [87] is formally (C/BH exchange), and probably also structurally, derived from dicarbaclovohexaborane(6) *(9)*. The five boron atoms give three doublets having an intensity ratio of 2:2:1 in the ^{11}B-NMR spectrum; the ^{1}H-NMR and IR spectra indicate a CH and a BH_bB grouping.



(18)

Several *B*- and *C*-alkylated derivatives of carbahexaborane(9) CB_5H_9 *(2)* have been described [20,88] and their ^{11}B-NMR, ^{1}H-NMR, and IR spectra indicate a pentagonal-pyramidal structure having a B atom at the apex.

The ^{11}B-NMR spectrum of the *C*-methylpentaethyl derivative [20] consists of three signals in the intensity ratio 2:2:1. The ^{1}H-NMR spectrum (cf. Fig. 10) contains the $C-CH_3$ singlet together with the signals of two different types of B-ethyl groups (ratio 4:1). The protons of the ethyl group on B-1 are split into a "methylene quartet" and a "methyl triplet", while the ethyl groups on the four boron atoms in the base give the same signal for the methyl and methylene protons.

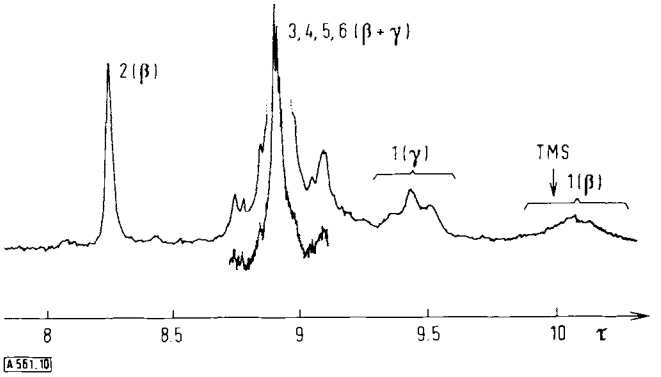
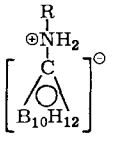


Fig. 10. ^{1}H-NMR spectrum of 2-methyl-1,3,4,5,6-pentaethyl-2-carbahexaborane(9) [64]. For definition of symbols see fig. 8 and 9.

The three BH_bB bridges can be detected from the IR spectrum, and probably link up the boron atoms in the base of the pyramid. In the ^{11}B-NMR spectrum of the 3-methyl derivative [88] of CB_5H_9 *(2)*, the asymmetric substitution leads, not only to splitting due to B–H coupling, but also to further complication. The spectrum contains four signals having an intensity ratio of 1(doublet):2(doublet):1(singlet):1(doublet). The positions of the signals due to the CH and the BCH_3 protons in the ^{1}H-NMR spectrum of the 3-methyl and 4-methyl derivatives differ only slightly.

The compound $RNH_2CB_{10}H_{12}$ (R = alkyl) contains only one carbon atom in the carborane skeleton and is assumed to be a zwitterionic derivative of the $CB_{10}H_{13}^{\ominus}$ ion, which is isoelectronic with dicarbanonaborane(13) [88a].



The ^{11}B-NMR spectrum contains six doublets in the intensity ratio 1:2:2:2:1:2. A BH_bB grouping is indicated by a weak broad band at 1975 cm^{-1} in the IR spectrum.

2.3.4. Carboranes with More Than Two Carbon Atoms in the Skeleton

2.3.4.1. *Carboranes with Three Carbon Atoms in the Skeleton*

One *C*-methyl and two *C,C'*-dimethyl derivatives of 2,3,4-tricarbahexaborane(7) *(5)* have been isolated (cf. Section 3.1.4.) [88b]. A pentagonal-pyramidal structure with three vicinal carbon atoms and one BH_bB grouping in the base of the pyramid [formula *(5)*] is deduced from the ^{1}H- and ^{11}B-NMR spectra and from the IR spectra (ν_{BH_bB} = 1500, 1900 cm^{-1}).

The ^{11}B-NMR spectra of the 2,3-dimethyl derivative *(5b)* and of the 2,4-dimethyl derivative *(5c)* are almost identical, and consist of two doublets having an intensity ratio of 2:1. In the spectrum of the 2-methyl derivative *(5a)*, the signal for the boron atom at the apex is slightly displaced. In addition to broad B–H multiplets, the ^{1}H-NMR spectra contain three singlets in the ratio 3:1:1 for *(5a)*, three singlets in the ratio 3:3:1 for *(5b)*, and two singlets in the ratio 6:1 for *(5c)*.

2.3.4.2. *Carboranes with Four Carbon Atoms in the Skeleton*

According to ^{11}B-NMR, ^{1}H-NMR, and IR spectra, the skeleton of tetracarbahexaborane(6) [diborahexacarbane(6)] $C_4B_2H_6$, several alkyl derivatives of which are known [6], has the pentagonal-pyramidal structure *(4)* predicted from theory [39]. One boron atom occupies the apex of the pyramid, while the other is situated in the base.

The ^{11}B-NMR spectrum of the hexamethyl derivative shows two boron atoms with different shielding (cf. Fig. 11). In agreement with this, the ^{1}H-NMR spectrum indicates two

[87] *T. P. Onak, R. Drake,* and *G. Dunks,* J. Amer. chem. Soc. *87,* 2505 (1965).

[88] *T. P. Onak, G. B. Dunks,* and *J. R. Spielman,* J. Amer. chem. Soc. *88,* 2061 (1966).

[88a] *D. E. Hyatt, D. A. Owen,* and *L. J. Todd,* Inorg. Chem. *5,* 1749 (1966).

[88b] *C. L. Bramlett* and *R. N. Grimes,* J. Amer. chem. Soc. *88,* 4269 (1966).

types of *B*-methyl groups as well as two pairs of equivalent *C*-methyl groups (Fig. 12). The protons of the *B*-methyl group at the base of the pyramid evidently give a sharp signal, whereas the remarkably broad signal at higher field strengths must be assigned to the protons of the *B*-methyl group at the apex [*].

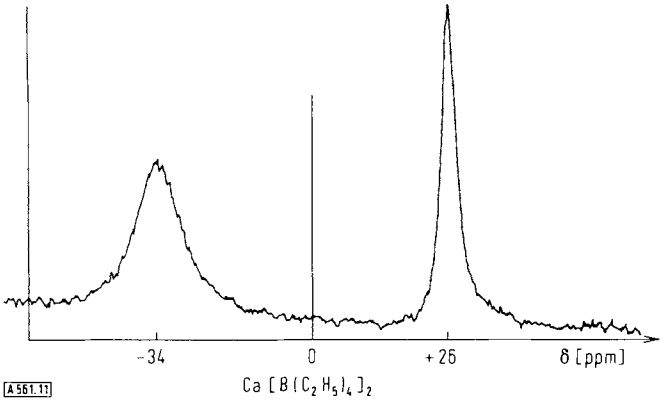


Fig. 11. ^{11}B-NMR spectrum of hexamethyl-2,3,4,5-tetracarbahexaborane(6). Line width (W_H) at −34 ppm; 234 Hz, at +26 ppm: 69 Hz [64].

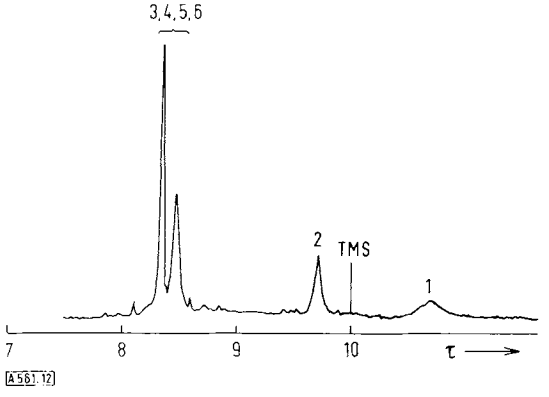


Fig. 12. ^{1}H-NMR spectrum of hexamethyl-2,3,4,5-tetracarbahexaborane(6) [64].

3. Preparation of Carboranes

No method based on readily obtainable derivatives of monoborane, corresponding *e.g.* to the preparation of the polyhedral $B_{12}H_{12}^{2\ominus}$ ion from sodium boranate and diborane [89],

$$2\ NaBH_4 + 5\ B_2H_6 \xrightarrow[100-180\,^\circ C]{N(C_2H_5)_3} Na_2B_{12}H_{12} + 13\ H_2$$

has so far been found for the unsubstituted carboranes. Acetylene and diborane react to give carboranes in small quantities only, and generally in the form of mixtures that are difficult to resolve [8, 11, 25, 59–61, 63].

Carboranes are generally prepared by the reaction of polyboranes [*e.g.* pentaborane(9), decaborane(14)] with an organic component (acetylene, other alkynes). Nearly all carboranes with no substituents on the boron have been prepared in this way, either directly or by degradation or transformation of the primary products (see Scheme 1).

Carboranes with alkyl groups attached to boron (organocarboranes), on the other hand, can also be prepared directly by condensation of simple organoboranes. For example, fully alkylated derivatives of 1,5-dicarbaclovopentaborane(5) *(6)* can be obtained, sometimes in very good yields, by several entirely different routes from alkylhalogenoboranes, alkyldiboranes, and alkynylboranes (cf. Section 3.2.2.) [21, 62].

3.1. Carboranes from Polyboranes

3.1.1. Carboranes from Decaborane(14)

3.1.1.1. *With Alkynes*

The preparation of 1,2-dicarbaclovododecaborane(12) [*o*-carborane *(7a)*] and its *C*-organo derivatives from decaborane(14) and acetylene or alkynes proceeds particularly smoothly in the presence of Lewis bases [9, 10, 30, 90–92].

$$B_{10}H_{14} + RC{\equiv}CR' \xrightarrow{L} RC\underset{\backslash O /}{-}CR' + 2\ H_2$$
$$B_{10}H_{10}$$

The reaction proceeds *via* disubstitution products $B_{10}H_{12}L_2$ (L = Lewis base) formed by elimination of 1 mole of hydrogen:

$$B_{10}H_{14} + 2\ L \rightarrow B_{10}H_{12}\cdot L_2 + H_2$$

These intermediates then react with the CC triple bond of the acetylene or alkyne, with elimination of a second mole of hydrogen and simultaneous regeneration of the free base.

The formation of *o*-carborane from acetylene and decaborane(14) in benzene takes place in the presence of only 0.1 mole of acetonitrile per mole of decaborane [9]; however, the optimum ratio of base to polyborane is 0.9:1.

Apart from acetonitrile, a number of other Lewis bases have also been used successfully, *e.g.* trialkylarsines [30, 92] and cyclic ethers such as dioxane and tetrahydrofuran [9]. However, the most suitable compounds are dialkyl sulfides and Lewis bases containing nitrogen, such as alkyl cyanides, trialkylamines, and dialkylamines [9, 10].

1-substituted or 1,2-disubstituted acetylenes give *C*-substituted or *C,C'*-disubstituted 1,2-dicarbaclovododecaboranes(12) [9, 10, 30, 91, 92]. However, unsubstituted 1,2-dialkylacetylenes react very poorly. For example, whereas 1-pentyne and even 1,4-dichloro-2-butyne react smoothy in benzene with decaborane(14) in the presence of acetonitrile to give the corresponding di-

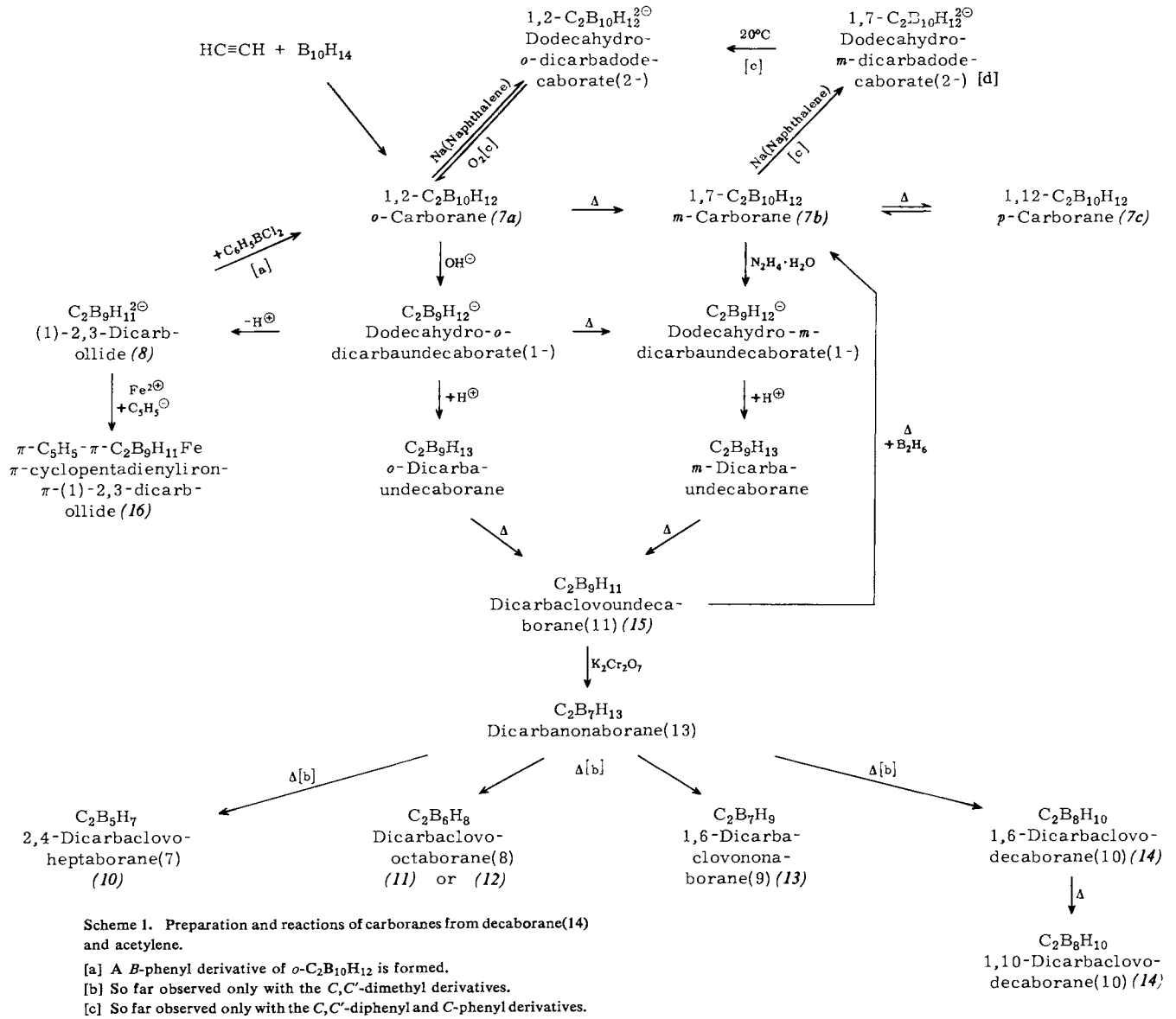
[*] The breadth of the signal has not yet been satisfactorily explained.

[89] *H. C. Miller, N. E. Miller,* and *E. L. Muetterties,* J. Amer. chem. Soc. *85,* 3885 (1963); *N. E. Miller* and *E. L. Muetterties,* ibid. *86,* 1033 (1964).

[90] *C. D. Ross,* US-Pat. 3028432 (1959), Callery Chemical Corp.; Chem. Abstr. *57,* 7308h (1962).

[91] *M. M. Fein, D. Grafstein, J. E. Paustian, J. Bobinski, B. M. Lichtstein, N. Mayes, N. N. Schwartz,* and *M. S. Cohen,* Inorg. Chem. *2,* 1115 (1963).

[92] *L. I. Zakharkin, V. I. Stanko, V. A. Brattsev, Yu. A. Chapovskii, A. I. Klimova, O. Yu. Okhlobystin,* and *A. A. Ponomarenko,* Doklady Akad. Nauk SSSR *155,* 1119 (1964); Chem. Abstr. *61,* 3131c (1964).



Scheme 1. Preparation and reactions of carboranes from decaborane(14) and acetylene.

[a] A *B*-phenyl derivative of $o\text{-}C_2B_{10}H_{12}$ is formed.
[b] So far observed only with the *C,C'*-dimethyl derivatives.
[c] So far observed only with the *C,C'*-diphenyl and *C*-phenyl derivatives.
[d] Not definitely detected [113a].

carbaclovododecaboranes(12) (> 50 and 74% yield respectively), 2-butyne and 2-pentyne give only traces of carboranes [9,91].

3.1.1.2. *With Alkyl Isocyanides*

Whereas the reaction of decaborane(14) with alkyl cyanides leads to elimination of hydrogen and formation of bis(alkylnitrile)decaboranes(12), the reaction with alkyl isocyanides leads to compounds having the composition $RNH_2CB_{10}H_{12}$ (R = alkyl), in which one carbon atom is joined to the $B_{10}H_{12}$ residue to give a carborane skeleton [88a] (cf. Section 2.3.3.).

3.1.2. Carboranes from Hexaborane(10)

When hexaborane(10) and acetylene are heated to 200 °C, traces of dicarbaclovooctaborane(8) [formula *(11)* or *(12)*] and dicarbahexaborane(8) *(3)* [57] are formed. 2-Butyne may also be used as the alkyne component in this reaction; *C,C'*-dimethyldicarbaclovooctaborane(8) is then formed in < 2% yield.

The formation of the carborane in this case is evidently not catalysed by Lewis bases. Thus no carborane can be detected even after prolonged heating of the adduct $B_6H_{10}\cdot P(C_6H_5)_3$ with an excess of 2-butyne at 100 °C. On the other hand, photochemical activation of the reaction mixture at 35 to 60 °C [57] gave up to 12% of *C,C'*-dimethyldicarbaclovooctaborane(8):

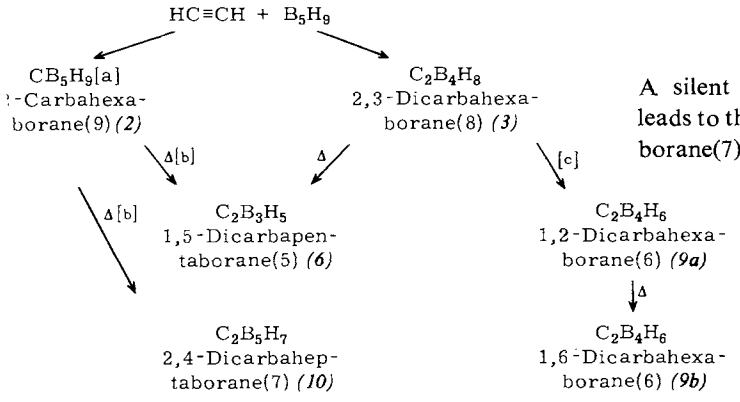
$$B_6H_{10} + CH_3\text{–}C{\equiv}C\text{–}CH_3 \xrightarrow{h\nu} (CH_3)_2C_2B_6H_6$$

An isomeric dicarbaclovooctaborane was also formed in trace amounts.

3.1.3. Carboranes from Pentaborane(9)

The reaction of pentaborane(9) with acetylene or alkynes always yields a mixture of carboranes, the composition of which depends on the reaction conditions. In contrast to the synthesis of *o*-carborane *(7a)* the manner in which these products are formed is not very clear. The mixture generally contains compounds having less boron than the polyborane used.

When a mixture of pentaborane(9) and acetylene is heated at reduced pressure [11,25] or exposed to a silent discharge [25,59,60], extremely small quantities of condensed carboranes $C_2B_nH_{n+2}$ (n = 3–5) can subsequently be detected.



Scheme 2. Preparation and reactions of carboranes from pentaborane(9) and acetylene.

[a] Three isomeric monomethyl derivatives are formed.
[b] So far observed only with fully alkylated derivatives.
[c] Silent discharge.

The pyrolysis of acetylene and pentaborane(9) in closed vessels, on the other hand, leads to the formation of 2,3-dicarbahexaborane(8) *(3)* in 30 to 40% yield [81,93] (see Scheme 2).

$$B_5H_9 + HC{\equiv}CH \xrightarrow{215\,^\circ C} \underset{(3)}{C_2B_4H_8}(30\text{–}40\%) + \underset{(1\text{–}2\%)}{CH_3{-}CB_5H_8}$$

Small quantities of isomeric methylcarbapentaboranes(9) $CH_3{-}CB_5H_8$ are also formed, as well as benzene and toluene [88].

Even better yields are obtained in some cases in the formation of *C*-substituted carboranes from alkynes. For example, 2-butyne and pentaborane(9) at 165 °C give the *C,C'*dimethyl derivative of 2,3-dicarbahexaborane in a yield of more than 50% [81].

These reactions are accelerated by many Lewis bases. Alkylated acetylenes and pentaborane(9) react even at room temperature in the presence of lutidine [81], the yields of carborane being strongly influenced by the alkyl substituents on the acetylene. Whereas acetylene gives only small quantities of the unsubstituted compound *(3)*, the *C,C'*-dimethyl compound is obtained in yields of up to 40% from 2-butyne under the same conditions [65]. The first step in the reaction could be a nucleophilic attack on the pentaborane(9) by the alkyne. However, 2-methylbut-1-en-3-yne, which reacts smoothly with decaborane(14) under similar conditions to give the 1-isopropenyl derivative of *o*-carborane [10], reacts only slowly with pentaborane(9), even in the presence of lutidine. No carborane is formed in the absence of bases [81].

3.1.4. Carboranes from Tetraborane(10)

The reaction of tetraborane(10) and acetylene in the gas phase at room temperature yields solid products together with small quantities (10^{-2} to 10^{-3} mmole per mmole of B_4H_{10} consumed [*]) of methylated 2,3,4-tricarbahexaboranes(7) *(5)* [88b]. The 2-methyl, 2,3-dimethyl, and 2,4-dimethyl derivatives of *(5)* were identified. A small quantity of pentaborane(9) is also formed.

3.1.5. Carboranes from Alkylated Polyboranes

A silent discharge in 1-methylpentaborane(9) vapor leads to the formation of small quantities of carbahexaborane(7) $CB_5{-}H_7$ *(18)* [87], the methyl carbon atom of the 1-methylpentaborane(9) being incorporated into the carborane skeleton. The mechanism of this reaction has not yet been explained; the reaction may become a general method for the synthesis of carboranes.

3.2. Carboranes from Mono- and Diboranes and Their Organo Derivatives

3.2.1. Carboranes from Diborane and Acetylene

The reactions of gaseous mixtures of acetylene and diborane in electric discharges have been extensively studied [63]. When diborane is present in excess, 10 to 15% of the acetylene can react to form volatile carboranes of the clovo type containing three to five boron atoms and methyl derivatives of these carboranes. 1,5-Dicarbaclovopentaborane(5) *(6)*, 1,6-dicarbaclovohexaborane(6) *(9b)*, and their 2-methyl derivatives, 2,4-dicarbaclovoheptaborane(7) *(10)* and its 1,3-dimethyl and 5-methyl derivatives, and a *C*,3-dimethyl-1,2-dicarbaclovopentaborane(5) have been detected. The reaction products also include pentaborane(9) and tetraborane(10), which may be intermediates in this carborane synthesis.

3.2.2. Carboranes from Organo Derivatives of Monoborane

3.2.2.1. *Dehalogenation of Alkylhalogenoboranes*

B- and *C*-alkylated carboranes containing 3 to 7 B atoms have been detected on dehalogenation of alkylhalogenoboranes with alkali metals [94]. Satisfactory

[*] In a reaction mixture containing 3.1 mmole of B_4H_{10} and 3.3 mmole of C_2H_2, nearly all the acetylene and 1.4 mmole of B_4H_{10} had reacted in 7 days.

[93] *I. Shapiro* and *H. G. Weiss*, US-Pat. 3086996 (1956), Olin Mathieson Chem. Corp.; Chem. Abstr. *60*, 548b (1964).

[94] *R. Köster* and *G. Benedikt*, Angew. Chem. *76*, 650 (1964); Angew. Chem. internat. Edit. *3*, 515 (1964).

yields of carboranes are obtained in particular by the use of lithium in tetrahydrofuran; diethyl ether and dimethoxyethane may also be used as solvents. However, not all dehalogenations of this type lead to the formation of carboranes; for example, when sodium-potassium alloy, in non-polar solvents such as hexane or toluene at room temperature, is used as the dehalogenating agent, alkali metal halide and diborylated alkanes are formed, but carboranes can be detected only in traces.

Suitable alkylhalogenoboranes for dehalogenation with lithium are dialkylchloroboranes, dialkylfluoroboranes, and alkyldifluoroboranes [20,94]. When alkyldichloroboranes are used, on the other hand, cleavage of the tetrahydrofuran, even at −30 °C, leads to quantitative formation of compounds containing BO bonds, *e.g.* *B*-alkylperhydrooxaborines [95].

The dehalogenation of organohalogenoboranes gives optimum yields of carboranes only within a relatively narrow range of temperatures. Below this range, the dehalogenation proceeds mainly on the ratio R:X in the alkylhalogenoborane $R_nX_{3-n}B$ (n = 1,2; X = halogen). For example, the reaction of diethylchloroborane and lithium at 0 °C in tetrahydrofuran yields *C*-methyl-*B*-ethyl derivatives of 2-carbahexaborane(9) *(2)* and of 2,4-dicarbaclovoheptaborane(7) *(10)*, together with triethylborane, which contains more than 50% of the *B*-ethyl groups used [55]. Thermally unstable and readily oxidizable organocarboranes, the structures of which are not yet known, are also formed. Small quantities of alkyl derivatives of other carboranes (up to 7 B atoms) forming homologous series can also be detected.

A total of 7 to 9% of the boron from the organohaloborane is used in the formation of stable, distillable organocarboranes, which are resistant to hydrogen peroxide in acidic solution. Approximately a further 5% of the boron is used for the formation of a compound $C_{12}H_{30}B_4$, the principal component of the distillable organoboranes that are unstable towards heat and oxidation (cf. Table 1). A substantial proportion of

Table 1. Composition of the identified organocarboranes formed in the dehalogenation of ethylhalogenoboranes in tetrahydrofuran at −5 to 0 °C.

Organocarboranes			obtained from					
			$(C_2H_5)_2BCl + Li$ isolated directly		$(C_2H_5)_2BCl + Li$ after heating at 200 °C		$C_2H_5BF_2 + 2\,Li$ isolated directly	
Formula [a]	Number of isomers [b]	Characterization	% B [d]	% C [d]	% B [d]	% C [d]	% B [d]	% C [d]
$C_{10}B_3H_{21}$	1	Derivative of 1,5-dicarbaclovopentaborane(5) *(6)*	—	—	2.42	2.02	—	—
$C_{12}B_4H_{30}$	1	Structure unknown [c]	*ca.* 5.0		*ca.* 0.50		—	—
$C_{10}B_5H_{23}$	5	Derivatives of 2,4-dicarbaclovoheptaborane(7) *(10)*	0.33	0.17	0.59	0.30	0.27	0.27
$C_{12}B_5H_{27}$	3		2.96	1.78	2.98	1.79	3.40	4.08
$C_{13}B_5H_{29}$	1		—	—	0.61	0.40	—	—
$C_{14}B_5H_{31}$	1		2.73	1.91	3.00	2.10	6.10	8.54
$C_{10}B_5H_{27}$	2	Derivatives of 2-monocarbahexaborane(9) *(2)*	1.07	0.53	1.17	0.59	1.61	1.61
$C_{12}B_5H_{31}$	1		0.85	0.51	0.76	0.46	7.28	8.86
round sum: (disregarding the compound $C_{12}B_4H_{30}$)			8.0	4.9	11.5	7.7	18.6	23.4

[a] Determined by mass spectrometry [97]; [b] Separated by gas chromatography [96]; [c] Thermally unstable and autoxidizable; [d] Percentage of boron and of all the carbon bound in the organocarborane, based on the boron and carbon in the organohalogenoborane.

smoothly, but leads mainly to polyorganoboranes, and not to carboranes. For example, carboranes are formed only in traces in the reaction of dialkylchloroboranes with lithium in tetrahydrofuran at −20 to −30 °C. This is shown by the decomposition, by D_2O, of the products formed on reaction with trialkylaluminum (cf. Section 2.3.2.1.), which yields monodeuterated and dideuterated alkane, while the 1,1,1-trideuteroalkane characteristic of carboranes is scarcely detectable. Interference by cleavage of tetrahydrofuran becomes noticeable above +10 °C in the reaction of dialkylmonochloroboranes. The preparation of carboranes from dialkylchloroboranes with lithium in tetrahydrofuran is therefore best carried out at about 0 °C. The most favorable temperature range for the alkyldifluoroboranes is between −10 and −5 °C, since the cleavage of the ether again becomes important at temperatures slightly above this range.

Provided that the reaction is conducted at a suitable temperature, the composition of the resulting mixture of organoboranes and organocarboranes depends

the boron is found in the compounds of the undistillable residue. These are evidently also carborane-like substances. When the distillation residue is heated with triethylborane in a closed vessel, the main products are alkyl derivatives of 1,5-dicarbaclovopentaborane(5) *(6)* and 2,4-dicarbaclovoheptaborane(7) *(10)*.

The carboranes that are unstable to heat and oxidation are partly converted into condensed carboranes at 150 to 200 °C. The total yield of stable carboranes can therefore be increased considerably by subsequent heating of the reaction mixture. The products consist mainly of alkyl derivatives of 1,5-dicarbaclovopentaborane(5). However, members of a new homologous series of carboranes having relatively high molecular weights are also formed (cf. Table 2).

The dehalogenation of ethyldifluoroborane rather than diethylchloroborane leads to much better yields of organocarboranes [20]; cf. Table 1. The directly formed distillable fraction contains alkyl derivatives of 2-carbahexaborane(9) *(2)* and of 2,4-dicarbaclovoheptaborane(7) *(10)*. The yield of derivatives of *(2)* is particularly high in relation to that obtained by the

[95] *R. Köster* and *G. Benedikt*, unpublished.

[96] *G. Schomburg*, Mülheim/Ruhr, gas-chromatographic separations.

[97] *D. Henneberg*, Mülheim/Ruhr, mass-spectrometric measurements, particularly investigations with a high-resolution mass spectrometer model CEC 21-110; cf. *D. Henneberg*, Z. analyt. Chem. *205*, 124 (1964).

Table 2. Mass-spectrometrically detected organocarboranes [a] from the dehalogenation of diethylchloroborane.

Derivatives of the carborane	Organocarborane: Formula found [b]	Molecular weight found [c]	[d]	Isomers separated by gas-liquid chromatography [96]
$1,5\text{-}C_2B_3H_5$	$C_9H_{19}B_3$	—	160	
	$C_{10}H_{21}B_3$	—	174	1
? $C_2B_4H_6$	$C_{10}H_{22}B_4$	—	186	
	$C_{12}H_{26}B_4$	—	214	
$2,4\text{-}C_2B_5H_7$		170	170	
		—	184	
	$C_{10}H_{23}B_5$	198	198	4–5
			212	
	$C_{12}H_{27}B_5$	226	226	3
	$C_{13}H_{29}B_5$	—	240	
	$C_{14}H_{31}B_5$	254	254	1
$2\text{-}CB_5H_9$	$C_{10}H_{27}B_5$	202	202	2
	$C_{12}H_{31}B_5$	230	230	1
? $C_2B_6H_8$	$C_{12}H_{18}B_6$	238	238	
			252	
	$C_{14}H_{32}B_6$	266	266	1
			280	
	$C_{16}H_{36}B_6$	294	294	
? $C_xB_7H_y$	$C_{14}H_{33}B_7$	—	278	
		—	292	
	$C_{16}H_{37}B_7$	—	306	
		—	320	
		—	334	

[a] The compounds are not attacked by 30% aqueous hydrogen peroxide in acidic solution at room temperature, and can be distilled under reduced pressure.

[b] Determined by high-resolution mass spectrometry [97] with a CEC 21-110 instrument.

[c] Directly after dehalogenation.

[d] After heating at about 200 °C.

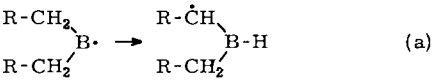
dehalogenation of dialkylchloroboranes. Practically no unstable compounds containing three to five boron atoms are formed. Up to 20% of the boron from the alkyldifluoroborane is utilised in the formation of distillable organocarboranes that are stable to oxygen. About half of the *B*-ethyl groups can be recovered as triethylborane.

Organocarboranes containing 3 to 7 B atoms are also formed in the reaction of diethylether-trifluoroborane with lithium at about −5 °C in the presence of triethylborane in tetrahydrofuran. As in the dehalogenation of alkylhalogenoboranes, the composition of the carborane mixture depends on the ratio R:X (R = C_2H_5, X = F). When R:X = 2:1 or 1:1, the thermally unstable carboranes predominate. At a ratio R:X = 1:2, the proportion of organocarboranes of the clovo type increases at the expense of the unstable compounds. At the same time, larger quantities of high-boiling organocarboranes and undistillable products are obtained.

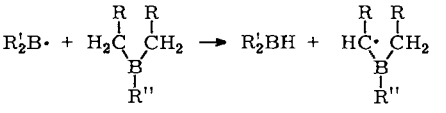
The process involved in the dehalogenation of alkylhalogenoboranes has not yet been fully explained. However, an essential part is probably played, not only by the formation and reaction of free radicals, but also by the catalysed exchange of substituents on boron by BH bonds [98]. Thus the dehalogenation of dialkylhalogenoboranes with lithium in the presence of alkenes yields only small quantities of carboranes, since the BH components required for ligand exchange are evidently taken up by the CC double bond [94]. This is also the case in dehalogenations below −15 °C, since the BH-catalysed exchange is then almost frozen.

[98] *R. Köster*, Angew. Chem. *73*, 66 (1961); *R. Köster* and *G. Schomburg*, Angew. Chem. *72*, 567 (1960).

The first step in the reaction presumably leads to the formation of short-lived *C*-radicals from the free alkylboron radicals [*] by migration of a hydrogen atom from an α-carbon atom to the boron [eq. (a)]. However, an intermolecular hydrogen transfer [eq. (b)] is not impossible. Thus when diethylchloroborane reacts with lithium at −30 °C in the



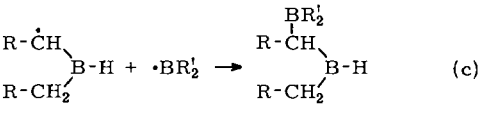
(a)



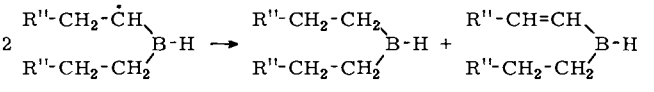
(b)

presence of tripropylborane, di-and-triborylated C_3 residues are found as well as di- and triborylated C_2 units. The C_3 units can be qualitatively detected *via* the corresponding deuterated hydrocarbons. The organoboranes are made to react with a suitable trialkylaluminum, *e.g.* trioctylaluminum [98a], and the resulting mixtures of organoaluminum and organoboron compounds are decomposed by D_2O.

The combination of a *C*-radical with a *B*-radical leads to the formation of a new BC bond [eq. (c)].



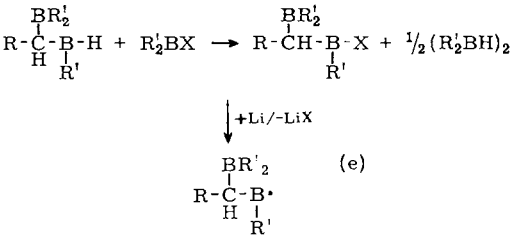
(c)



(d)

Disproportionation of the *C*-radical in accordance with equation (d) can be largely ruled out since alkenyl groups attached to boron have never been detected after dehalogenations in the presence of an excess of olefin.

New dialkylboryl radicals may also be formed, *e.g.* in accordance with eq. (e).



(e)

Contrary to an earlier assumption [94], intermediates of the type $R\text{–}C(BR_2)_3$ probably play no part, or at least no important part, in the formation of carboranes by dehalogenation. Investigations on the hydroboration of dialkyl-(1-alkynyl)boranes with alkyldiboranes (cf. Section 3.2.2.4.2.) have now shown [21] that compounds of this type form trialkylboranes and alkylated 1,5-dicarbaclovopentaboranes(5) *(6)* at room temperature or on gentle heating. However, no derivatives of *(6)* have been detected as primary products in the dehalogenation of alkylhalogenoboranes (c. f. Table 2).

A variant of the dehalogenation that also leads to stable BC compounds has been found for arylated boranes [99]. Di-

[*] In some cases it was possible to intercept these free radicals as stable free BN radicals [98b] by the addition of pyridine [95].

[98a] *R. Köster* and *G. Bruno*, Liebigs Ann. Chem. *629*, 89 (1960).

[98b] *R. Köster, G. Benedikt*, and *H. W. Schrötter*, Angew. Chem. *76*, 649 (1964); Angew. Chem. internat. Edit. *3*, 514 (1964); *R. Köster, H. Bellut*, and *E. Ziegler*, Angew. Chem. *79*, 241 (1967).

[99] *F. Joy, M. F. Lappert*, and *B. Prokai*, J. organometallic Chem. *5*, 512 (1966).

bromophenylborane and diphenylacetylene react in the presence of metallic potassium to form a compound that, because of its stability to oxygen and the absence of C=C stretching vibrations, was assigned the structure, not of hexaphenyl-1,4-diboracyclohexa-2,5-diene, but of an octahedral C_4B_2 skeleton.

However, by analogy with the results obtained in the aliphatic series (cf. Section 2.3.4.2.), this product could be a hexaphenylated C_4B_2 carborane having a pentagonal-pyramidal structure with a boron atom at the apex, as in *(4)*.

3.2.2.2. *Carboranes from Alkyldiboranes and Alkali Metals*

Alkylated carboranes containing three to five boron atoms are also formed in the preparation of alkali metal boranates from alkyldiboranes and alkali metals [100]. For example, the reaction of 2.3 g of sodium with 28 g of tetraethyldiborane at 100–110 °C gives sodium boranate and triethylborane as the principal products [100a], together with 1.5 g of a mixture of carboranes, about 15 % of which consists of compounds that are stable to hydrogen peroxide at room temperature. These are mainly alkyl derivatives of 2-carbahexaborane(9) *(2)* and of 2,4-dicarbaclovoheptaborane(7) *(10)* (c.f. Table 3). The small quantities of 1,5-dimethyl-2,3,4-triethyl-1,5-dicarbaclovopentaborane(5) that can also be detected are presumably formed during distillation by the thermal degradation of unstable carboranes. The higher-boiling fraction consists mainly (about 60 %) of compounds that are unstable to heat and to hydrogen peroxide and oxygen. The proportion of these compounds increases in relation to the proportion of stable organocarboranes as the ratio C_2H_5: H in the ethyldiborane used is increased, and ultimately reaches a value of about 75 % in the reaction of ethyldiborane having 0.6 % of hydride hydrogen. If lithium is used instead of sodium, the same carboranes are obtained from the alkyldiboranes in lower yields and at much lower reaction rates. With sodium-potassium alloy (K_2Na), the reaction is fairly fast at 50 °C, but the result is essentially the same as when sodium is used.

Table 3. Mass-spectrometrically detected organocarboranes [a] from ethyldiboranes and alkali metals.

Organocarboranes		
Molecular weight found	Formula [b]	Assignment
174	$C_{10}H_{21}B_3$	Derivative of 1,5-$C_2B_3H_5$
190		Derivatives of an unknown compound
218		
198		Derivatives of 2,4-$C_2B_5H_7$
212		
226	$C_{12}H_{27}B_5$	
240		
254	$C_{14}H_{31}B_5$	
202		Derivatives of 2-CB_5H_9
230	$C_{12}H_{31}B_5$	
238		Presumably derivatives of $C_2B_6H_8$
266	$C_{14}H_{32}B_6$	

[a] The compounds are not attacked by 30 % aqueous hydrogen peroxide in acidic solution at room temperature, and can be distilled under reduced pressure.

[b] Determined by high-resolution mass spectrometry [97] with a CEC 21-110 instrument.

The formation of carboranes from alkyldiboranes and alkali metals is probably initiated by the formation of an $R_2B\cdot$ radical:

$$^1/_2(R_2BH)_2 + M \rightarrow R_2B\cdot + MH \qquad (f)$$

The further course of the reaction is probably substantially the same as in the dehalogenation of alkylhalogenoboranes (cf. Section 3.2.2.1.). However, the BH-catalysed ligand exchange is facilitated by the relatively high concentration of BH groups. The synthesis of 2,4-dimethyl-1,3,5,6,7-pentaethyl-2,4-dicarbaclovoheptaborane(7) from triethyldiborane and sodium can be represented by the overall equation (g):

$$22[(C_2H_5)_2BH]_2 + 12\ Na \rightarrow 12\ NaBH_4 + 27\ B(C_2H_5)_3 + C_{14}H_{31}B_5 \qquad (g)$$

Salt-like compounds containing several boron atoms have not, as yet, been detected.

3.2.2.3. *Carboranes by Pyrolysis of Alkyldiboranes*

The pyrolysates of alkyldiboranes contain up to 5 % of organocarboranes having three to eight, and possibly even more boron atoms [101]. When ethyldiboranes are heated to about 170 °C, the products consist mainly of alkyl derivatives of 2,4-dicarbaclovoheptaborane(7), together with 1,5-dimethyl-2,3,4-triethyl-1,5-dicarbaclovopentaborane(5) (cf. Table 4). The

Table 4. Mass-spectrometrically detected organocarboranes [a] from the pyrolysis of ethyldiboranes.

Organocarboranes		
Molecular weight found	Formula [b]	Assignment
160	$C_{10}H_{21}B_3$	Derivatives of 1,5-$C_2B_3H_5$
174		
198		Derivatives of 2,4-$C_2B_5H_7$
212		
226		
240	$C_{13}H_{27}B_5$	
254	$C_{14}H_{31}B_5$	
266	$C_{14}H_{32}B_6$	Presumably derivatives of a $C_2B_6H_8$
280		
294		
236		unknown
250		
264	$C_{14}H_{33}B_7$	
278		
292		
234	$C_{10}H_{26}B_8$	unknown
248	$C_{11}H_{28}B_8$	
262		
276		
290		
304		
318	$C_{16}H_{30}B_8$	

[a] The compounds are not attacked by 30 % aqueous hydrogen peroxide in acidic solution at room temperature, and can be distilled under reduced pressure.

[b] Determined by high-resolution mass spectrometry [97]) with a CEC 21-110 instrument.

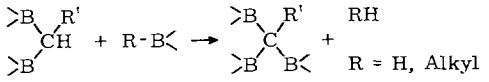
[100] *R. Köster* and *M. A. Grassberger*, Angew. Chem. *77*, 457 (1965); Angew. Chem. internat. Edit. *4*, 439 (1965).

[100a] *R. Köster*, Angew. Chem. *68*, 383 (1956).

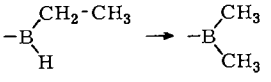
[101] *R. Köster, W. Larbig*, and *G. W. Rotermund*, Liebigs Ann. Chem. *682*, 21 (1965).

presence of an alkylated carborane $C_{14}H_{32}B_6$ has also been detected by high-resolution mass spectrometry [97].

The formation of carboranes from simple alkylated monoboranes probably proceeds *via* CB_2 and CB_3 groupings resulting from intermolecular elimination of hydrogen or of alkane [102].



However, C–C bonds are also broken during the pyrolysis, with the result that *B*-methyl groups are formed from the *B*-ethyl groups [103].

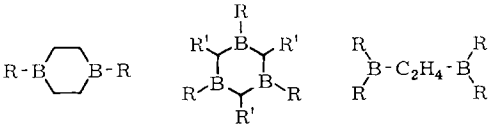


Consequently, the molecular weights of the homologous carboranes formed by the pyrolysis of ethyldiboranes differ only be the mass of one CH_2 group (cf. Table 4).

3.2.2.4. *Carboranes by Hydroboration of Dialkyl-1-alkynylboranes*

3.2.2.4.1. *From Acetylene and Ethyldiboranes*

Whereas an electric discharge in a mixture of diborane and acetylene yields only small quantities of carboranes (cf. Sections 3.1.3. and 3.1.4.) [63], *B*-alkylcarboranes can be obtained in preparative quantities by the rapid introduction of acetylene into tetraethyldiborane at room temperature followed by heating under pressure [19,62]. In addition to simple cyclic [*(19)*, *(20)*] and acyclic hydroboration products *(21)*, the reaction



R = C_2H_5 *(19)* *(20)* *(21)*

R′ = CH_3

leads in particular to 1,5-dimethyl-2,3,4-triethyl-1,5-dicarbaclovopentaborane(5) in yields of 10 to 15%, depending on the conditions [62]. Very small quantities of homologues of this carborane can also be detected.

In agreement with the results described in the following Section, this synthesis probably proceeds *via* diethylethynylborane, which must be formed from acetylene and the tetraethyldiborane with elimination of hydrogen:

$$^1/_2[(C_2H_5)_2BH]_2 + HC{\equiv}CH \rightarrow (C_2H_5)_2BC{\equiv}CH + H_2 \quad (h)$$

The hydroboration of the diethylethynylborane with tetraethyldiborane then presumably leads to the formation of 1,1,1-tris(diethylboryl)ethane, which is finally disproportionated to form triethylborane and the 1,5-dicarbaclovopentaborane(5) derivative [eq. (i)].

$$(C_2H_5)_2BC{\equiv}CH + [(C_2H_5)_2BH]_2 \rightarrow [(C_2H_5)_2B]_3C{-}CH_3$$
$$2[(C_2H_5)_2B]_3C{-}CH_3 \rightarrow (CH_3C)_2B_3(C_2H_5)_3 + 3(C_2H_5)_3B \quad (i)$$

Acetylene and ethyldiborane also react to form higher carboranes, and particularly derivatives of 2-carbahexaborane(9) *(2)* and of 2,4-dicarbaclovoheptaborane(7) *(10)* (cf. Table 5).

Table 5. Mass-spectrometrically detected organocarboranes [a] from the hydroboration of acetylene with ethyldiborane.

Organocarboranes		Number of isomers detected by gas chromatography [96]	Assignment
Molecular weight	Formula [b]		
174	$C_{10}H_{21}B_3$	1	Derivative of 1,5-$C_2B_3H_5$
198	$C_{10}H_{23}B_5$		Derivatives of 2,4-$C_2B_5H_7$
212	$C_{11}H_{25}B_5$		
226	$C_{12}H_{27}B_5$	3	
240	$C_{13}H_{29}B_5$	2	
254	$C_{14}H_{31}B_5$	1	
202	$C_{10}H_{27}B_5$		Derivatives of 2-CB_5H_9
230	$C_{12}H_{31}B_5$		
266	$C_{14}H_{32}B_6$	1	Presumably derivative of $C_2B_6H_8$

[a] The compounds are not attacked by 30% aqueous hydrogen peroxide in acidic solution at room temperature, and can be distilled under reduced pressure.

[b] Determined by high-resolution mass spectrometry [97] with a CEC 21-110 instrument.

Carboranes containing more than five boron atoms can also be detected. One of the compounds isolated has the formula $C_{14}H_{32}B_6$; from its ^{1}H-NMR spectrum, this compound is probably the *C,C′*-dimethylpentaethyl derivative of a dicarbaclovooctaborane(8) [*(11)* or *(12)*].

3.2.2.4.2. *From Alkyldiboranes and Dialkyl-1-alkynylboranes*

The formation of carboranes by the action of acetylene on ethyldiboranes, for which the above reaction path was postulated, led to the development of a synthesis of carboranes by hydroboration of alkynylboranes with alkyldiboranes. It was found that the alkyl derivatives of 1,5-dicarbaclovopentaborane(5) can be obtained in relatively high yields by this method [21]

An essential requirement for this synthesis was the development of a method for the preparation of uncomplexed dialkyl-1-alkynylboranes, which were unknown until recently [104]. The trimethylamine adducts of these compounds can

[102] It had been observed earlier, in the hydrogenation of trialkylboranes with hydrogen under pressure to obtain alkyldiboranes and/or diborane, that condensations take place particularly readily when the boron hydride content is too high and the reaction mixture is heated to 180 °C or higher (*R. Köster*, *G. Bruno*, and *P. Binger*, Liebigs Ann. Chem. *644*, 1 (1962).

[103] *R. Köster* and *W. Larbig*, Angew. Chem. *73*, 620 (1961).

[104] *H.-J. Horstschäfer*, Diploma Thesis, Technische Hochschule Aachen, 1966.

be obtained in high yields from alkynyl-lithium and the trimethylamine-dialkylfluoroborane adduct, and can be converted into the free dialkyl-1-alkynylboranes *e.g.* by treatment with the boron trifluoride-diethyl ether adduct:

$$LiC{\equiv}C{-}CH_3 + FBR_2{-}N(CH_3)_3 \rightarrow LiF + CH_3C{\equiv}C{-}BR_2{-}N(CH_3)_3 \quad (j)$$

$$\xrightarrow{+F_3B-OR_2} F_3B{-}N(CH_3)_3 + OR_2 + R_2BC{\equiv}CCH_3$$

$R = C_2H_5$

The hydroboration of these dialkyl-1-alkynylboranes with alkyldiboranes leads to the formation of alkyl derivatives of 1,5-dicarbaclovopentaborane(5) in yields of more than 50%. If the hydroborating agent contains alkyl groups different from those in the dialkyl-1-alkynylboranes, the reaction leads to 1,5-dicarbaclovopentaboranes having different alkyl groups on the boron atoms[21]. Reactions studied so far include the hydroborations of diethyl-1-propynylborane and of diethyl-1-octynylborane with ethyl- and methyldiboranes.

In the case of the methyl and ethyl compounds, the distribution of the alkyl groups on the boron atoms of the carborane and of the trialkylborane does not correspond entirely to the expected statistical distribution[105].

The formation of C_2B_3 carboranes evidently involves intermediates containing CB_3 groupings, which disproportionate to form the more stable C_2B_3 carboranes [eq. (k)].

$$R_2BC{\equiv}C{-}CH_3 + (R_2BH)_2 \rightarrow R_2B{-}\underset{R_2B}{\overset{R_2B}{C}}{-}CH_2{-}CH_3 \quad (k)$$

$$2\,(R_2B)_3C{-}C_2H_5 \rightarrow (C_2H_5C)_2B_3R_3 + 3\,BR_3$$

$R = C_2H_5, C_3H_7$

In addition to the derivatives of 1,5-dicarbaclovopentaborane(5) *(6)*, small quantities of high-boiling organocarboranes with up to five boron atoms in the skeleton are also formed. The undistillable fractions also contain compounds having carborane-like structures.

Further carboranes are obtained by subsequent heating of the reaction mixtures, probably as a result of isomerization of 1,1,2-triborylated alkanes[21] [eq. (1)].

$$R_2BC{\equiv}C{-}CH_3 + (R_2BH)_2 \rightarrow (R_2B)_2CH{-}CH(BR_2)CH_3$$

$$(R_2B)_2CH{-}CH(BR_2)CH_3 \xrightarrow{\Delta} (R_2B)_3C{-}CH_2{-}CH_3 \quad (1)$$

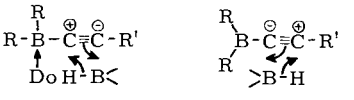
$$\downarrow$$

$$^1/_2\,(C{-}C_2H_5)_2R_3B_3 + {}^3/_2\,BR_3$$

$R = C_2H_5, C_3H_7$

The yields of 1,5-dicarbaclovopentaborane(5) derivatives are highest when the reactions are carried out in dilute solutions of the tetraalkyldiboranes in trialkylborane. The hydroborating agents is then almost free from RBH_2- and BH_3-components, and consists of dialkylboron hydrides R_2BH[106]. This permits a highly selective addition of BH, which, with the 1-alkynylboranes, leads to the formation of 1,1,1-triborylated alkanes.

It is also very important that uncomplexed dialkyl-1-alkynylboranes should be used in the synthesis of the C_2B_3 carboranes and that addition compounds with amines should be absent since they, like the alkali metal trialkyl-1-alkynylboranates $M[R_3BC{\equiv}CR']$ *(24)*, react with alkyldiboranes to give mainly 1,2-diborylated alkenes *(23)*. The polarization of the C≡C bond is then opposite [*(22a)*] to that in the free 1-alkynylboranes *(22b)*.



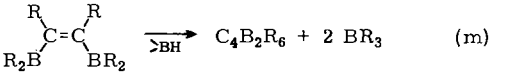
(22a) *(22b)*

Do = electrondonator

If 1,2-diborylated alkenes *(23)* are formed, they disproportionate very readily in the presence of boron hydrides to form stabilized C_4B_2 compounds (cf. Section 3.2.2.5.). Thus in the presence of Lewis bases, C_2B_3 organocarboranes can no longer be prepared by hydroboration of dialkyl-1-alkynylboranes.

3.2.2.5. *Carboranes ("Boracarbanes") from 1,2-Diborylated Alkenes*

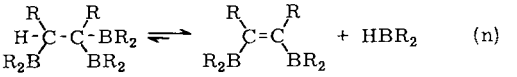
The disproportionation of 1,2-bis(dialkylboryl)alkenes *(23)* leads to fully alkylated derivatives of tetracarbahexaborane(6) *(4a)* [6].



$$\xrightarrow{>BH} C_4B_2R_6 + 2\,BR_3 \quad (m)$$

(23) *(4a)*

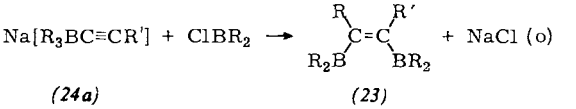
The ligand exchange in accordance with equation (m) takes place at temperatures above 40 °C in the presence of alkyldiboranes and proceeds almost quantitatively, since the triborylated alkanes formed by hydroboration readily decompose into their components [eq. (n)].



$$+ HBR_2 \quad (n)$$

(23)

The compounds *(23)* can be obtained *e.g.* from sodium trialkyl-1-alkynylboranates *(24a)* and dialkylchloroboranes in yields of up to 80% [eq. (o)] [107].



$$+ NaCl \quad (o)$$

(24a) *(23)*

The reaction (o) leads exclusively to *cis-(23)*, and takes place with many dialkylchloroboranes R_2BCl (R = CH_3, C_2H_5, C_3H_7) and sodium trialkyl-1-alkynylboranates $Na[R_3BC{\equiv}CR']$ (R = CH_3, C_2H_5; R′ = CH_3, C_2H_5). 2,3-Bis(diethylboryl)-2-pentene, for example, reacts in five to six hours to give isomeric tetraethyl-C,C′-dimethyl-2,3,4,5-tetracarbahexaboranes(6) *(4a)* as well as triethylborane.

However, the compounds *(4a)* can also be obtained from sodium 1-alkynyls and tetraalkyldiboranes in the presence of trialkylboranes, in accordance with equation (p), without isolation of *(23)*.

$$2\,NaC{\equiv}CR' + 2\,BR_3 + 4\,(R_2BH)_2 \rightarrow 2\,NaBH_4 + 6\,BR_3 + R'_2R_2C_4B_2R_2 \quad (p)$$

e.g. R = C_2H_5; R′ = C_3H_7 *(4a)*

[105] *R. Köster* and *H.-J. Horstschäfer*, unpublished.

[106] *R. Köster*, *G. Griasnov*, *W. P. Larbig*, and *P. Binger*, Liebigs Ann. Chem. *672*, 1 (1964).

[107] *P. Binger* and *R. Köster*, Tetrahedron Letters *1965*, 1901.

(4a) is obtained in yields of more than 50%, together with sodium boranate and trialkylborane. When the reaction is carried out in the absence of trialkylborane, the products consist mainly of high molecular weight compounds, together with small quantities of alkyl derivatives of 1,5-dicarbaclovopentaborane(5) *(6)* [eq. (q)].

$$2\,NaC{\equiv}CC_3H_7 + 6\,((C_2H_5)_2BH)_2 \rightarrow 2\,NaBH_4 + 7\,B(C_2H_5)_3 + (C_4H_9)_2C_2B_3(C_2H_5)_3 \quad (q)$$

(6a)

The organo derivatives having the C_4B_2 skeleton *(4a)* are closer in many respects to the organocarboranes than to the organoboranes. The BC bonds of the compounds *(4a)* are practically unaffected by heating for several hours with 6N sulfuric acid. They are also stable to methanol and ethanol up to a temperature of 150 °C. However, the compounds react with boiling propionic acid to give tetrapropionylpyroboric acid $(C_3H_7OCO)_2BOB(OCOC_3H_7)_2$, *cis*-pentene, and a mixture of isomeric decenes.

Trimethylamine *N*-oxide, which smoothly oxidizes all the BC bonds in organoboranes at temperatures slightly above room temperature[107a], does not attack the C_4B_2 compounds even in boiling benzene. Slow oxidation takes place even at room temperature with molecular oxygen and hydrogen peroxide[6]. This illustrates the difference between the organo-substituted tetracarbahexaboranes (diborahexacarbanes) and the condensed organocarboranes of the series $C_2B_xR_{x+2}$ (cf. Section 3.2.2.1.).

When the 1,2-diborylated alkenes are heated above 80 °C in the presence of BH compounds, C–C cleavage and other irreversible reactions (*e.g.* cyclization) take place[108]. The *B*-ethylated compounds yield mainly diboracyclopentenes and similar products, whereas *(23)* with methyl groups on the boron can be converted predominantly into the C_4B_2 compounds even at 150 °C.

The disproportionation of the *cis*-1,2-diborylated alkenes in accordance with equation (o) can also take place at room temperature in the presence of UV radiation[6], but side reactions then become more important.

3.3. Interconversions of Carboranes

3.3.1. Thermal Isomerizations

At present there are only a few cases in which all the theoretical skeletal isomers of a particular carborane are known. The isomers can sometimes be interconverted by heating, but activation energies may be high.

3.3.1.1. *Isomerization of the Dicarbaclovodecaboranes(12)*

The best-known example of the isomerization of a carborane is the formation of 1,7-dicarbaclovododecaborane(12) [*m*-carborane *(7b)*] at 450–500 °C from *o*-carborane *(7a)*[31,109], which is less stable according to LCAO calculations[28].

The experimental data give an activation energy of 62 kcal/mole[110]. The boron and carbon atoms could conceivably be arranged in the form of a cuboctahedron in the transition state[68,111]; cf. Figure 13.

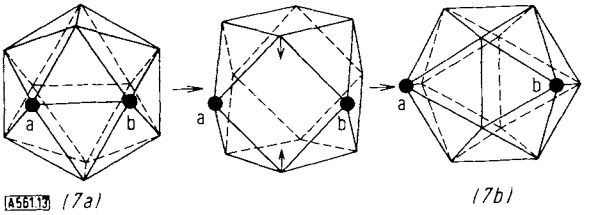
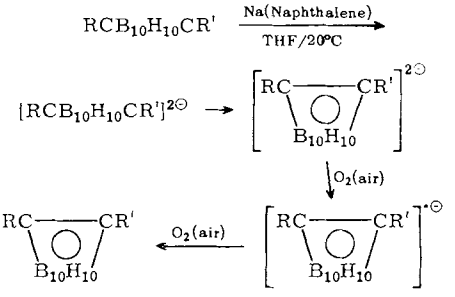


Fig. 13. Skeletal isomerization of dicarbaclovododecaboranes(12) *(7)*. [*o*-carborane *(7a)* → *m*-carborane *(7b)*].

Some of the *C*-substituted *o*-carboranes can also be converted into the more stable *m*-compounds by heating[31,109,110,112,113]. Steric as well as electronic effects often play a part in this isomerization, *e.g.* 1,2-bis (methyldiphenylsilyl) - 1,2 - dicarbaclovododecaborane(12) rearranges at 260 °C to form the *m*-isomer; the activation energy, as found experimentally, is only 45 kcal/mole[110].

Conversely, derivatives of *m*-carborane can be converted into *o*-carboranes *via* the dianion of dicarbadodecaboranes(14)[113a].



R = Phenyl, R' = H, Phenyl

This is in agreement with *Lipscomb*'s predictions[4].

Finally, when *m*-carborane is heated almost to its decomposition point (about 630 °C), it is partly converted into 1,12-dicarbaclovododecaborane(12) *(7c)* (*p*-carborane)[76]. The composition of the resulting mixture of *m*- and *p*-carboranes is in good qualitative agreement with LCAO–MO calculations, which give the same energy content for both isomers[28].

3.3.1.2. *Isomerization of Dodecahydrodicarbaundecaborates(1-)*

Dodecahydro-*o*-dicarbaundecaborate(1-) $C_2B_9H_{12}^{\ominus}$ can be converted into the *m*-isomer by heating at 300 °C[114]; this product is identical with that obtained

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[108] *P. Binger*, unpublished.

[109] *D. Grafstein* and *J. J. Dvorak*, US-Pat. 3226429, (1961), Thiokol Chem. Corp.; Chem. Abstr. *64*, 8235b (1966).

[110] *R. M. Salinger* and *C. L. Frye*, Inorg. Chem. *4*, 1815 (1965).

[111] *R. Hoffmann* and *W. N. Lipscomb*, Inorg. Chem. *2*, 231 (1963).

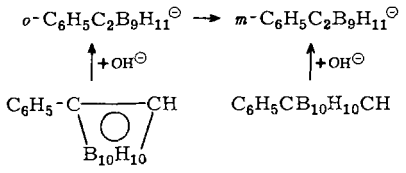
[112] *S. Papetti* and *T. L. Heying*, Inorg. Chem. *3*, 1448 (1964).

[113] *L. I. Zakharkin* and *V. N. Kalinin*, Izvest. Akad. Nauk SSSR Ser. chim. *1965*, 2206; Bull. Acad. Sci. USSR Div. Chem. Sci. *1965*, 2173; Chem. Abstr. *64*, 9751d (1966).

[113a] *L. I. Zakharkin*, *V. N. Kalinin*, and *L. S. Podvisotskaya*, Izvest. Akad. Nauk SSSR, Ser. Chim. *1966*, 1495.

[114] *P. M. Garret*, *F. N. Tebbe*, and *M. F. Hawthorne*, J. Amer. chem. Soc. *86*, 5016 (1964).

by degradation of *m*-carborane with bases (cf. Section 3.3.3.1.).



3.3.1.3. *Isomerization of Dicarbaclovodecaborane(10)*

According to LCAO–MO calculations [111], the stability of the seven possible isomeric dicarbaclovodecaboranes(10) *(14)* decreases in the order (a,b = indices of the C atoms): 1,10 > 1,6 > 1,2 > 2,4 > 2,8 > 2,3 > 2,7.

Dimethyl-1,6-dicarbaclovodecaborane, which can be obtained by pyrolysis of *C,C'*-dimethyldicarbanonaborane(13) (cf. Section 3.3.3.2.), rearranges almost quantitatively into the more stable 1,10-isomer at 350 °C [67]; cf. Figure 14.

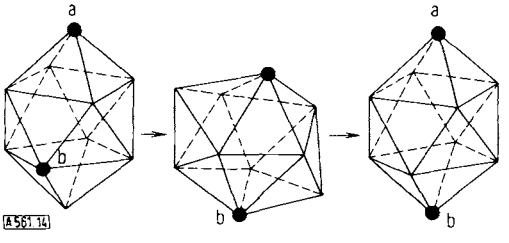


Fig. 14. Skeletal isomerization of dicarbaclovodecaboranes(10) *(14)*; conversion of the 1,6-into the 1,10-isomer.

3.3.1.4. *Isomerization of Dicarbaclovohexaborane(6)*

The octahedral 1,2-dicarbaclovohexaborane(6) *(9a)* can be almost quantitatively converted into the more stable symmetrical 1,6-isomer *(9b)* by heating at 250 °C [81]. The rearrangement could proceed *via* a pentagonal pyramid [68, 111]; cf. Figure 15. However, a trigonal prism having symmetry D_{3h} cannot be entirely ruled out as an intermediate [68, 111].

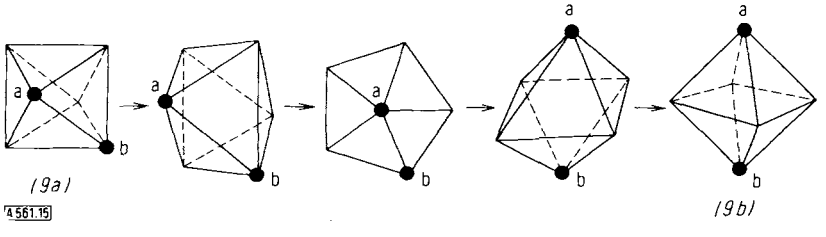
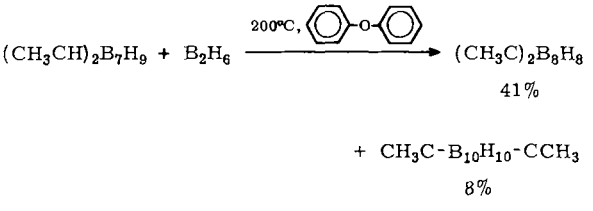


Fig. 15. Skeletal isomerization of dicarbaclovohexaboranes(6); conversion of *(9a)* into *(9b)*.

3.3.2. Carboranes by Synthesis from Lower Carboranes

Only a very small number of new carboranes have so far been obtained by synthesis from lower carboranes. The insertion of a B_1 unit into the $C_2B_9H_{11}^{2\ominus}$ ion *(8)* to form the neutral *B*-phenyl-*o*-carborane occurs in the reaction of the disodium salt of the (1)-2,3-dicarbollide ion *(8)* with phenyldichloroborane (−40 °C, THF) [115]; the 3-phenyl derivative of *(7a)* is thought to be formed (cf. also Scheme 1).

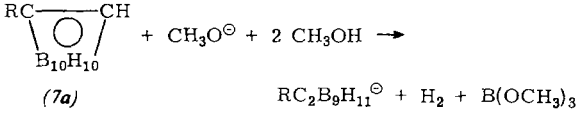
The results of the pyrolysis of dicarbanonaborane(13) (cf. Section 2.3.2.3.) in the presence of diborane [67] also indicate the general feasibility of the stepwise synthesis of higher condensed carboranes from lower, incompletely condensed compounds. *C,C'*-Dimethyl-1,6-dicarbaclovodecaborane(10) *(14)* is formed in a relatively high yield (41 %), together with small quantities (8 %) of the *C,C'*-dimethyl derivative of *m*-carborane *(7b)* in the reaction of *C,C'*-dimethyldicarbanonaborane(13) with diborane at about 200 °C in the presence of diphenyl ether.



3.3.3. Carboranes by the Degradation of Higher Carboranes

3.3.3.1. *Degradation with Bases*

o-Carborane *(7a)* and its *C*-substituted derivatives are rapidly degraded by strong bases, such as ethanolic potassium hydroxide solution, amines, alkali metal amides, or hydrazine, with elimination of a boron atom and formation of dodecahydrodicarbaundecaborates [56, 83, 116–118].



Kinetic measurements with 1-phenyl-*o*-carborane in 50 % ethanolic potassium hydroxide solution [83] show that the reaction is first order with respect to the car-

[115] *M. F. Hawthorne* and *P. A. Wegner*, J. Amer. chem. Soc. *87*, 4392 (1965).

[116] *D. Grafstein, J. Bobinski, J. Dvorak, H. Smith, N. N. Schwartz, M. S. Cohen*, and *M. M. Fein*, Inorg. Chem. *2*, 1120 (1963).

[117] *L. I. Zakharkin* and *V. N. Kalinin*, Tetrahedron Letters *1965*, 407; Izvest. Akad. Nauk SSSR, Ser. chim. *1965*, 579; Bull. Acad. Sci. USSR Div. Chem. Sci. *1965*, 567; Chem. Abstr. *63*, 622f (1965).

[118] *M. F. Hawthorne, P. A. Wegner*, and *R. C. Stafford*, Inorg. Chem. *4*, 1675 (1965).

borane and the hydroxide ion. Experiments with deuterated carborane [83] have shown that the boron atom is removed from position 3 or 6. *m*-Carborane is more resistant to nucleophilic attack than the *o*-isomer.

It is not attacked by boiling methanolic potassium hydroxide solution, but is slowly (R = H, CH_3) or relatively quickly (R = C_6H_5, *p*-Cl–C_6H_4) degraded by boiling hydrazine hydrate to *m*-undecaborate [31, 119].

$$RCB_{10}H_{10}CH + N_2H_4 \cdot H_2O + 2\,H_2O \rightarrow N_2H_5^{\oplus}RC_2B_9H_{11}^{\ominus} + H_2 + B(OH)_3$$

(7b)

R = H, CH_3 [31] R = C_6H_5, *p*-Cl–C_6H_4, *p*-Br–C_6H_4 [119]

Acidification of the *m*- and *o*-$C_2B_9H_{12}^{\ominus}$ anions *e.g.* with phosphoric acid [53,83] yields the neutral dicarbaundecaboranes(13) $C_2B_9H_{13}$.

On the other hand, when the $C_2B_9H_{12}^{\ominus}$ ion is treated with sodium or sodium hydride [77], further proton abstraction leads to the "potlike" dianion $C_2B_9H_{11}^{2\ominus}$ (dicarbollide ion) *(8)*.

By analogy with the reactions of the cyclopentadienyl anion, the reaction of the dicarbollide ion with salts of the transition metals yields compounds in which the transition metal and the carborane nucleus are linked by π bonds, *e.g.* π-cyclopentadienyliron(III)-π-2,3-dicarbollide *(16)* [32, 77–79].

$$[C_5H_5]^{\ominus} + [C_2B_9H_{11}]^{2\ominus} + Fe^{2\oplus} \xrightarrow[-e\ominus]{} \pi\text{-}C_5H_5\text{–}Fe\text{–}\pi\text{-}C_2B_9H_{11}$$

(16)

3.3.3.2. *Oxidative Degradation*

Whereas 1,2-$C_2B_{10}H_{12}$ *(7a)* in acidic media is not attacked by hydrogen peroxide, peroxy acids, or chromic acid [10,92,116], the dicarbaundecaborane(11) $C_2B_9H_{11}$ *(15)* can be smoothly degraded to the dicarbanonaborane(13) $C_2B_7H_{13}$ even by dichromate ions in acetic acid solution [86] (76% yield).

The *C*-methyl and *C*-phenyl derivatives react in the same manner to form the substituted dicarbanonaboranes(13).

3.3.3.3. *Pyrolytic Degradation*

The polyhedral BC compounds with higher hydrogen contents are much less stable than the condensed carboranes $C_2B_nH_{n+2}$. Consequently, compounds such as 2,3-dicarbahexaborane(8) *(3)* or *o*-dicarbaundecaborane(13) cannot be converted by heat into isomers in which the carbon atoms are separated by B atoms; on heating they lose hydrogen to form stable condensed carboranes, and in some cases the reaction proceeds smoothly to give homogeneous products in high yield. *o*- and *m*-dicarbaundecaborane(13) $C_2B_9H_{13}$ both give the same dicarbaundecaborane(11) $C_2B_9H_{11}$ *(15)* with non-adjacent carbon atoms when heated [53, 54, 114].

The removal of hydrogen from the *m* compound is easier than from the *o*-isomer [54]. The pyrolysis of *o*-dicarbaundecaborane(13) probably leads first to isomerization into *m*-dicarbaundecaborane(13); the C-substituted dicarbaundecaboranes(13) behave similarly. On the other hand, the *B*-iodo derivative $C_2B_9H_{12}I$ forms high molecular weight products when heated [120].

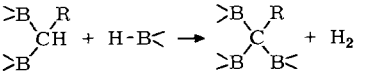
Dicarbanonaborane(13) disproportionates at 200 °C with loss of hydrogen, the main products being dicarbaclovooctaborane(8) [structure *(11)* or *(12)*] and 1,6-dicarbaclovodecaborane(10) [cf. *(14)*] [67, 86].

Small quantities of dicarbaclovononaborane(9) *(13)* are also formed.

$$R_2C_2B_7H_{11} \xrightarrow{200\,^{\circ}C} \underset{28\%}{R_2C_2B_8H_8} + \underset{30\%}{R_2C_2B_6H_6} + \underset{7\%}{R_2C_2B_7H_7}$$

R = H, CH_3 (R = CH_3) (R = CH_3) (R = CH_3)

The pyrolysis must (cf. Section 3.2.2.3.) involve the formation of new BC bonds, since investigations carried out so far indicate that dicarbanonaborane(13), unlike the condensed carboranes, contains only methylene groups [86] and no methine groups.



(p)

The pyrolysis of 2,3-dicarbahexaborane(8) *(3)* (dihydrocarborane) at 295 °C leads mainly to 2,4-dicarbaclovoheptaborane(7) *(10)*, together with 1,5-dicarbaclovopentaborane(5) *(6)* and 1,6-dicarbaclovohexaborane(6) *(9b)* [81].

$$2,3\text{-}R_2C_2B_4H_6 \xrightarrow{295\,^{\circ}C} 2,4\text{-}R_2C_2B_5H_5 + 1,5\text{-}R_2C_2B_3H_3 + 1,6\text{-}R_2C_2B_4H_4$$

R = H	28%	2%	1%
R = CH_3	25%	5%	–

C-alkylated 1,6-dicarbaclovohexaboranes(6) and 2,4-dicarbaclovoheptaboranes(7) can be obtained in the same way as the unsubstituted compounds from the *C*-alkyl-2,3-dicarbahexaboranes(8) [65, 81]. The *C,C'*-dimethyl compound gives mainly 2,4-dimethyl-2,4-dicarbaclovopentaborane(7), together with a little 1,6-dimethyl-1,6-dicarbaclovohexaborane(6). Much more of the C_2B_4 carborane is formed in the presence of an amine, even at lower temperatures [65].

$$2.3\text{–}R_2C_2B_4H_6 \xrightarrow{260\,^{\circ}C;\ N(CH_3)_3} 2.4\text{–}R_2C_2B_5H_5 + 1.6\text{–}R_2C_2B_4H_4$$

R = CH_3 15% 25%

The following reaction course has therefore been proposed for the formation of 1,6-dicarbaclovohexaborane(6) and of 2,4-dicarbaclovoheptaborane(7) [65]:

$$2.3\text{–}C_2B_4H_8 \rightarrow 1.2\text{–}C_2B_4H_6 + H_2 \text{ (slow)}$$

(13) *(9a)*

$$1.2\text{–}C_2B_4H_6 \rightarrow 1.6\text{–}C_2B_4H_6$$

(9a) *(9b)*

} catalysed by NR_3

$$1.2\text{–}C_2B_4H_6 + 2.3\text{–}C_2B_4H_8 \rightarrow 2.4\text{–}C_2B_5H_7 + \text{tarry products}$$

(9a) *(3)* *(10)*

[119] *L. I. Zakharkin* and *V. N. Kalinin*, Ž. obšč. Chim. *35*, 1691 (1965); Chem. Abstr. *63*, 18135f (1965).

[120] *F. P. Olsen* and *M. F. Hawthorne*, Inorg. Chem. *4*, 1839 (1965).

The *B*- and *C*-alkylated 2-carbahexaboranes(9) are also converted into condensed carboranes by heat. The *C*-methylpentaethyl derivative of CB_5H_9 reacts at 200–250 °C to give hydrogen, ethane, and unidentified high molecular weight products, together with 1,5-dimethyl-2,3,4-triethyl-1,5-dicarbaclovopentaborane(5) and a mixture of three isomeric *C*,*C'*-dimethyltetraethyl derivatives of 2,4-dicarbaclovoheptaborane(7) [20].

3.3.3.4. *Photolytic Degradation*

2,3-Dicarbahexaboranes(8) *(3)* can also be degraded to condensed carboranes by the action of light [121]; however, this method, unlike pyrolysis, leads mainly to carboranes in which the number of boron atoms is smaller than or equal to that in the starting compound. Hydrogen, diborane, and pentaborane(9) are formed as by-products.

$$\underset{(3)}{2.3\text{-}C_2B_4H_8} \xrightarrow[2\ h]{h\nu/60\,^\circ C} \underset{(9a),\,14\%}{1.2\text{-}C_2B_4H_6} + \underset{(9b),\,22\%}{1.6\text{-}C_2B_4H_6} + \underset{(6),\,17\%}{1.5\text{-}C_2B_3H_5}$$

The maximum total yield of new carboranes, based on the consumed 2,3-dicarbahexaborane(8), is 60%. The yield decreases when the irradiation time is increased, and only a trace of the less stable 1,2-dicarbaclovohexaborane(6) *(9a)* is formed.

[121] *J. R. Spielman* and *J. E. Scott jr.*, J. Amer. chem. Soc. *87*, 3512 (1965).

4. Outlook

Though a large volume of data on the carboranes and carborane-like compounds has already been accumulated in a relatively short time, research in this new branch of boron chemistry is still in its infancy. Suggestions have already been made for the industrial utilization of the new BC compounds; for example, numerous polymers have been synthesized from derivatives of 1,2-dicarbaclovododecaborane(12) and their properties been tested [122]. Production costs are, however, very high.

The discovery of new BC systems, and refinement of the syntheses of the carboranes already known, will undoubtedly give fresh impetus to the discussion of possible applications of these compounds.

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Translated by Express Translation Service, London

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Reactions of Halogen Azides

BY K. DEHNICKE [*]

Until recently, the explosive nature of halogen azides made these compounds unsuitable for preparative uses and greatly impeded investigation of their physical properties. Reactions of ClN_3 and BrN_3 with metal halides, metal carbonyls, and organometallic compounds to form metal azide halides, nitride halides, carbonyl azide halides, and alkylmetal azides were reported only very recently. The stability relationships of the halogen azides are discussed.

A. Preparation of Halogen Azides

The first halogen azide, iodine azide, was prepared by *Hantzsch* and *Schümann* [1] in 1900 from silver azide and iodine in ether at 0 °C:

$$AgN_3 + I_2 \rightarrow AgI + IN_3 \qquad (a)$$

These authors obtained the explosive substance in the crystalline form by careful evaporation of the ether. Soon afterward, *Raschig* [2] synthesized the gaseous chlorine azide by acidification of solutions of sodium azide and sodium hypochlorite with boric or acetic acid:

$$N_3^- + ClO^- + 2\,H^+ \rightarrow ClN_3 + H_2O \qquad (b)$$

The formation of chlorine azide is betrayed by the yellow solution obtained when it dissolves in water. In 1943, *Frierson, Konrad*, and *Browne* [3] obtained

[*] Priv.-Doz. Dr. K. Dehnicke
Laboratorium für Anorganische Chemie
der Technischen Hochschule Stuttgart
Schellingstr. 26
7 Stuttgart-N (Germany)

[1] *A. Hantzsch* and *M. Schümann*, Ber. dtsch. chem. Ges. *33*, 522 (1900).

[2] *F. Raschig*, Ber. dtsch. chem. Ges. *41*, 4194 (1908).

[3] *W. F. Frierson, J. Kronrad*, and *A. W. Browne*, J. Amer. chem. Soc. *65*, 1696 (1943).

ethereal solutions of chlorine azide by method (a) when Cl_2 was passed into a suspension of AgN_3 in ether. These methods prove unsuitable when the halogen azides are required for preparative purposes. In 1965 a preparation of chlorine azide in large quantities was described, in which a stream of chlorine diluted with nitrogen is passed into an aqueous solution of sodium azide at 0 °C:

$$N_3^- + Cl_2 \rightarrow ClN_3 + Cl^- \quad (c)$$

Under these conditions, the chlorine reacts quantitatively in the exothermic reaction (c); after drying over P_4O_{10}, the resulting chlorine azide can be used directly for syntheses [4].

Almost 20 years after the discovery of chlorine azide, *Spencer* [5] obtained bromine azide as a mobile orange liquid which is very sensitive to hydrolysis. This compound is prepared by passing a stream of bromine diluted with nitrogen over dry sodium azide:

$$NaN_3 + Br_2 \rightarrow BrN_3 + NaBr \quad (d)$$

Fluorine azide was first prepared in 1942. It is a very unstable yellowish-green gas which is formed on reaction of fluorine with hydrazoic acid [6,7]:

$$4\,HN_3 + 2\,F_2 \rightarrow 3\,FN_3 + N_2 + NH_4F \quad (e)$$

Fluorine azide has so far been characterized only by qualitative analysis, by its molecular weight, and with the aid of the decomposition reaction (j) [6]. FN_3 is also formed as a by-product in the synthesis of N_2F_2 from fluorine and solid sodium azide moistened with a trace of water [8]; the sodium azide may be diluted with CaF_2 to avoid local overheating [9].

B. Chemical Properties of the Halogen Azides

The halogen azides are hydrolysed in aqueous media, particularly in the presence of OH^- ions:

$$XN_3 + 2\,OH^- \rightarrow N_3^- + XO^- + H_2O \quad (f)$$
$$X = Cl, Br, I$$

This reaction led at an early stage to the conclusion that the halogens X are electropositive in these compounds [1,2]. The formation of hypochlorite is utilized for analytical determination; arsenite is oxidized smoothly to arsenate [10]:

$$AsO_3^{3-} + XN_3 + 2\,OH^- \rightarrow AsO_4^{3-} + N_3^- + X^- + H_2O \quad (g)$$

Only ClN_3 and IN_3 dissolve in water without decomposing [1,2], whereas BrN_3 decomposes in water to form HN_3 and HOBr; when heated, the reaction products undergo a redox reaction:

$$2\,BrN_3 \quad H_2O \xrightarrow{H_2O} 3\,N_2 + Br_2 \quad (h)$$

ClN_3 BrN_3, and IN_3 dissolve readily in solvents such as ether, benzene, carbon tetrachloride, carbon disulfide, and pentane. Although solutions of ClN_3 in these solvents can be stored for a few days at 20 °C [2], the BrN_3 solutions, which can be kept for only a few hours, must be stored in the dark [5]; IN_3 solutions decompose slowly at 0 °C [1]. Reaction occasionally takes place with the solvent, as in the slow reaction of ClN_3 with pentane according to equation (i) [3]:

$$C_5H_{12} + ClN_3 \rightarrow C_5H_{11}Cl + HN_3 \quad (i)$$

ClN_3 undergoes a complex reaction with an excess of ammonia in the gas phase, which yields N_2, NH_4Cl, and NH_4N_3 [3]. Violent explosions occur when ClN_3, BrN_3, and IN_3 are brought into contact with Na, Mg, Zn, or white phosphorus. When the reaction mixture is diluted with solvents, the reaction products are found to be mixtures of the chloride and azide of the element in question [1,3,5].

All the halogen azides are extremely explosive. The stability appears to increase slightly in the order

$$FN_3 < IN_3 < BrN_3 < ClN_3$$

The halogen azides explode particularly readily in the solid state; however, the utmost caution is advised, even in reactions in the gas phase. Fluorine azide explodes "regularly" on vaporization of the condensate [6]; the reasons for this are largely unknown. It is known that in the presence of nitrogen, even very small pressure variations (Δp = 0.05 mm Hg) can cause chlorine azide and bromide azide to explode [11]. In our experience, explosions are avoided completely if pressure variations are kept within this Δp limit.

The slow decomposition of ClN_3, BrN_3, and IN_3 affords the elements, whereas fluorine azide yields difluorodiazene [6,8,9]:

$$2\,FN_3 \rightarrow N_2F_2 + 2\,N_2 \quad (j)$$

FN_3 reacts slowly with an excess of fluorine in the gas phase to form nitrogen trifluoride [6]:

$$FN_3 + F_2 \rightarrow NF_3 + N_2 \quad (k)$$

An interesting reaction takes place between chlorine azide and silver azide in diethyl ether at −78 °C; a deep blue to black substance is formed which evidently contains an Ag(II) compound [12]:

$$2\,AgN_3 + 2\,ClN_3 \rightarrow 2\,N_3AgCl + 3\,N_2 \quad (l)$$

Silver(II) azide chloride is very sensitive to shock; decomposition into AgCl and N_2 begins at −30 °C [12].

[4] *K. Dehnicke*, J. inorg. nuclear Chem. *27*, 809 (1965).

[5] *D. A. Spencer*, J. chem. Soc. (London) *127*, 216 (1925).

[6] *J. F. Haller*, Dissertation, Cornell University, 1942.

[7] *S. H. Bauer*, J. Amer. chem. Soc. *69*, 3104 (1947).

[8] *H. W. Roesky*, *O. Glemser*, and *D. Bormann*, Chem. Ber. *99*, 1589 (1966).

[9] *A. F. Pankratof*, *O. M. Ssokolof*, and *N. I. Ssavenkova*, Ž. neorg. Chim. *9*, 1095 (1964); Chem. Abstr. *61*, 10299 (1964).

[10] *A. Gutmann*, Ber. dtsch. chem. Ges. *57*, 1956 (1924).

[11] *K. Dehnicke*, Habilitation Thesis, Technische Hochschule Stuttgart. 1965,

[12] *W. J. Frierson* and *A. W. Browne*, J. Amer. chem. Soc. *65*, 1698 (1943).

C. Physical Properties of the Halogen Azides

Owing to the instability and explosive nature of the halogen azides, very few of their physical data are known. Determination of the magnetic susceptibility of chlorine azide dissolved in carbon tetrachloride showed a slight paramagnetism of $\chi_{mole} = 16.5 \times 10^{-6}$ [12a].

Table 1. Melting points and boiling points of the halogen azides.

	M.p (°C)	B.p. (°C/mm)	Ref.
FN_3	−154	−82/760 [*]	[6]
ClN_3	−100	15/760	[3]
BrN_3	−45	?	[5]
IN_3	(solid)	?	[1]

[*] The boiling point of FN_3 could be determined only as the condensation point.

Gaseous chlorine azide can be exploded even at low pressures (< 0.1 mm Hg) by the action of an electric discharge [13a]; light is emitted in the wavelength range of 5000 to 5500 Å. The kinetics of the explosion can be represented by equation (m) [13]:

$$ClN_3 \rightarrow Cl + 3\,N \qquad (m)$$

Milligan and *Jacox* studied the UV-induced reactions of FN_3, ClN_3 and BrN_3; when fixed in an argon matrix at 4 °K, these compounds yielded the radicals NF, NCl, and NBr. The IR spectra of these radicals and of the halogen azides (the fundamental vibrations of which are given, with their assignments, in Table 2) have been recorded [14, 15]. The halogen azide molecules all belong to the symmetry class C_s, the angle at the α-N atom being less than 180° [14].

Table 2. IR spectra of the halogen azides in an Ar matrix, after *Milligan* and *Jacox* [14].

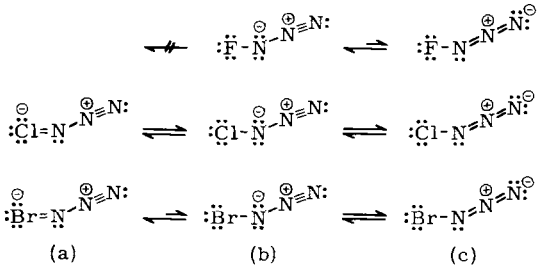
	ν (NX)	ν_{as} (N_3)	ν_s (N_3)	δ (N_3)
FN_3	869	2034	1086	503, 654
ClN_3	721(^{37}Cl)724(^{35}Cl)	2060, 2072	1144	520
BrN_3	687	2053, 2070	1160	530

Comparison with the N-halogen stretching vibrations of other molecules shows that only the N–F stretching vibration occurs at a "normal" [16] frequency; the NCl stretching vibration of ClN_3 occurs at the extremely high frequency of 724 cm^{-1} [16–18]. Though no data for comparison are available for NBr stretching vibrations, the NBr stretching frequency in BrN_3 also appears to be very high from its relationship with the N–Cl frequency of ClN_3. This must be interpreted as resulting from an increase in the strength of the N-halogen bond from fluorine azide to bromine azide, which can only be due to interaction of the π-electrons of the N_3 group with free d orbitals of the chlorine or bromine. Since there are no d orbitals available in fluorine, there is no strengthening of the F–N bond, with the result that the F–N stretching vibration occurs in the normal position.

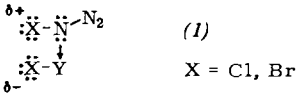
The situation changes when we turn from the halogen azides to the halogen-nitrogen radicals XN. Bond strengthening can now occur in the FN radical owing to the electron deficiency on the N atom. This should give rise to a considerable increase in frequency, and the N–F frequency is in fact found to increase from 869 to 1115 cm^{-1} [14]. A much smaller increase in frequency, *i.e.* only 98 cm^{-1}, is found for the transition from ClN_3 to ClN; this is in agreement with the view that the Cl–N bond is already considerably strengthened in ClN_3. There is no difference between the NBr frequencies of BrN_3 and BrN, evidently because the d orbitals of bromine and its ease of polarization render a very high bond order possible in BrN_3. This explanation agrees with Goubeau's rule [19], according to which groups of atoms tend to form multiple bonds only when the sum of the electronegativities, owing to electron deficiency and low polarity of the bond, is greater than 5.

This casts considerable doubt on the "electropositive" character of the halogens in the halogen azides, because the above discussion suggests that the halogen is the electronegative partner; the relationships are summarized in Table 3.

Table 3. The probable resonance relationships in the halogen azides.



It can be seen that resonance form (a) cannot occur in fluorine azide, but can occur in ClN_3 and to an even greater extent in BrN_3; nevertheless, the halogen azides react as if the halogen atoms were electropositive, *e.g.* in hydrolysis or in substitutions. The explanation of this apparent contradiction must be sought in the kinetics of the first step in the reactions of the halogen azides. In every case studied, this step consists in an attack by an electron acceptor Y (Lewis acid), which is a proton in hydrolysis, on the α-N atom of the halogen azide; this attack leads to the formation of the transition complex *(1)*.



(1)

X = Cl, Br

The attack by the acceptor atom Y, *e.g.* antimony in $SbCl_5$, favors the resonance form (b) (cf. Table 3).

If Y is attached to an electronegative partner X (*e.g.* $Cl^{\ominus}$ in $TiCl_4$; XY = $TiCl_4$), a redox neutralization of

[12a] *K. Krogmann, H. D. Hausen,* and *K. Dehnicke,* unpublished.

[13] *G. Pannetier,* C. R. hebd. Séances Acad. Sci. *233,* 168(1951).

[13a] *G. Pannetier* and *M. Lecamp,* Bull. Soc. chim. France *1954,* 1068.

[14] *D. E. Milligan* and *M. E. Jacox,* J. chem. Physics *40,* 2461 (1964).

[15] *D. E. Milligan,* J. chem. Physics *35,* 372 (1961).

[16] *H. Siebert*: Anwendungen der Schwingungsspektroskopie in der anorganischen Chemie. Springer, Göttingen-Heidelberg-Berlin-New York, 1966.

[17] *F. Moll,* Naturwissenschaften *52,* 559 (1965).

[18] *J. Strähle* and *K. Dehnicke,* Z. anorg. allg. Chem. *338,* 287 (1965).

[19] *J. Goubeau,* Angew. Chem. *69,* 77 (1957).

the two oppositely charged halogen species can lead finally to the formation of X_2 [4, 11]. The result is therefore the replacement of halide by azide. This view is substantiated by the fact that ClN_3 and BrN_3 do not react with halides that are not pronounced Lewis acids, *e.g.* $SiCl_4$ or $POCl_3$ [11]. Since the resonance form (a) is more strongly favored in bromine azide, whereas the initial reaction with the acceptor depends on form (b) or (c), reactions with BrN_3 should be inhibited; this agrees with observations [20]. Thus it may be concluded the halogen azides are not *a priori* electropositive, but become so only as a result of reversal of polarization during reactions. The halogen azides might therefore be better described as "azidium halides".

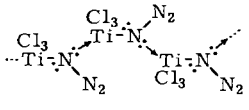
D. Reactions of Halogen Azides Used in Preparative Work

1. Reactions with Metal Halides

When gaseous chlorine azide, diluted with nitrogen, is passed into metal halides such as $TiCl_4$, $VOCl_3$, or $SnCl_4$ at room temperature, an exothermic reaction takes place in accord with equation (n) (cf. also Section C) and metal monoazide halides are precipitated [4].

$$TiCl_4 + ClN_3 \rightarrow TiCl_3N_3 + Cl_2 \qquad (n)$$

This reaction can be used for the synthesis of Cl_3SnN_3, $VOCl_2N_3$ [4], and CrO_2ClN_3 [21]. These metal azide chlorides are crystalline, generally explosive solids; in solution in $POCl_3$ they are monomeric, but in the solid state they tend to associate [4] and are thus stabilized (cf. Section 5):



Not all metal halides containing the metal in its highest valence state are known. However, metal halides of lower valence states, *e.g.* VCl_4 or $MoCl_5$, can be oxidized with ClN_3 [18, 21]:

$$VCl_4 + ClN_3 \rightarrow VCl_4N_3 + {}^1/_2\, Cl_2 \qquad (o)$$

Metal halides that are solid at room temperature and are only slightly soluble in CCl_4 will react, as a slurry, with ClN_3. This method has been used for the conversion of $MoCl_5$ into $MoCl_5N_3$, WCl_6 into WCl_5N_3 [21], and UCl_5 into UCl_5N_3 [22]. The monoazide chlorides of molybdenum and tungsten dissolve readily in CCl_4 to give deep red solutions, in which the compounds are probably present in the monomeric form. $MoCl_5N_3$ and WCl_5N_3 are extremely explosive; in these compounds the stability is considerably decreased by the coordinative saturation of the central atoms Mo and W, which prevents association of the α-N atom of the azide group with a neighboring metal atom [21].

The reactions of chlorine azide with metal chlorides can, in principle, also be applied to bromine azide and metal bromides; this reaction is illustrated by equation (p).

$$WBr_5 + BrN_3 \rightarrow WBr_5N_3 + {}^1/_2\, Br_2 \qquad (p)$$

The properties of WBr_5N_3 [22] are similar to those of WCl_5N_3.

Sometimes, a second azide group can also be introduced with the aid of chlorine azide. Thus $MoCl_5N_3$, which is readily soluble in CCl_4, reacts to form the diamagnetic, highly explosive $MoCl_4(N_3)_2$ as shiny black crystals [21]:

$$MoCl_5N_3 + ClN_3 \rightarrow MoCl_4(N_3)_2 + Cl_2 \qquad (q)$$

In the metal azide halides discussed so far, the bonding of the azide group to the metal is essentially homopolar. This conclusion is based on the characteristic IR vibrations of the N_3 group, which are typical of homopolar bonding of the azide group, and on the metal-nitrogen stretching vibration, which cannot occur in an azide ion. The metal-azide group in every case forms an angle other than 180° at the α-N atom [4, 18, 21, 22]:

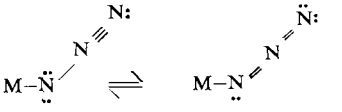


Table 4. Characteristic IR vibrations of azide groups in some metal azide chlorides.

	ν_{as} (N_3)	ν_s (N_3)	δ (N_3)	ν (M–N)	Ref.
$TiCl_3N_3$	2135	1230	659	565	[4]
$VOCl_2N_3$	2130, 2095	1249	698	560	[4]
CrO_2ClN_3	2145	1223	637	495	[21]
VCl_4N_3	2105	1190	703	556	[18]
$MoCl_4(N_3)_2$	2120, 2050	1260, 1230, 1215	683, 614	552	[21]
$SnCl_3N_3$	2158, 2137	1238, 1227	696	556	[4]

Whereas the metal azide halides discussed above associate only in the crystalline state, if at all, the reaction of chlorine azide with $SbCl_5$, which is analogous to the reaction (n), affords dimeric antimony azide tetrachloride [23, 25] $[SbCl_4N_3]_2$, which is soluble even in nonpolar solvents. In agreement with a suggestion of *Wiberg* and *Schmid* [24], this compound forms a four-membered Sb–N ring *(2)* using the α-N atoms of the azide groups. The vibration spectra (IR and Raman) indicate that this four-membered ring is planar (symmetry D_{2h}) both in the solid phase and in solution [25]. The ring can be cleaved with pyridine to form the adduct $[SbCl_4N_3 \cdot C_5H_5N]$, in which the

[20] *K. Dehnicke* and *U. Müller*, unpublished.

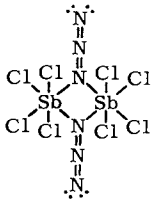
[21] *K. Dehnicke* and *J. Strähle*, Z. anorg. allg. Chem. *339*, 171 (1965).

[22] *K. Dehnicke, G. Lange, J. Müller, D. Seybold*, and *J. Strähle*, Angew. Chem. *78*, 339 (1966); Angew. Chem. internat. Edit. *5*, 322 (1966).

[23] *K. Dehnicke* and *U. Müller*, Angew. Chem. *76*, 385 (1964); Angew. Chem. internat. Edit. *3*, 448 (1964).

[24] *N. Wiberg* and *K. H. Schmid*, Angew. Chem. *76*, 380 (1964); Angew. Chem. internat. Edit. *3*, 444 (1964).

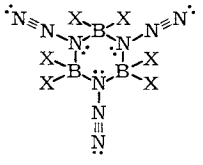
[25] *U. Müller* and *K. Dehnicke*, Z. anorg. allg. Chem., in press.



(2)

α-N atom of the azide group and the nitrogen atom of the pyridine occupy the *trans* positions on the octahedrally coordinated antimony [25].

The reaction of BCl_3 or BBr_3 with chlorine azide or bromine azide yields interesting products, namely the boron azide dihalides $[BX_2N_3]_3$ [26], which dissolve as the trimers in CCl_4 and benzene; the chlorine compound has also been prepared by another route [27]. The vibration spectra indicate that these compounds contain six-membered B–N rings *(3)*, which are characterized in particular by their planarity (symmetry D_{3h}) and a diazonium structure [26]:



(3)

Finally, it should be mentioned that ClN_3 and BrN_3 also take part in addition reactions. Thus ClN_3 reacts with PCl_3 to form the very unstable PCl_4N_3, which reacts further with PCl_3 to give the known compound $[Cl_3P{=}N{-}PCl_3]^{\oplus}Cl^{\ominus}$ [20] [25a] .Antimony azide tetrabromide can be obtained from $SbBr_3$ and BrN_3 in CCl_4 [20]:

$$SbBr_3 + BrN_3 \rightarrow SbBr_4N_3 \qquad (r)$$

2. Reactions of the Metal Azide Halides

Some metal azide halides decompose gently and in a definite manner under the influence of solvents, and are therefore of interest for the synthesis of nitride compounds.

It is possible to distinguish several types of decomposition:

1. In one case, nitrogen and chlorine are split off simultaneously, *e.g.*:

$$TiCl_3N_3 \rightarrow TiNCl + N_2 + Cl_2 \qquad (s)$$

$$VOCl_2N_3 \rightarrow VON + N_2 + Cl_2 \qquad (t)$$

The polymeric nitride compounds $(TiNCl)_x$ and $(VON)x$ are formed quantitatively in a very pure state when carbon tetrachloride solutions of the azide chlorides are heated [4].The decomposition of $MoCl_5N_3$ or WCl_5N_3 in CCl_4 under the same mild conditions leads, again quantitatively, to precipitates having the composition $MoNCl_3$ or $WNCl_3$:

$$MoCl_5N_3 \rightarrow MoNCl_3 + N_2 + Cl_2 \qquad (u)$$

The IR spectra of these substances indicate that the metal atoms have deformed tetrahedral coordination (site symmetries C_s or C_i) in the lattice, and Mo≡N and W≡N triple bonds are detected [21]. Mass-spectrometric examination shows that, in agreement with these findings, $MoNCl_3$ vaporizes as the monomer [28]. $MoNCl_3$ and $WNCl_3$ form adducts with pyridine in the molar ratio of 1:3 [21].

2. In another case, the metal azide halides decompose in a definite manner with elimination of nitrogen only, the initially formed radical being stabilized by migration of Cl from the metal to the nitrogen. Hexachloroborazole has been prepared in this way from $[BCl_2N_3]_3$ [27]. Another example is the decomposition of VCl_4N_3, which proceeds at room temperature and yields *N*-chlorovanadium imide trichloride:

$$Cl_4V{-}N_3 \xrightarrow{-N_2} [Cl_4V{=}N{:}] \rightarrow Cl_3V{=}N{-}Cl \qquad (v)$$

This type of reaction (v) is reminiscent of the Curtius acid degradation. IR-spectroscopic studies indicate that the intermediate radical probably contains a V=N double bond [18]. $VNCl_4$ sublimes readily, is soluble as the monomer in benzene, and, according to the IR spectrum, has a molecular symmetry C_s with an angular V=N–Cl grouping [18]. $VNCl_4$ forms adducts *via* the Cl atom attached to the nitrogen both with Lewis acids and with Lewis bases. Thus it forms a 1:1 adduct *(4)* with $SbCl_5$, and a 1:2 adduct *(5)* with pyridine.

$[Cl_3V{=}N]^{\oplus}\ [SbCl_6]^{\ominus}$ *(4)* $[Cl_3V{\equiv}N]^{\ominus}\ [Cl(C_5H_5N)_2]^{\oplus}$ *(5)*

Both compounds may be regarded as ionic [18], because they crystallize well, are insoluble in nonpolar solvents, and have no definite melting point. The IR spectra do not contain the characteristic N–Cl vibrations of $VNCl_4$. On the other hand, the spectrum of *(4)* contains the two IR-active vibrations (class F_{1u}) of the $SbCl_6^-$ octahedron, as well as the characteristic vibrations of the cation. The IR spectrum of the anion $VNCl_3^-$ in *(5)* agrees with that of the isoelectronic $VOCl_3$ [18].

3. Finally the metal azide halide may also react with the solvent. Owing to the high energy of the azide, reactions of this type can take place even under mild conditions. For example, antimony azide tetrachloride reacts with boiling CCl_4 to form triazidocarbonium hexachloroantimonate [28a]:

$$3\ SbCl_4N_3 + CCl_4 \rightarrow [C(N_3)_3^{\oplus}\ [SbCl_6]^{\ominus} + 2\ SbCl_5 \qquad (w)$$

According to its IR spectrum, the triazidocarbonium cation consists of a planar CN_3 skeleton with azido groups bent out of the plane (symmetry C_{3v}). The CN stretching frequencies agree with those of the guanidinium ion [28a].

[25a] *M. Becke-Goehring* and *W. Lehr*, Z. anorg. allg. Chem. *327*, 136 (1964).

[26] *P. I. Paetzold, M. Gayoso*, and *K. Dehnicke*, Chem. Ber. *98*, 1173 (1965).

[27] *P. I. Paetzold*, Z. anorg. allg. Chem. *326*, 47 (1963).

[28] *H. Schäfer* and *K. Rinke*, personal communication.

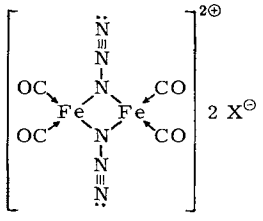
[28a] *U. Müller* and *K. Dehnicke*, Angew. Chem. *78*, 825 (1966); Angew. Chem. internat. Edit. *5*, 841 (1966).

3. Reactions of the Halogen Azides with Metal Carbonyls

Chlorine azide and bromine azide react with the metal carbonyls $Fe(CO)_5$, $Mo(CO)_6$, and $W(CO)_6$ to form carbonylmetal azide halides $M(CO)_2N_3Cl$ [29]:

$$Fe(CO)_5 + ClN_3 \rightarrow Fe(CO)_2N_3Cl + 3\ CO \qquad (x)$$

According to the IR spectra and magnetic behavior, the iron compound $Fe(CO)_2N_3X$ consists of substantially planar four-membered Fe–N rings *(6)*, the halogen being ionically bonded (pseudosymmetry D_{2h}) [29]:

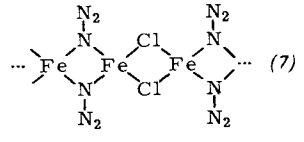


(6), X = Cl, Br

These compounds exhibit the paramagnetism of the unperturbed Fe(II) ion (μ = 5.29 B.M.) and obey the Curie law (θ = 0 °C); they are the first paramagnetic carbonyliron derivatives [29]. The Fe–C bonds appear to be pure σ bonds without any back-donation. Thermal degradation under vacuum at 80 °C yields the CO-free azide halides of Fe^{II}, $FeClN_3$ and $FeBrN_3$, which are also paramagnetic:

$$Fe(CO)_2N_3Cl \rightarrow FeClN_3 + 2\ CO \qquad (y)$$

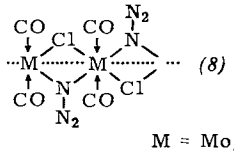
The IR spectra of the iron(II) azide halides indicate that they are polymeric *(7)*, the azide groups retaining their bridge function [29]:



(7)

The genetic relationship with the carbonylmetal azide is obvious. Neither the carbonylmetal azide halides nor the CO-free azide halides of Fe^{II} are explosive; utilization of the lone pair of electrons on the α-N atom offers an explanation of these facts.

The carbonylmetal azide halides of Mo and W are also polymeric *(8)*, but in this case both Cl and N_3 assume bridge functions [29].



(8)

M = Mo, W

This leads to strong metal-metal interactions, as can be seen from the magnetic behavior: $[Mo(CO)_2ClN_3]_\infty$: μ = 0.81 B.M., θ = −20 °C; $[W(CO)_2ClN_3]_\infty$: $\chi_{mole} = -74.9\times10^{-6}$. The carbon monoxide cannot be removed completely from these compounds without risk of explosion [29].

[29] *G. Lange* and *K. Dehnicke*, Z. anorg. allg. Chem. *344*, 167 (1966).

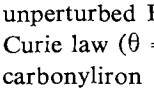
4. Reactions of the Halogen Azides with Organometallic Compounds

Chlorine azide can react with organometallic compounds according to equation (z). These reactions can be carried out in solvents (*e.g.* benzene, pentane, CCl_4) or in the absence of solvents, and lead to excellent yields of metal monoazide derivatives [30]:

$$MR_x + ClN_3 \rightarrow MR_{x-1}N_3 + RCl \qquad (z)$$

For example, dimethylcadmium gives the hygroscopic, white, crystalline methylcadmium azide $[H_3C\text{-}Cd]^{\oplus}N_3^{\ominus}$, which appears from its IR spectrum to be ionic (symmetry of the cation C_{3v}) [30].

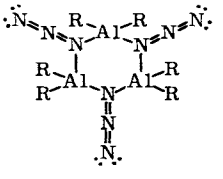
On the other hand, the alkylmercury and arylmercury azides obtained by reaction (z) form white, readily sublimable, non-hygroscopic crystals, which are soluble in benzene (monomeric), and whose vibration spectra (IR and Raman) indicate the presence of linear C–HgNNN groups [30,31]:



R = CH_3, C_2H_5, n-C_3H_7, i-C_3H_7 n-C_4H_9, C_6H_5

Ethylzinc azide and phenylzinc azide can also be prepared as in equation (z) from carefully purified chlorine azide. These compounds form white, hygroscopic, explosive crystals, whose physical and chemical properties are intermediate between those of the corresponding cadmium and mercury compounds [31a].

Trialkylaluminums also react readily with chlorine azide to form dialkylaluminum azides [30,32]. The ethyl compound (m.p. −130 °C) dissolves in benzene as the trimer, can be distilled (10^{-3}mm Hg) at 63 °C without decomposition, and is not exploded either by shock or by heat. According to the vibration spectrum, the aluminum atoms are linked with the α-N atoms to form a planar, six-membered Al–N ring *(9)* (symmetry D_{3h}) [30,32]. The indicated electron distribution on the N_3 groups is deduced from thermal and spectroscopic behavior.



(9)

The same structure, with a six-membered Ga–N ring, is found in diethylgallium azide $[(C_2H_5)_2GaN_3]_3$, which is obtained from $Ga(C_2H_5)_3$ and chlorine azide; this compound is again trimeric, and is a colorless, distillable liquid [32a]. In contrast with the diethylalu-

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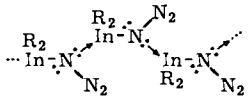
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minum azide, the gallium compound does not react with water [32a].

On the other hand, diethylindium azide, which is prepared from triethylindium and chlorine azide, forms crystals that are insoluble in benzene, the α-N atom of the azide group giving rise to polymerisation [32b] in accordance with formula *(10)*.



(10)

5. The Stability Relationships of the Azides

Relatively little is known at present of the thermodynamics of azides; a review has been published by *Gray* [33]. However, chemists are also interested in kinetic aspects, since *e.g.* a prerequisite for handling of an azide is that the activation energy for its decomposition must be sufficiently high. In the case of the diorganylborazides, the kinetics of the decomposition depend on both the bulk and the inductive effect of the organic ligands [33a].

The above discussions show that the classification into stable "azide ions" and "unstable homopolar azides" will have to be extended. Thus it has been seen that stabilization of covalently bonded azide groups is also possible. From experience gained so far, such groups are always stabilized when the α-N atom of the N_3 group forms an additional bond. It is possible to distinguish two cases.

1. The formation of the additional bond by the α-N atom may lead to a multiple bond (dπ–pπ interaction) between the metal and the N_3 group. This requires a sufficiently large d-orbital contribution of the metal, and leads to widening of the bond angle at the α-N atom. Stable conditions of this nature are observed in the monomeric alkylmercury azides $R-Hg=N=N=\dot{N}:$, which contain linear structural groups [30]. The electron requirements of the mercury appear to be satisfied in this way. A second azide group cannot lead to further stabilization; $Hg(N_3)_2$ is explosive.

This case also includes the very stable alkyl and aryl azides of elements of group IV [34,35], though this appears to contradict the calculated force constants for the Si–N bond in trimethylsilyl azide [36].

If the electron requirements of the central atom are satisfied by other ligand atoms, the N_3 group cannot be stabilized in this way, and the resulting azide derivatives are explosive. This situation is found in metal azide halides such as $MoCl_5N_3$, $MoCl_4(N_3)_2$, WCl_5N_3 [21], and WBr_5N_3 [22], in which the electron requirements of the metal are evidently satisfied by the halogen atoms. This concept also explains, in principle, the increase in the stability of the halogen azides from FN_3 to BrN_3 (cf. Section C). FN_3 is the least stable, since no strengthening of the F–N bond is possible; consequently the α-N atom cannot reduce its excess of electrons. HN_3 and CH_3N_3 are also explosive because electrons cannot be transferred into the H–N or C–N bond.

2. Another possibility for the stabilization of covalently bonded N_3 groups is found in the azide derivatives that associate *via* the α-N atom. This always occurs when the central atom is coordinatively unsaturated, so that an additional bond can be formed between this atom, as a Lewis acid, and the α-N atom as a Lewis base. The result is the formation of four-membered or six-membered rings or of polymers *e.g.* the dimeric antimony azide tetrachloride *(2)*, the trimeric diethylaluminum azide *(9)*, and the polymeric diethylindium azide *(10)*. A special case of this mode of stabilization is the protonation of hydrazoic acid $H_2N_3^+$ (as the hexachloroantimonate) [37]. This stabilization results mainly from the possibility of resonance in the N_3 group:



Additional stabilization is to be expected in ring formation (provided that the rings are strainless) as a result of the entropy effect.

Many azidometal complexes are known, *e.g.* $[Pt(N_3)_6]^{2-}$, in which additional stabilization is achieved by the incorporation of bulky cations, *e.g.* $[As(C_6H_5)_4]^+$ [39].

Table 5. Some stabilized azides.

Type *(1)*		Type *(2)*	
$N_2N_3^+$	[37]	R_3MN_3	[34, 35]
$CH_3N_3 \cdot SbCl_5$	[38]	(R = Alkyl, Aryl;	
$[SbCl_4N_3]_2$	[23–25]	M = Si, Ge, Sn, Pb)	
$[MR_2N_3]_3$	[30, 32, 32a]	R–HgN_3	[30, 31]
(M = Al, Ga)			
$[Fe(CO)_2N_3]_2^{2+}$	[29]		

I am grateful to my co-workers, particularly Fräulein Dipl.-Chem. Gertrud Lange, Dr. J. Strähle, Dr. Ulrich Müller, Dipl.-Chem. Joachim Müller, Dipl.-Chem. Herbert Müller, and Dipl.-Chem. D. Seybold, without whose imagination and fearlessness this work would not have been possible. I thank Prof. Dr. J. Goubeau for his confidence and for his help. Acknowledgment is also due to the Deutsche Forschungsgemeinschaft and to the Fonds der Chemischen Industrie for financial support.

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Formation of Amino Acids and their Precursors from Primitive Compounds by High-Temperature Synthesis

By *M. Taube, St. Z. Zdrojewski, K. Samochocka*, and *K. Jezierska*[*]

On high-temperature synthesis of amino acids from methane, ammonia, and water vapor we have found numerous intermediates as well as three amino acids (lysine, tryptophane, and β-alanine) whose formation had not previously been reported[1–3]. We obtained the best yields of amino acids in a streaming apparatus under the following conditions: CH_4 0.5 l/min, NH_3 0.3 l/min, and H_2O 0.2 l/min; the residence time of the gases in the reaction zone was 0.125 sec; warming of the gases from 100 to 800 °C required 0.28 sec, and cooling to 20 °C required 0.4 sec; the optimal temperature in the reaction zone was 1000 °C, 95.4% of the NH_3 in the reaction mixture then undergoing conversion. Yields of amino acids were very low at 900 °C, and at 1150 °C the methane was converted into graphite. At 1050 °C aromatic hydrocarbons and oxygen compounds (mainly acetaldehyde and propionaldehyde) constituted up to 1% of the total product; at this temperature the proportion of nitrogen compounds (methylamine, ethylamine, hydrogen cyanide) amounted to 10 mole-%. The reaction zone was filled with silica gel (particle size 3 to 6 mm).

The products of synthesis were identified by gas chromatography and the individual amino acids by high-voltage paper electrophoresis (50 V/cm).

The compounds identified are listed in the following table.

C, H, N, O compounds identified by gas chromatography (mole-%)

Hydrocarbons		Oxygen compounds	
Benzene	0.16–0.58	Acetaldehyde	0.05–0.29
Toluene	0.01–0.02	Propionaldehyde	0.03–0.2
p-, *m*-, *o*-Xylene	0.12–0.04	Acrolein	0–0.02
Naphthalene	0.002–0.004	Methanol	0.02–0.11
Ethane	10^{-5} to 10^{-3}	Ethanol	0.001–0.14
Propane	10^{-7}–10^{-5}	Acetone	0–0.03
Cyclobutane	0.02–0.06	Volatile acids	0.005–0.09
Cyclohexane	0–0.012	Involatile acids	0.01–0.29
Tars	0.005–0.02	Carbon monoxide	0.001–0.3
Acetylene	0.13–0.83	Formamide	0–0.09
Nitrogen compounds			
Hydrogen cyanide	0.07–0.6	Acetonitrile	0.03–0.3
Methylamine	0.04–0.5	Propionitrile	0.1–0.7
Dimethylamine	0.72–0.82	Acrylonitrile	0–0.12
Diethylamine	0–0.04	3-Butenonitrile	0–0.02
Aniline	0–0.01		
Amino acids (10^{-2} mole-%)			
Glycine	1.8–12	Lysine	2.3–2.4
α-Alanine	1.3–2.0	Proline	3.0
β-Alanine	1.9–6.3	Tryptophan	0.08
Serine	0.6–5.3	Phenylalanine	0.1
Glutamic acid	2.8–6.2	Valine	1.5–3.2
Asparagic acid	1.0–1.6	Leucine	1.2–2.6
Aminobutyric acid	0.2–2.0		

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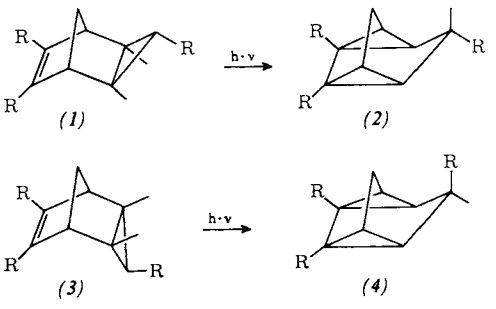
[*] Doz. Dr. M. Taube, mgr. St. Z. Zdrojewski, Dr. K. Samochocka, and mgr. K. Jezierska
Uniwersytet Warszawski, Katedra Radiochemii
Zwirki i Wigury 101
Warszawa (Poland)

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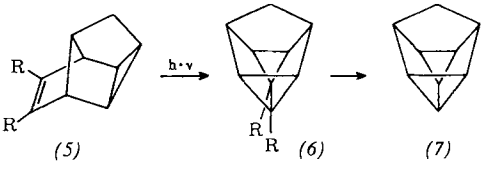
Pentacyclo[4.3.0.0^{2,4}.0^{3,8}.0^{5,7}]nonane

By *H. Prinzbach* and *D. Hunkler*[*]

The differing rates of the light-induced valence isomerizations *(1)* → *(2)* and *(3)* → *(4)* have been ascribed to the differing overlaps between the π- and the Δ-orbitals[1] in *(1)* and *(3)*[2].



We have now isomerized compounds of type *(5)* photochemically to the corresponding pentacyclic compounds *(6)*. Compound *(6a)* is not formed in isolable amounts under the conditions that are optimal for the change *(1)* → *(2)* (R = CO_2H; yield in water > 90%); further, the yield of *(6b)* is only a few percent when the ester *(5b)* is irradiated in ether. However, isomerization of *(5b)* in glacial acetic acid and of *(5a)* in this solvent, dioxane, or in tetrahydrofuran-ether (5:1 to 7:4)[3] can be achieved, giving (so far) yields of 15 to 30%[4].



(a) R = CO_2H
(b) R = CO_2CH_3 (d) R = CN
(c) R = $CONH_2$ (e) R = $CO_3C(CH_3)_3$

The structure of *(6a)* is proved by the several reactions *(6b)*–*(6e)* as well as by NMR results.

	M.p. (°C)	^{1}H–NMR (τ-values)			
(6a)	246–247	6.69 (4H)	6.98 (2H)	7.82 (2H)	(in CF_3CO_2H)
(6b)	64	6.31 (6H)	7.20 (6H)	8.08 (2H)	(in CCl_4)
(6e)	93–94	7.20 (6H)	8.07 (2H)	8.72 (18H)	(in CCl_4)

On pyrolysis of the di-t-butyl peroxyester *(6e)* in 1,3,5-triisopropylbenzene (N_2 stream; 150–155 °C) we obtained pentacyclo[4.3.0.0^{2,4}.0^{3,8}.0^{5,7}]nonane *(7)*, m.p. 82–84 °C (after repeated sublimation) in 40% yield.

IR: 3067, 2994, 2959, 1302, 1040, 1014, 970, 897, 889, 881, 783, 766, 754 cm^{-1}.

UV: no maximum above 210 μm.

NMR[5]: τ = 7.47 (2H), 7.80–8.20 (8H) in $CDCl_3$ (100 MHz).

Mass spectrum[5]: M^+ = 118 (base peak), and readily assignable peaks *m/e* = 116, 103, 91, 78, 65, 51, 39, and 27, as well as *m/2e* = 57.5.

The pentacycles *(6b)* and *(7)* are very stable thermally. For instance, heating *(6b)* alone or in dimethyl acetylenedicarboxylate (300 °C) does not cause isomerization to *(5b)* or

addition analogous to that of quadricyclene[6] or oxaquadricyclene[7]. Furthermore, heating *(7)* in perchlorobutadiene to 300 °C (50 min) is not sufficient to cause valence isomerization.

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[*] Prof. Dr. H. Prinzbach
Université de Lausanne, Laboratoire de Chimie organique
3, Place du Château
Lausanne (Switzerland)

Dipl.-Chem. D. Hunkler
Chemisches Laboratorium der Universität
Albertstr. 21
78 Freiburg (Germany)

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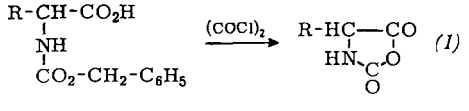
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Synthesis of *N*-Carboxy-α-amino Acid Anhydrides

By *D. Konopińska* and *I. Z. Siemion*[*]

N-Carboxy-α-amino acid anhydrides *(1)* are starting materials for the synthesis of polypeptides. We have found a new process for the preparation of these anhydrides, namely, treatment of *N*-(benzyloxycarbonyl)amino acids with oxalyl chloride. The acid chloride[1] is first formed, and then cyclizes to form the anhydride.



1 mmole of an *N*-(benzyloxycarbonyl)amino acid is allowed to react with 2 mmoles of oxalyl chloride in 1.5 to 2.5 ml of boiling benzene for 2 to 3 min. The reaction mixture is cooled in a refrigerator and after a short time the amino acid anhydride crystallizes. The leucine derivative is an exception, crystallizing only after addition of petroleum ether.

Parent amino acid	Anhydride		M.p. (°C) lit.
	Yield (%)	M.p. (°C) found	
D,L-Phenylalanine	92	124–125	125–126 [2]
L-*S*-Benzylcysteine	74	102–104	105–106 [3]
D,L-Alanine	69.9	4–46	44–45 [2]
D,L-Valine	71	78–79	77–70 [2]
L-Leucine	65	71–73	76–77 [4]

Prolonged heating of the components leads to formation of polymeric products. If *N*-(benzyloxycarbonyl)glycine is heated with oxalyl chloride for only 2 to 3 min, a product is obtained that does not melt sharply and contains appreciably more nitrogen than is calculated for the anhydride *(1)*.

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[*] Dr. D. Konopińska and Dr. I. Z. Siemion
Akademia Medyczna, Zaklad Chemii Fizjologicznej
ul. Chalubińskiego 10
Wroclaw (Poland)

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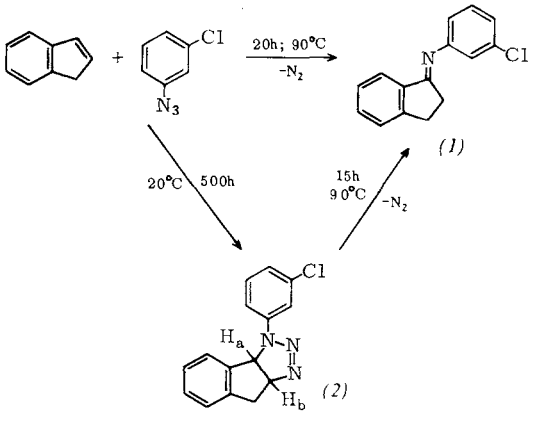
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Synthesis and Reactions of *m*-Chloro-*N*-1-indandylideneaniline

By *J. Jaz* and *A. Gerbaux*[*]

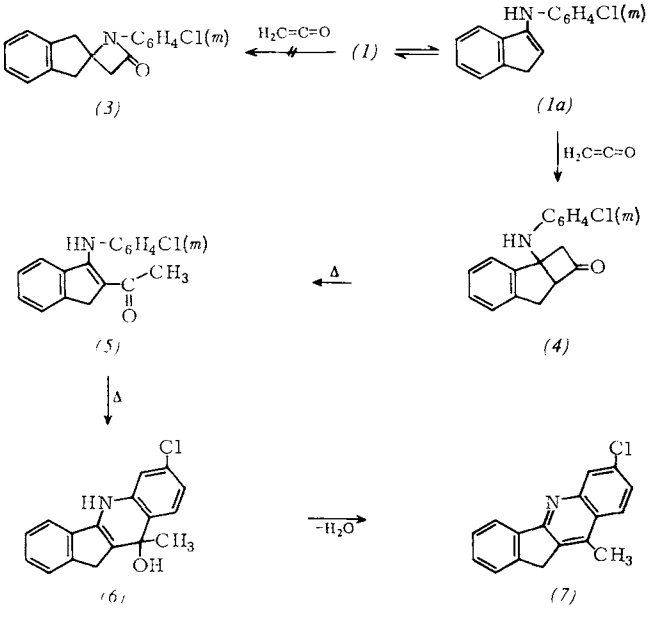
We have obtained various derivatives of *N*-1-indanylideneaniline by cycloaddition of substituted phenyl azides to indene[1]. We have now prepared the first *meta*-phenyl-substituted derivative, *m*-chloro-*N*-1-indanylideneaniline *(1)*, by heating an equimolar mixture of *m*-chlorophenyl azide[3] and indene for 20 h, distillation in a high vacuum after gas evolution had ceased, and recrystallization from ether (yield 60%; m.p. 50–52 °C).



If, however, the reaction mixture is left for three weeks at room temperature, substance *(2)* in 40% yield (m.p. 124 to 125 °C; decomp. with gas evolution) is isolated, whose IR spectrum (in CCl_4) shows the bands between 940 and 1000 cm^{-1} that characterize triazolines. The ^1H–NMR spectrum (TMS/$CDCl_3$) shows a methylene doublet at $\tau = 6.45$ (J = 5 Hz), the signals of the angular hydrogen atoms H_a and H_b at $\tau = 4.67$ (J = 9 Hz), and a band system centred at $\tau = 2.75$ to be assigned to the aromatic protons. Compound *(2)* is thus 1-(*m*-chlorophenyl)indano[1,2-*d*]-Δ^2-1,2,3-triazoline. *cis*-Addition has occurred, as proved by the dihedral angle of 20 °C calculated for the protons H_a and H_b by the *Karplus* equation[4].

When heated at 90 °C compound *(2)* undergoes thermal decomposition to *(1)* (yield 82%), with violent evolution of gas. The structure of compound *(1)* was proved by its IR spectrum (CCl_4; imine band at 1600 cm^{-1}), elemental analysis, and chemical reactions: acid hydrolysis affords, as well as *m*-chloroaniline, 1-indanone (yield 20%; m.p. 39–40.5 °C), which was identified by its IR spectrum (CCl_4; carbonyl band at 1720 cm^{-1}), UV spectrum [in C_2H_5OH λ_{max} = 244 nm (ε = 10550), 286 nm (2650), 292 nm (2550)[5]], ^1H–NMR spectrum (TMS/$CDCl_3$; methylene triplet at $\tau = 7.37$ and 6.88; complex band system centered at $\tau = 2.53$, corresponding to four aromatic protons), and its 2,4-dinitrophenylhydrazone (m.p. 259–260 °C).

Passing ketene into the molten compound *(1)* did not give a spirolactam *(3)*[6,7] or a tricyclic cyclobutanone *(4)*, but instead a crystalline product $C_{17}H_{12}NCl$ (yield 75%; m.p. 138–138.5 °C), which, on the basis of its IR, UV, and ^1H–NMR spectra, is 9-chloro-6-methylindeno[3,2-*b*]quinoline *(7)* [IR (CCl_4) methyl bands at 1390 and 2980 cm^{-1};



UV (C_2H_5OH) λ_{max} = 210 nm (ε = 20600), 256 nm (9000), 366 nm (15500); ^1H–NMR (TMS/$CDCl_3$) 7 aromatic protons centered at τ = 2.60, 2-methylene protons at τ = 6.3, methyl protons at τ = 7.8].

The formation of compound *(7)* can be understood if one assumes that the enamine form *(1a)* reacts with ketene to yield *(4)*, which according to *Opitz*[8] is thermolabile and undergoes ring opening and acetylation to give *(5)*. At the reaction temperature, *(5)* (which is molten) undergoes intramolecular addition and cyclization to give *(6)*, which aromatizes to *(7)*. The position of the chlorine atom follows from the ^1H–NMR spectrum and from consideration of molecular models that show cyclization at the 4-position to be sterically hindered.

Thermal decomposition of compound *(2)* yields only *(1)*, whereas the formation of aziridines has been demonstrated for the *para*-substituted analogues of *(1)*[9]. On reaction of *para*-substituted phenyl azides (excepting the *p*-nitro derivative), 2:1 adducts to indene have been isolated and characterized.

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[*] Doz. Dr. J. Jaz and Lic. Sci. A. Gerbaux
Laboratory for General and Organic Chemistry
University of Louvain
48 Overstraat
Veltem-Louvain (Belgium)

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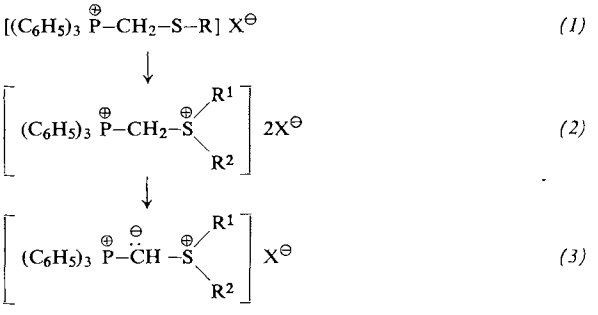
Dialkyl(triphenylphosphoniomethyl)sulfonium Bis-salts and their Conversion into Stable Ylide Salts

By *J. Gosselck, H. Schenk*, and *H. Ahlbrecht*[*]

Reaction of α-chloro sulfides[1] with triphenylphosphine in benzene gives (alkyl-, aralkyl-, or aryl-thiomethyl)triphenylphosphonium chlorides *(1a)–(1f)* in 50–80% yields. If these compounds are warmed in acid-free dimethyl sulfate for 1 to 2 h at 90–100 °C, the group R is removed in all cases and dimethyl(triphenylphosphoniomethyl)sulfonium bismethyl sulfate) *(2a)* is formed. It is precipitated by anhydrous ether and isolated from aqueous solution as the bistetrafluoroborate or dipicrate.

Alkylation of the salts *(1b)–(1f)* with triethyloxonium tetrafluoroborate in nitromethane at 50 °C yields the diethyl compound *(2b)*. Treatment of *(1a)* with triethyloxonium tetrafluoroborate gives the ethylmethyl compound *(2c)*. The salts *(2b)* and *(2c)* were isolated by precipitation with anhydrous ether and recrystallized from anhydrous ethanol.

If suspensions of the salts *(2a)–(2c)* in cold anhydrous ethanol are treated with equimolar amounts of sodium ethoxide, ylide salts *(3a)–(3c)* (readily soluble in ethanol) are formed in 70 to 80% yield. These compounds are colorless and stable in air, crystallize well, and are isolated by removal of the solvent and repeated precipitation from methylene chloride/ether (1:5 v/v). Addition of tetrafluoroboric acid to ethanolic solutions of the ylide salts *(3a)–(3c)* regenerates the salts *(2a)–(2c)*.



	R or R^1	R^2	$X^⊖$	M.p. (°C)	τCH_2 or τCH [a]	J_{HP}(Hz)
(1a)	CH_3		$B(C_6H_5)_4$	210–211		
			[2]			
			Picrate	102–103		
(1b)	C_2H_5		BF_4	159–160		
			Picrate	103–104		
(1c)	*t*-$C(CH_3)_3$		$B(C_6H_5)_4$	162–163		
(1d)	$-CH_2-C_6H_5$		$B(C_6H_5)_4$	187–188		
			BF_4	133–134		
(1e)	C_6H_5		$B(C_6H_5)_4$	165–167		
(1f)	*p*-Cl–C_6H_4–		$B(C_6H_5)_4$	183–184		
			BF_4	131–132		
(2a)	CH_3	CH_3	BF_4	234–235	4.67	10.0
			Picrate	156–157		
(2b)	C_2H_5	C_2H_5	BF_4	194–195	4.73	10.0
(2c)	CH_3	C_2H_5	BF_4	223–224	4.67	10.0
(3a)	CH_3	CH_3	BF_4	147–148	7.50	17.0
(3b)	C_2H_5	C_2H_5	BF_4	119–120	7.77	17.0
(3c)	CH_3	C_2H_5	BF_4	121–122	7.67	17.0

[a] Chemical shift for the proton attached to the carbon atom between S and P. Meas- ured in CD_3NO_2 for *(2)* and in $CDCl_3$ for *(3)*. In both cases tetramethylsilane was used as internal standard.

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[*] Doz. Dr. J. Gosselck, Dr. H. Schenk, and H. Ahlbrecht
Institut für Organische Chemie der Universität
Ludwigstr. 21
63 Giessen (Germany)

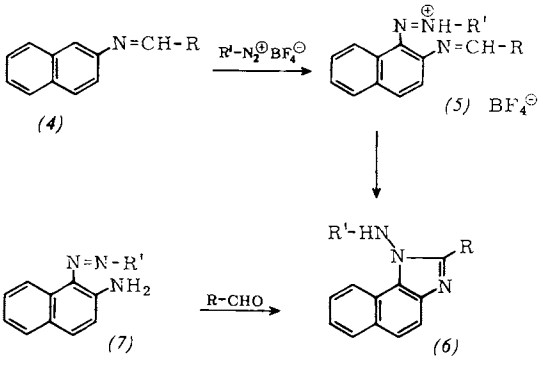
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Azo Coupling to Schiff Bases. A New Synthesis of Naphthimidazole Derivatives

By *A. Messmer* and *O. Szimán*[*]

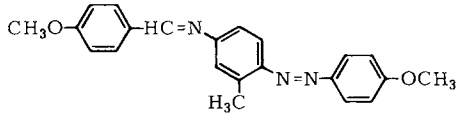
We have found that, in dipolar solvents that cannot take up a proton (nitromethane, nitrobenzene, acetonitrile), arenediazonium fluoroborates react by azo coupling with aromatic amines, and, surprisingly, also with Schiff bases from aromatic amines and aromatic aldehydes, whereas no reaction occurs with phenols. Adding ether to the reaction mixture precipitates the intensely colored fluoroborates of the aminoazo compounds. If the azo group is in the *para*-position to the amino group, the free base is liberated from the salt by pyridine; but if the azo group is in the *ortho*-position to the amino group, salts are formed on addition of pyridine and ring closure takes place to give condensed imidazole derivatives.



R	R′	(5) M.p. (°C)	(5) Yield (%)	(6) M.p. (°C)	(6) Yield (%)
p-CH_3O–C_6H_4	*p*-CH_3O–C_6H_4	168	70	177	80 [b]
C_6H_5	*p*-CH_3O–C_6H_4	165	81	185	88
C_6H_5	C_6H_5	175	72	199	62
p-O_2N–C_6H_4	*p*-Br–C_6H_4	[a]		249	95
p-O_2N–C_6H_4	*p*-O_2N–C_6H_4	[a]		304	99

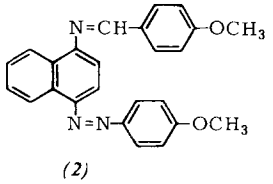
[a] Not isolated. [b] The same product is obtained from *(7)* and *p*-anisaldehyde [1], whereby the structure of *(6)* is proved.

The reaction of *N*-(*p*-anisylidene)-*m*-toluidine with *p*-methoxybenzenediazonium fluoroborate in nitromethane or acetonitrile, gives the brownish-red, crystalline *N*-(*p*-anisylidene)-4-(*p*-methoxyphenylazo)-3-methylanilinium fluoroborate, m.p. 239 °C (yield 67%), which is quantitatively converted into the red free base *(1)*, m.p. 108 °C, by pyridine. Its structure is established by the fact that the same base can be prepared from 3-amino-4′-methoxy-2-methylazobenzene and *p*-anisaldehyde.

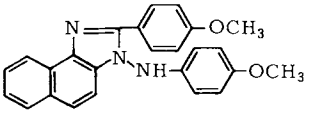


(1)

N-(*p*-Anisylidene)-α-naphthylamine and *p*-methoxybenzenediazonium fluoroborate in nitromethane give a dark blue mixture from which a mixture of red and white crystals is precipitated on addition of pyridine; these can be separated by recrystallization from ethanol. The red crystals are 4-(*p*-aminophenylazo)-*N*-(*p*-anisylidene)-1-naphthylamine *(2)*, m.p. 167 °C (yield 23%); the white crystals are *N*,2-di-(*p*-methoxyphenyl)naphtho[1,2-*d*]imidazol-3-ylamine *(3)*, m.p. 195 °C (yield 30%).



(2)



(3)

N-(*p*-Anisylidene)-β-naphthylamine *(4)*, R = *p*-CH_3O–C_6H_4, has been observed to couple with *p*-methoxybenzenediazonium fluoroborate in the *ortho*-position only. In this case a blue color develops within 30 min of mixing equivalent amounts of the reactants in acetonitrile ar room temperature. On addition of ether *N*-(*p*-anisylidene)-1-(*p*-methoxyphenylazo)-2-naphthylammonium fluoroborate *(5)*, R = R′ = *p*-CH_3O–C_6H_4, is precipitated as deep blue crystals. With pyridine these give white crystalline *N*,2-bis-(*p*-methoxyphenyl)naphtho[1,2-*d*]imidazol-1-ylamine *(6)*, R = R′ = *p*-CH_3O–C_6H_4.

The azo coupling of aromatic amines in nitrobenzene at 20.0 ± 0.1 °C is a reaction of the third order: $v = k$ [Diaz] [Amine]^2 (measurement of unused diazonium salt). The azo coupling of Schiff bases is autocatalytically accelerated after a slow start. Apparently, in coupling with amines, the proton is removed from the σ-complex by the amine, whereas, in coupling with the less basic Schiff bases, the product is necessary for this purpose.

The Schiff bases react only at concentrations above 10^{-2} mole/l. Schiff bases from ketones do not react.

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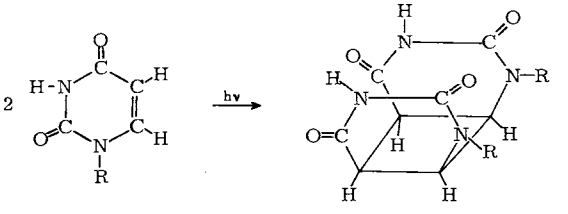
[*] Dr. A. Messmer and Dipl.-Chem. O. Szimán
Central Research Institute for Chemistry of the
Hungarian Academy of Sciences
Pusztaszeri ut 57/69
Budapest, II (Hungary)

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The Structure of the Uridine Dimer Produced by UV Irradiation of Uridine [1]

By *E. Fahr*, *G. Fürst*, *G. Dörhöfer*, and *H. Popp*[*]

UV irradiation of uracil or thymine in an ice matrix affords dimeric pyrimidines that are interesting for interpretation of biological radiation damage. We have been able to isolate the dimeric uridine[2], which is produced on UV irradiation of uridine *(1)*, and have proved its structure to be that of *(2)*.



(1) R = Ribosyl

(2), R = Ribosyl
(3), R = H

Frozen aqueous uridine solutions (*ca.* −5 °C) were irradiated with a low-pressure Hg lamp (Hanau NK 6/20)[3] and the products were separated by column chromatography on

cellulose (liquid phase: butan-1-ol/propan-1-ol/water = 1:1:1 v/v). Dimeric uridine (R_F = 0.13) appeared as third fraction, after uridine and 5,6-dihydro-6-hydroxyuridine, and was obtained analytically pure: colorless crystals, m.p. 178–179 °C (from ethanol); Mol. wt. (cryoscopically and osmometrically in water) 480 (calc. 488).

By degradation of the dimeric uridine *(2)* with concentrated hydrochloric acid [80 mg (0.16 mmole) in 10 ml conc. HCl, 4 h reflux] and thin-layer chromatographic separation we obtained uridine and uracil [fission of the cyclobutane ring of *(2)*], as well as the dimeric uracil *(3)* of known structure[4] (identified by comparison of IR data with data for a sample of *(3)* prepared by UV irradiation of uracil; and by chromatographic data: thin-layer chromatography on silica gel (n-propanol/water, 7:3 v/v) R_F = 0.47, (n-butanol/water (saturated)) R_F = 0.18).

Since *(3)* is unchanged under the conditions used (as proved by boiling a solution of *(3)* in conc. HCl for 4 h) the dimeric uridine has structure *(2)*.

Contrary to expectation, the irradiation of uridine in an ice matrix leads to a dimer[5] in which the sugar residues are oriented next to one another.

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[*] Prof. Dr. E. Fahr, cand. chem. G. Fürst, Dr. G. Dörhöfer, and cand. rer. nat. H. Popp
Institut für Organische Chemie der Universität
Röntgenring 11
87 Würzburg (Germany)

[1] Part VIII of "Effect of Radiation on Nucleic Acid Components"; Part VII: [4].

[2] Cf. *A. Wacker, D. Weinblum, L. Träger,* and *Z. H. Moustafa,* J. molecular Biol. *3,* 790 (1961).

[3] Irradiation data: 10^{-2} mol. aqueous solution, frozen in a layer of 1–2 mm, time of irradiation: 30 min, distance from the UV source: 5 cm.

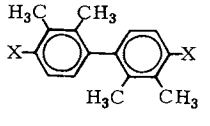
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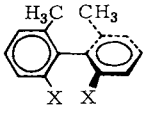
Optically Active 2,2'-Dimethylbiphenyl, the Simplest Atropisomeric Hydrocarbon

By *W. Theilacker* and *Horst Böhm*[*]

2,2',3,3'-Tetramethylbenzidine *(1a)* can be obtained relatively easily in optically active form[1], and optically active 2,2',3,3'-tetramethylbiphenyl *(1b)* can be obtained from it by deamination[2]. Both compounds have considerable optical stability although the atropisomerism is caused only by two relatively small *ortho*-substituents in the biphenyl molecule. This stability is caused on the one hand by the support



(1a), X = NH_2
(1b), X = H



(2), X = NH_2
(3), X = H

(buttressing effect) given by the methyl groups in the 3,3'-positions to the 2,2'-substituents and on the other to the fact that these compounds have a relatively large negative racemization entropy. If the buttressing substituents are removed, the optical stability decreases appreciably; earlier unsuccessful attempts to obtain optically active 2,2'-dimethylbenzidine confirmed this.

For the preparation of optically active 2,2'-dimethylbiphenyl we therefore started from optically stable (+)- or (−)-2,2'-dimethylbiphenyl-6,6'-diamine[3] *(2)*. We diazotized this in hydrochloric acid solution at −10 °C and deaminated it with hypophosphorous acid and copper(I) oxide/copper(II) sulfate at approximately −35 °C. The solution was extracted with isobutene at −50 °C, the extract poured through aluminum oxide at −50 °C, and the isobutene evaporated at −78 °C. The optically active 2,2'-dimethylbiphenyl *(3)* obtained in this way was dissolved in dimethylformamide at −55 °C, and the optical rotation of this solution was measured after various times at temperatures between −30 °C and −36 °C.

The following data were obtained for the racemization:

T (°C)	−35.46	−34.42	−33.04	−32.28	−30.94
$k_{rac} \times 10^3$ [s^{-1}]	1.035	1.182	1.426	1.569	1.876

E_A = 15.1 ± 0.4 kcal mole^{-1}; $\Delta H^{\ddagger}$ = 14.6 ± 0.4 kcal mole^{-1}; $\Delta S^{\ddagger}$ = −11.6 ± 1.8 cal mole^{-1} deg^{-1} (calc. for inversion); $\Delta G^{\ddagger}$ = 17.4 kcal mole^{-1} at −35 °C, 18.1 kcal mole^{-1} at + 25 °.

The half-reaction time for racemization at −32 °C is 7 min; that calculated for +25 °C is 1.1 sec.

Since the absolute configuration of *(2)* is known[4] and configuration is not reversed on deamination, the absolute configuration of *(3)* is also established. (+)-*(2)* ($[\alpha]_{546}^{+20}$ = + 53.8°; c = 1.13; ethanol) receives the chirality symbol *(R)*[5]; the (−)-form of *(3)* (maximum value: $[\alpha]_{546}^{-33}$ = −26°; c = 2.7, dimethylformamide) resulting therefrom receives the same chirality symbol.

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[*] Prof. Dr. W. Theilacker and Dipl.-Chem. H. Böhm
Institut für organische Chemie der Technischen Hochschule
Callinstr. 46
3 Hannover (Germany)

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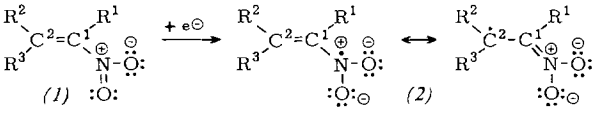
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Anion Radicals from 1-Nitroolefins

By *A. Berndt*[*]

Independently of recent papers[1,2] concerning radicals of unproved[1] or, in the light of our results, incorrectly assigned structure[2], that were formed on reduction of 1-nitroalkenes, we have studied electrolytic one-electron reduction[3] of substituted 1-nitroalkenes *(1)* in acetonitrile. We have thus obtained the first anion radicals from 1-nitroolefins that have been conclusively characterized as radicals of type *(2)* by electron spin resonance (ESR) spectra[4]. The radicals were generated at a platinum cathode in acetonitrile containing 10^{-3} mole/l of *(1)* and 10^{-1} mole/l tetra-n-propylammonium perchlorate as supporting electrolyte, within the ESR spectrometer cavity.



The lifetimes of the new radicals lie between a few minutes and some hours, according to the substituents, the nature of R^1 being of little influence. Substituents R^2 and R^3 that

contribute to delocalization of the unpaired electron, or by their space-filling reduce the chemical reactivity at C^2, are particularly effective in prolonging the life. When R^2 or R^3 = H no anion radical was observed.

Table 1 shows the properties of the new nitroalkenes *(1)*, together with the nitrogen and proton coupling constants a_N and a_H, respectively, of the radicals *(2)* that could be unambiguously assigned. Fig. 1 illustrates a particularly simple ESR spectrum.

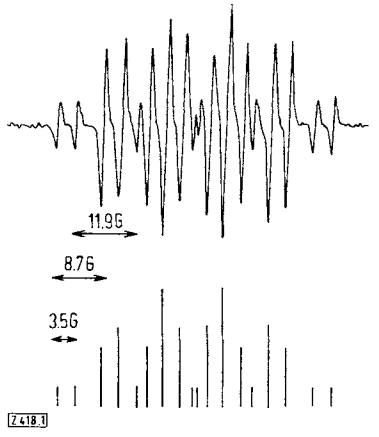


Fig. 1. ESR spectrum of the anion radical from 2-methyl-1-nitro-2-t-butylethylene *(2f)*, and the line spectral diagram.

Table 1. Properties of nitroalkenes *(1)* and radicals *(2)*.

	R^1	R^2	R^3	*(1)* M.p. (°C) or b.p. (°C/mm)	*(2)* a_N	*(2)* $a_H(R^1)$	*(2)* $a_H(R^3 = CH_3)$
(a)	C_6H_5	C_6H_5	C_6H_5		6.0	—	—
(b)	H	C_6H_5	C_6H_5				
	H	C_6D_5	C_6D_5	85	6.3	3.2	— [a]
(c)	CH_3	C_6H_5	C_6H_5	56	7.0	3.5	
(d)	H	C_6H_5	CH_3				
	H	C_6D_5	CH_3	(72/0.05)	7.9	2.8	9.3
(e)	H	C_6H_5	$C(CH_3)_3$	(93/0.14)	10.4	3.0	—
(f)	H	$C(CH_3)_3$	CH_3	(99/20)	11.9	3.5	8.7
(g)	H	CH_3	CH_3		11.6	3.2	9.0
(h)	NO_2	C_6H_5	C_6H_5				
	NO_2	C_6D_5	C_6D_5	149	2.8	—	—

[a] Coupling constants (in gauss) of the phenyl protons: a_o and a_p = 1.2; a_m = 0.6.

[b] Stable radicals are also obtained from 9-nitromethylenefluorene (R^1 = H, $R^2 + R^3$ = biphenylylene) and 9-(α-nitrobenzylidene)fluorene ($R^1 = C_6H_5$, $R^2 + R^3$ = biphenylylene), m.p. 123 °C. Their ESR spectra are under study.

The spin density distribution was calculated [7] by *McLachlan*'s method [5] with the parameters for aromatic nitro anion radicals [6]. The nitrogen coupling constants a_N were calculated from the resulting spin densities on nitrogen ρ_N and oxygen ρ_O from equation (a) [6].

$$a_N = (99.0 \pm 10.2)\,\rho_N - (71.6 \pm 11.8)\,\rho_O \qquad \text{(a)}$$

The calculated and the experimental coupling constants are compared in Table 2.

Table 2. Experimental and calculated nitrogen coupling constants a_N (in gauss).

	(2b)	*(2c)*	*(2d)*	*(2e)*	*(2f)*	*(2g)*	*(2h)*
exp.	6.3	7.0	7.9	10.4	11.9	11.6	2.8
calc.	5.4	6.5	9	12	11.8	11.8	2.1

Nitrogen coupling constants of 24.0 and 23.3 gauss have been given for the reduction products of 2-nitropropene [2] and ω-nitrostyrene [2], respectively. According to our calculations 11 gauss and 6–7 gauss, respectively, are to be expected for these anion radicals. a_N values of *ca.* 24 gauss are characteristic of anion radicals from aliphatic nitro compounds [8]. The existence of radicals of this structure is also indicated by the number of proton coupling constants that has been given [2] for the radicals from 2-nitropropene and ω-nitrostyrene.

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[*] Dr. A. Berndt
Institut für Organische Chemie der Universität
Bahnhofstr. 7
335 Marburg (Germany)

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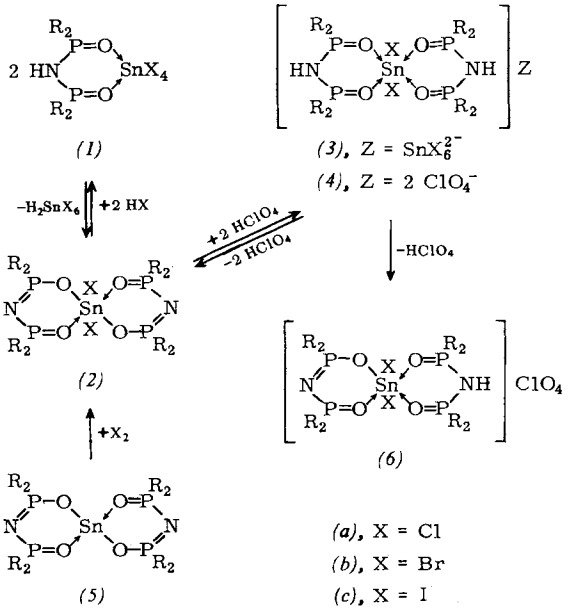
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Imidophosphinatotin Halides [1]

By *A. Schmidpeter* and *K. Stoll* [*]

Diphosphinic imides $(R_2PO)_2NH$ (imidodiphosphinic acids) behave as univalent bidentate ligands toward transition metals [2, 3] and toward main group elements [4] of coordination number 6; in the latter case a larger variety of types of compounds are formed.



$SnCl_4$ or $SnBr_4$ and $((C_6H_5)_2PO)_2NH$ give first adducts *(1)*, which yield bis(imidodiphosphinatotin dihalides *(2)* under the action of a weak base, *e.g.* when boiled with water. This reaction appears to indicate structure *(3)* for the adduct which however is not in accord with the Mössbauer spectrum (only one resonance line with an isomeric shift that is distinctly different from that of SnX_6^{2-}; on the other hand the shifts come close to those of 2,2'-dipyridyltin(IV) halide adducts [5]).

	M.p. (°C)	Sn isomeric shifts (mm/sec) [a]	ν (Sn–X) (cm^{-1})
(1a)	286–292	0.40	342, 330, 304, 170
(1b)	278–280	0.63	244, 226, 209

[a] Relative to SnO_2. – Shifts for $SnCl_6^{2-}$ 0.50 mm/sec, for $SnBr_6^{2-}$ 0.87 mm/sec [5].

In agreement with structure *(1)* the IR spectra contain three to four absorption bands assignable, very probably, to SnX vibrations; the presence of the HN group is shown by a band at 3130 cm^{-1}. The molecular size could not be determined since *(1a)* and *(1b)* are insoluble in non-solvolysing media, *(2a)* and *(2b)* are formed, not only by the solvolytic disproportionation of *(1a)* and *(1b)*, but also by melting *(1a)* or *(1b)* with further $((C_6H_5)_2PO)_2NH$, from SnX_4 and $((C_6H_5)_2PO)_2NNa$, and by addition of Cl_2 or Br_2 to tin(II) bis(tetraphenylimidodiphosphinate) *(5)*.

(5) is formed on melting together tin(II) acetate and $((C_6H_5)_2PO)NH$ in a vacuum. It is soluble and monomolecular in polar organic solvents and aromatic compounds, and according to its ^{31}P–NMR spectrum it contains only equivalent phosphorus atoms, so that it is also a chelate.

(2c) is obtained directly from SnI_4 and $((C_6H_5)_2PO)_2NH$. The complexes *(2)* apparently exist in the *cis*-form; their dipole moments in dioxane amount to 7 to 8 Debyes. *(2c)* in CH_2Cl_2 gives two ^{31}P-resonance signals of comparable intensity.

	(2a)	*(2b)*	*(2c)*	*(5)*
M.p. (°C)	325–327	283–285	yellow, 258–260 (dec.)	215–217
δ (^{31}P) (ppm) [b]	−28.8	−28.4	−28.0; −26.3	−17.9
	(4a)	*(4b)*	*(4c)*	
δ (^{31}P) (ppm) [b]	−45.8	−44.5	−43.3	

[b] Measured in CH_2Cl_2; relative to 85% H_3PO_4; negative values refer to lower field strengths.

Compounds *(2)* are cleaved back to *(1)* and $((C_6H_5)_2PO)_2NH$ by hydrogen halides; anhydrous perchloric acid, however, is added, yielding *(4)*. Structure *(4)* is proved by equivalence of the phosphorus atoms in the ^{31}P–NMR spectrum, the appearance of NH bands at 2925 and 2640 cm^{-1}, and solvolytic removal of $HClO_4$ by acetonitrile or methanol, to give *(6)* or *(2)*, respectively.

The IR spectra of *(4)* do not correspond with those of the adducts from SnX_4 and $((C_6H_5)_2PO)_2NH$. This confirms chemically that the correct formula for the adduct is *(1)*, and not *(3)*.

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[*] Dr. A. Schmidpeter and Dipl.-Chem. K. Stoll
Institut für Anorganische Chemie der Universität
Meiserstr. 1
8 München 2 (Germany)

[1] Part 6 of Phosphazenes. – Part 5: *A. Schmidpeter* and *J. Ebeling*, Angew. Chem. *79*, 100 (1967); Angew. Chem. internat. Edit. *6*, 87 (1967). – The ^{31}P–NMR spectra were determined by Dipl.-Chem. *H. Brecht*. We are grateful to Prof. *N. N. Greenwood*, Dr. *B. P. Straughan* and Mr. *J. N. R. Ruddick*, Newcastle, for determination of the Mössbauer and IR spectra in the long-wave region and for discussions.

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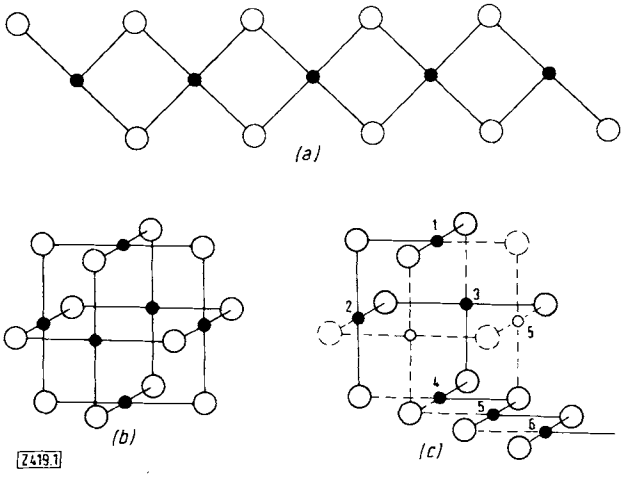
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The Molecules Pd_6Cl_{12} and Pt_6Cl_{12} in the Gaseous State. A Contribution to the Problem of M_6X_{12} Groups

By *H. Schäfer, U. Wiese, K. Rinke*, and *K. Brendel*[*]

Palladium(II) chloride crystallizes in an α-form which, according to *Wells*[1], contains endless chains of coplanar $PdCl_{4/2}$ units ($_\infty[PdCl_{4/2}]$; Fig. 1a). We have found a β-form which, according to Guinier photographs, is isotypic with the modification of platinum(II) chloride described by *Broderson, Thiele*, and *von Schnering*[2]. Thus the Pd_6Cl_{12} molecules assume a space-centered arrangement $I\bar{4}3m$ ($[Pd_6Cl_{12}]$; Fig. 1b). When tempered at 500 °C, this β-form passes into the α-form. The β-modification $[Pd_6Cl_{12}]$ is formed when either form is sublimed in a vacuum.



In the mass spectrometer both modifications yield Pd_6Cl_{12} molecules (mean mol. wt. 1064) with high intensity; $(PdCl_2)_n$ molecules with $n \neq 6$ do not occur. It is therefore improbable that the Pd_6Cl_{12} molecules observed have a chain or ring structure. Pd_6Cl_{12} molecules (as in Fig. 1b) apparently occur in the gas phase, as in the β-modification[3].

Particular interest attaches to the ready transition: chain ⇄ polyhedron. We attribute this to the fact that a Pd_6Cl_{12} polyhedron can be developed from a $[PdCl_{4/2}]$ chain (Fig. 1c). Starting from the end of the chain, one has only to break one of the four bonds attached to each Pd atom, whereby the connection through the chain remains but free rotation becomes possible around each bond. In terms of molecular kinetics this doubtless occurs by opening of alternate bonds and reclosure thereof in their new positions. All the bond angles (Pd–Cl–Pd and Cl–Pd–Cl) remain unchanged. It should be emphasized that this is the first reasonable demonstration of the way in which such M_6X_{12} groups can be formed.

Evaluation of data in the literature[3,4] gives the following bond energies for the Pd–Cl bond: $_\infty[PdCl_{4/2}]$ chain (α-$PdCl_2$) 48 kcal; gaseous Pd_6Cl_{12} 46 kcal; gaseous monomeric $PdCl_2$ 62 kcal. The bond energy for the chain is almost identical with that for the polyhedron. It is significant that the first of the four Pd–C bonds of a $PdCl_{4/2}$ unit is more easily broken than the others and it is for this reason that the chain is not disrupted in forming the polyhedron.

On vaporization of the platinum(II) chloride from a preparation that contains a high proportion of the $[Pt_6Cl_{12}]$ modification, the heaviest particles seen in the mass spectrometer are Pt_6Cl_{12} molecules (mean mol. wt. 1596)[5]. However, ions such as $Pt_4Cl_8^{\oplus}$ and $Pt_5Cl_{10}^{\ominus}$ (of somewhat lower intensity than $Pt_6Cl_{12}^{\oplus}$) are found. This behavior is different from that of Pd_6Cl_{12}.

If the dsp^2-orbitals of the metal atom are used for binding $Cl^{\ominus}$ ions in planar arrangement, the remaining d-orbitals of the palladium or platinum are fully occupied and are not available for metal-metal bonding. The existence of Pd_6Cl_{12}

and Pt_6Cl_{12} in the gas phase expressly confirms the fact that $[M_6Cl_{12}]$ polyhedra are held together by Cl bridges. The importance and the choice of the "inner" atoms X^i [6] that are multiply bound to the M_6 octahedra in such polyhedra (also where M = Nb, Ta, Mo, or W) thus appear in a new light.

Metal atoms in compounds of the type $[Nb_6Cl_{12}]Cl_{4/2}$ or $[Mo_6Cl_8]Cl_2Cl_{4/2}$ have also the same arrangement of chlorine atoms corresponding to the dsp^2-hybridization [7]. However, the atomic distances found show that in these cases there are also metal-metal bonds:

In the $[Nb_6Cl_{12}]^{2\oplus}$ group the available six 4d-orbitals of the niobium atoms combine to give 8 fully occupied three-centre bonds [8] that lie on the faces of the octahedron.

In the $[Mo_6Cl_8]^{4\oplus}$ group the 6×4 d-orbitals of the Mo atoms combine to give 12 fully occupied single bonds that lie along the edges of the M_6 octahedron.

Finally the p_z orbitals of the metal atoms can be occupied. This enables further "outer" [6] atoms X^a to be bound. So groups can be joined by atoms X^a, *e.g.* in $[Nb_6Cl_{12}^i]$-$Cl_{4/2}^a$ [9] and $[Mo_6Cl_8^i]Cl_2^aCl_{4/2}^a$ [6], or there may be complete saturation without further connection, *e.g.* in $K_4[Nb_6Cl_{12}^i]Cl_6^a$ [10] or $\{[Mo_6Cl_8^i]Cl_6^a\}^{2\ominus}$ [11].

Pd_6Cl_{12} and Pt_6Cl_{12} should also have the capacity to bind electron-donors; this should be tested.

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[*] Prof. Dr. H. Schäfer, Dipl.-Chem. U. Wiese,
Dipl.-Chem. K. Rinke, and K. Brendel
Anorganisch-Chemisches Institut der Universität
Hindenburgplatz 55
44 Münster (Germany)

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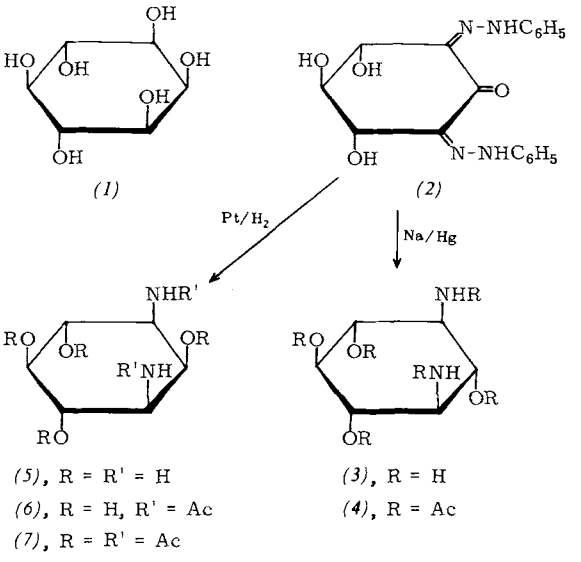
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A Simple Synthesis of Streptamine and Actinamine

By *F. W. Lichtenthaler, H. Leinert*, and *T. Suami* [*]

Three syntheses are known [1] for streptamine, a building unit of streptomycin and related antibiotics, and one for actinamine [2], a unit in the antiobiotic actinospectacin. We have devised a simple synthesis of these two units, starting from *myo*-inositol and requiring, respectively, four and six steps.

trans-3,4,5-Trihydroxy-2,6-phenylhydrazonocyclohexanone *(2)*, which can be prepared from *myo*-inositol *(1)* in 10 % yield in three steps [3], is converted on reduction by sodium amalgam in glacial acetic acid into a single isomer that was identified as streptamine *(3)* by paper and thin-layer chromatography.



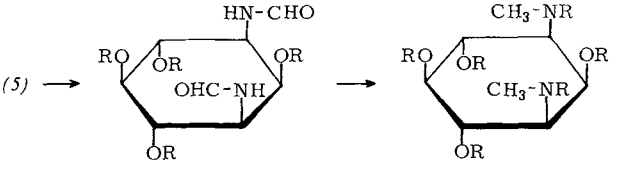
(5), R = R' = H
(6), R = H, R' = Ac
(7), R = R' = Ac

(3), R = H
(4), R = Ac

It affords a hexaacetate which was isolated in 30 % yield [calculated on *(2)*] and was identical with authentic streptamine hexaacetate in melting behavior (partial melting at 245–250 °C, then resoldification [4]) and IR and NMR data.

Catalytic hydrogenation of the product *(2)* over platinum in 20 % methanolic acetic acid led, however, to *myo*-inosa-1,3-diamine *(5)* [m.p. 230 °C (decomp.)], which was further characterized as the di-*N*-acetate *(6)* (decomp. 310 °C) and the hexaacetate *(7)* (m.p. 270–271 °C; [2] 269 °C).

Di-*N*-formylation with acetic formic anhydride [5] to give *(8)* (m.p. 265 °C) and subsequent reduction of the tetraacetate *(9)* (m.p. 223–224 °C) by $LiAlH_4$ in tetrahydrofuran proved to be the simplest way of converting the diamine *(5)* into its *N,N'*-dimethyl derivative, actinamine *(10)*. Hexaacetylactinamine *(11)*, identical in melting point and IR and NMR spectra with the product prepared from actinospectacin [6], could thus be isolated in 23 % yield [calc. on *(5)*], whereas other methods used for the di-*N*-methylation [2] gave yields of about 8 %.



(8), R = H
(9), R = Ac

(10), R = H
(11), R = Ac

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[*] Doz. Dr. F. W. Lichtenthaler and Dipl.-Ing. H. Leinert
Institut für Organische Chemie der Technischen Hochschule
61 Darmstadt (Germany)
Prof. Dr. T. Suami
Institute for Applied Chemistry
Keio University
Tokyo (Japan)

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[6] We thank Dr. *P. F. Wiley* (Upjohn Co., Kalamazoo, Michigan) for supplying a sample of the authentic material.

Pyridines as Stabilisers of Free Boron Radicals

By *R. Köster, H. Bellut,* and *E. Ziegler* [*]

Whereas free BN radicals with unresolved ESR signals are formed on dehalogenation of pyridine- and 2-alkylpyridine-dialkylchloroboranes by lithium in tetrahydrofuran [1] at 0 to 5 °C, associated radicals *(1)*, whose ESR spectra show a hyperfine structure of ten lines (distances: 3.83 gauss), are obtained from the adducts of dialkylchloroboranes and 4-alkylpyridines. The resolution can be ascribed to the coupling of the free electron to three boron atoms [2]. In the spectrum of *(1)* in 10^{-2} M solution, an additional hyperfine structure (see Fig. 1) also appears, the resolution of which varies with the linewidth associated with the substituent R in the aromatic ring, in the order
$CH_2C_6H_5 \approx CH_3 \approx C_2H_5 > C_3H_7 > CH(CH_3)_2 > C(CH_3)_3$.
Simultaneously the association (measured cryoscopically in benzene) decreases from $x \approx 3$ to $x \approx 1.5$.

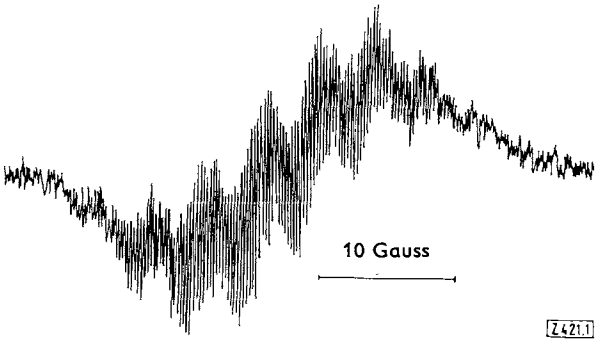
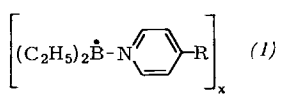
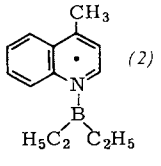


Fig. 1. ESR spectrum of the 4-methylpyridine-diethylboryl radical; *ca.* 0.001 M in diethyl ether.

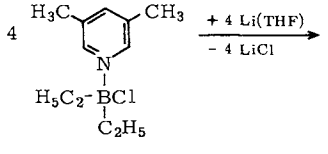
The 4-methylquinoline-diethylboryl radical *(2)* is monomeric in benzene. In agreement with this fact the hyperfine structure of the ESR spectrum shows a clear (1:1) splitting (14 gauss), which can be ascribed to the coupling of the free electron with one proton. *(1)* and *(2)* are highly colored, very viscous liquids, which are decolored by air.

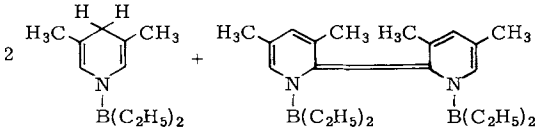

(1)


(2)

R = $CH_2C_6H_5$, CH_3, C_2H_5, C_3H_7, $CH(CH_3)_2$, $C(CH_3)_3$
x = 1,5-3

Dehalogenation of 3-alkylpyridine-dialkylchloroboranes,even at 0 °C, gives either no (3,5-lutidine, 3,4,5-trimethylpyridine) or only a very unstable free radical (3-methylpyridine). From 3,5-lutidine-chlorodiethylborane one obtains a dark red, diamagnetic liquid (b.p. 48 °C/10^{-3} mm) which is composed mostly of *N*-diethylboryl-1,4-dihydro-3,5-dimethylpyridine *(3)* and yellow crystalline *N,N'*-bis(diethylboryl-1,1'-2,2'-tetrahydro-3,3',5,5'-tetramethyl-$\Delta^{2,2'}$-bipyridine *(4)*, m.p. 93 °C; 85 % yield). Structures *(3)* and *(4)* were proved by ^{1}H–NMR.




(3) *(4)*

If pyridine-chlorodiethylborane is dehalogenated in boiling tetrahydrofuran no free radical is formed, but instead a disproportionation product (b.p. 88–89 °C/14 mm) analogous to *(3)*; the dehydrogenated portion corresponding to *(4)* is a dark solid.

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[*] Dr. R. Köster, Dipl.-Chem. H. Bellut, and Dr. E. Ziegler
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1
4330 Mülheim-Ruhr (Germany)

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[2] Coupling of the spin of the unpaired electron with three symmetrical equivalent ^{11}B-nuclei ($I = 3/2$) leads to $2(3 \times 3/2) + 1 = 10$ hyperfine structure lines.

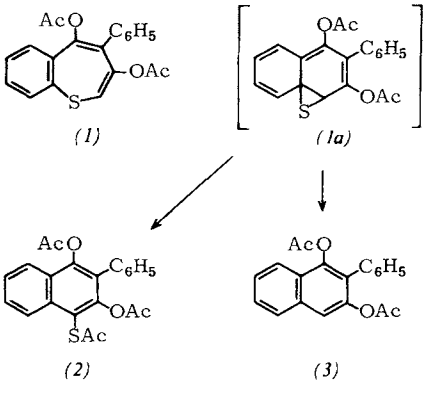
Rearrangements of Derivatives of Benzo[*b*]thiepin and Benzo[*b*]thiepin 1,1-Dioxide [**]

By *H. Hofmann* and *H. Westernacher* [*]

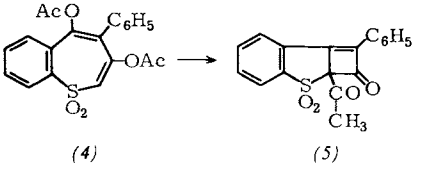
Thiepins contain a cyclic 8π-electron system, so that, as with oxepins, rearrangements to more stable ring systems are to be expected. Indeed, when 3,5-diacetoxy-4-phenylbenzo[*b*]-thiepin *(1)* [1] is heated under reflux with sodium acetate in acetic anhydride for 6 hours, 1,3-diacetoxy-4-acetylthio-2-phenylnaphthalene *(2)*, m.p. 175–176 °C (from methanol), is formed in 53 % yield.

The rearrangement is thus analogous to that observed with benzo[*b*]oxepin derivatives [2]. The structure *(2)* is proved by elemental analysis, the IR spectrum [in KBr; $\nu_{C=O}$ = 1764 cm^{-1} (aromatic acetate), $\nu_{C=O}$ = 1710 cm^{-1} (aromatic thioacetate)], the NMR spectrum [in $CDCl_3$; τ = 8.15 and 8.03 (each 3 H of the two acetate groups), τ = 7.65 (3 H of the thioacetate groups], and by oxidation in an aqueous alkaline (KOH) solution to 2-hydroxy-3-phenyl-1,4-naphthoquinone [3]. However, treatment of the thiepin *(1)* with acetic anhydride in pyridine (15 min at 60 to 70 °C) gives a 66 % yield of a sulfur-free product that was identified by its IR spectrum and mixed m.p. as 1,3-diacetoxy-2-phenylnaphthalene [4].

We assume that in both rearrangements an episulfide *(1a)*, a valence tautomer of *(1)* which has not yet been isolated, is first formed.


(1) *(1a)* *(2)* *(3)*

The same products *(2)* and *(3)* are obtained if 2,3,4,5-tetrahydro-4-phenylbenzo[*b*]thiepin-3,5-dione [1] or 5-acetoxy-2,3-dihydro-4-phenylbenzo[*b*]thiepin-3-one [1] is used in place of *(1)*.


(4) *(5)*

Attempted rearrangement of 3,5-diacetoxy-4-phenylbenz[*b*]-thiepin 1,1-dioxide *(4)* [1] by heating it for 4 hours with sodium acetate in acetic anhydride under reflux gave a completely different result. In this reaction, 2a-acetyl-2,2a-dihydro-4-phenylcyclobutadieno[1,2-*b*]thionaphthen-2-one 3,3-dioxide *(5)*, m.p. 213–215 °C (from methanol; 65 % yield) was formed instead of *(3)*. We suspect that in this case the episulfone corresponding to *(1a)* is not formed but that 1 mol. equivalent of acetic acid is first eliminated followed by ring contraction and subsequent *O*-acyl → *C*-acyl migration to yield compound *(5)*.

Structure *(5)* was proved by elemental analysis, determination of the molecular weight, the IR spectrum (in KBr; $\nu_{C=O}$ = 1733 cm^{-1} for both carbonyl groups; $\nu_{C=C}$ = 1652 cm^{-1}; $\nu_{S=O}$ 1313 and 1160 cm^{-1}), the NMR spectrum (in $CDCl_3$; in addition to the signals of the 9 aromatic H atoms, only one signal for 3 H atoms at τ = 7.3), and by degradation to the known 2,3-dihydrothionaphthen-3-one 1,1-dioxide [5].

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[*] Priv.-Doz. Dr. Hans Hofmann and
Dipl.-Chem. H. Westernacher
Institut für Organische Chemie
der Universität Erlangen-Nürnberg
Henkestr. 42
852 Erlangen (Germany)

[**] We thank the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for financial support.

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Cesium and Rubidium Pentafluoroethoxide

By *F. Seel*, *R. Budenz*, and *W. Gombler* [*]

Trifluoroacetyl fluoride *(1)* reacts with cesium or rubidium fluoride, preferably in acetonitrile, to give the compounds $CsF{\cdot}C_2F_4O$ *(2a)* and $RbF{\cdot}C_2F_4O$ *(2b)*, respectively. Their compositions were determined from the ^{19}F–NMR spectra of the solutions and by wet analysis of the substances that crystallized from the solutions. When the temperature is raised, compounds *(2a)* and *(2b)* decompose reversibly into their components [vapor pressure of *(2a)* = 110 mm at 60 °C, of *(2b)* 48 mm at 25 °C].

On addition of even small amounts of CsF or RbF, or of potassium fluoride, to solution of *(1)* in acetonitrile the multiplet structure of the ^{19}F–NMR signals of *(1)* [$\delta(CF_3)$ = 78.6 ppm and $\delta(CF)$ = −11.3 ppm ($CFCl_3$ as an external standard), J = 6.1 Hz] disappears. This indicates fluoride ion exchange of the type:

$$CF_3COF \rightleftarrows CF_3CO^+ + F^- \quad (A)$$

$$\text{or } CF_3COF + F^- \rightleftarrows CF_3CF_2O^- \quad (B)$$

The fact that alkali-metal fluorides are anion-donors and not anion-acceptors suggests that reaction (B) is favored. The assumption that *(2a)* and *(2b)* are pentafluoroethoxides is supported by the chemical shifts of the CF_3 signal of *(1)* [δ = 85.3 ppm at 0 °C for *(2a)*] to the region of CF_3 groups bound to CF_2 (80 to 93 ppm) and the shift of the CF signal [δ = 36.4 ppm for *(2a)*] towards the signal of the CF_2 group of ethers containing the group $-CF_2OCF_2-$ (70 to 90 ppm) [1]. The ^{19}F–NMR spectrum of a suspension of KF in a solution of *(1)* in acetonitrile shows that *(1)* reacts only partly with KF to give pentafluoroethoxide. $CsF{\cdot}C_2F_4O$ *(2a)* can be included in the series of compounds $CsF{\cdot}SO_2$ [2], $CsF{\cdot}OSF_4$ [3], and in particular in the series $CsF{\cdot}OCF_2$ [4] and $CsF{\cdot}OC(CF_3)_2$ [5].

Pentafluoroethoxides are very sensitive to moisture. It was shown by IR spectroscopy that *(2a)* and water vapor react to give cesium trifluoroacetate:

$$CF_3CF_2OCs + H_2O \longrightarrow CF_3CO_2Cs + 2\ HF$$

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[*] Prof. Dr. F. Seel, R. Budenz, and W. Gombler
Institut für Anorganische Chemie der Universität
66 Saarbrücken 15 (Germany)

[1] Cf. *H. Suhr*: Anwendungen der kernmagnetischen Resonanz in der organischen Chemie. Springer, Heidelberg 1965, p. 287.

[2] *F. Seel* and *L. Riehl*, Z. anorg. allg. Chem. *282*, 293 (1955); *F. Seel* and *J. Boudier*, *ibid. 342*, 173 (1966)

[3] *W. C. Smith* and *V. A. Engelhardt*, J. Amer. chem. Soc. *82*, 3838 (1960).

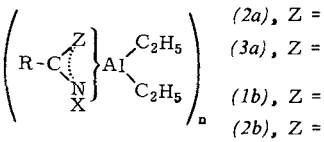
[4] *M. E. Redwood* and *C. J. Willis*, Canad. J. Chem. *43*, 1893 (1965).

[5] *Ch.T. Ratcliffe* and *J.M. Shreeve*, Chem. Commun. *1966*, 674.

2,3-Diazabuta-1,3-diene-1,4-diamines (1,4-Disubstituted) and N^1-Acylamidrazones from Nitriles and Bis(diethylalumino)-Substituted Amidrazones and Acid Hydrazides

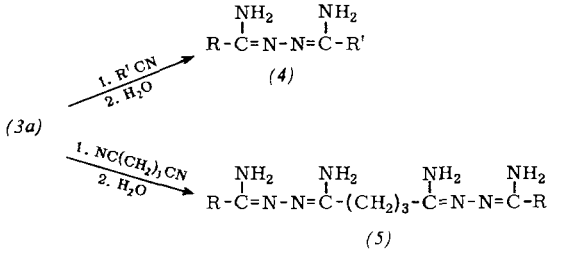
By *Th. Kauffmann*, *L. Bán*, and *D. Kuhlmann* [*]

When 1 molar equivalent of triethylaluminium reacts with amidrazones in benzene under nitrogen at 20 °C, one equivalent of ethane is evolved and mono(diethylalumino)amidrazones *(2a)* are formed [1], which, like the diethylalumino-derivatives *(1a)* [2] of amidines, do not add to nitriles.



(1a), Z = NH, X = H [3]
(2a), Z = NH, X = NH_2 [3]
(3a), Z = NH, X = $NHAl(C_2H_5)_2$ [3]
(1b), Z = O, X = H [3]
(2b), Z = O, X = NH_2 [3]
(3b), Z = O, X = $NHAl(C_2H_5)_2$ [3]

If, however, two molar equivalents of triethylaluminum are used, then two equivalents of ethane are evolved and bis-(diethylalumino)amidrazones *(3a)* [1] are formed, which are readily soluble in benzene and add readily to nitriles and dinitriles in benzene at 70–80 °C (reaction time 20 h), giving the asymmetrically 1,4-disubstituted diazabuta-1,3-diene-1,4-diamines *(4)* [and *(5)*] listed in Table 1. Their structures follow from the fact that, analogously to the symmetrically disubstituted diazabuta-1,3-diene-1,4-diamines [4], they are converted, when heated to *ca.* 250 °C, into 3,5-disubstituted triazoles in 90–95 % yield, with evolution of NH_3.



(4)

(5)

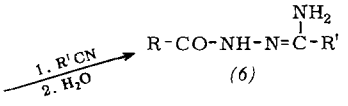
Table 1.

(3a), bis(diethylalumino)-substituted:	R'—CN	*(4)*, *(5)*	Yield (%)	M.p. (°C)
		(4):		
Benzamidrazone	Benzonitrile	R = R' = C_6H_5	95	203
Benzamidrazone	2-Cyanopyridine	R = C_6H_5; R' = 3-pyridyl	88 [a]	186
Benzamidrazone	4-Cyanopyridine	R = C_6H_5; R' = 4-pyridyl	91 [a]	207
Hexanoic acid amidrazone	Benzonitrile	R = n-pentyl; R' = C_6H_5	87 [a]	95
Hexanoic acid amidrazone	Propionitrile	R = n-pentyl; R' = C_3H_7	81 [a]	29
Dodecanoic acid amidrazone	Propionitrile	R = n-undecyl; R' = C_3H_7	80 [a]	82
		(5):		
Benzamidrazone	Glutarodinitrile	R = C_6H_5	53 [a]	205—206

[a] This represents the first preparation of these compounds.

Attempts to add sodio-substituted amidrazones to nitriles were unsuccessful. That bis-2-chloro(diethylalumino)benzamidrazones do not add to nitriles indicates a stabilizing coordinate bond between the chlorine atom and an aluminum atom.

Compounds *(1b)* [2], *(2b)* [1], and *(3b)* [1] are obtained from acid hydrazides in benzene at 20—30 °C analogously to the formation of compounds *(1a)*, *(1b)*, and *(1c)*. Treatment of bis(diethylalumino)-carboxylic acid hydrazides *(3b)* with nitriles for 6—8 h leads to the N^1-acylamidrazones *(6)* and *(7)* listed in Table 2; those products which were not new were identified by comparison with authentic specimins.



(3b)

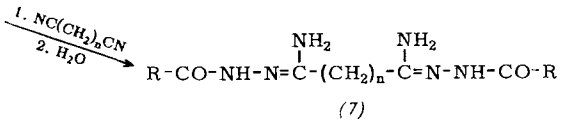


Table 2.

(3b), bis(diethylalumino)-substituted:	R'—CN	*(6)*, *(7)*	Yield (%)	M.p. (°C)
		(6):		
Acethydrazide	Acetonitrile	R = R' = CH_3	75	172
Acethydrazide	Benzonitrile	R = CH_3; R' = C_6H_5	73	163
Acethydrazide	4-Cyanopyridine	R = CH_3; R' = 4-pyridyl	70.5	200
Benzhydrazide	Benzonitrile	R = R' = C_6H_5	71	180
		(7):		
Acethydrazide	Succinodinitrile	R = CH_3; n = 2	64 [a]	198—200
Benzhydrazide	Malodinitrile	R = C_6H_5; n = 1	56 [a]	167
Benzhydrazide	Adipodinitrile	R = C_6H_5; n = 4	64	185

[a] As for Table 1.

Bis(diisobutylalumino)-carboxylic acid hydrazides also add to nitriles, but more slowly [5]. Attempts to add sodio-substituted acid hydrazides to nitriles were unsuccessful.

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[*] Prof. Dr. Th. Kauffmann and cand. chem. D. Kuhlmann
Organisch-Chemisches Institut der Universität
Hindenburgplatz 55
44 Münster (Germany)
Dipl.-Ing. László Bán
Institut für Organische Chemie der Technischen Hochschule
Schlossgartenstr. 2
61 Darmstadt (Germany)

[1] Not yet obtained pure.

[2] *J. Albrecht*, Planned Diploma Thesis, Universität Münster.

[3] According to molecular-weight determinations (cryoscopic in benzene) these compounds are not monomeric: when R = C_6H_5, for *(1a)* and *(1b)* $n = 2$ [2], for *(3a)* $n = 4$, and for *(3b)* $n = 3$—4.

[4] *A. Pinner*, Liebigs Ann. Chem. *297*, 228 (1897).

[5] From studies to date on the reactivity of diylkylaluminated primary amines [2], hydrazines [6], hydrazones [6], amidines, amidrazones, and acid amides and hydrazides it can be seen that dialkylaluminated nitrogen compounds often react differently from the corresponding alkali-metalated or trimethylsilylated [7] compounds; this can be ascribed to differences in solubility and to the electron deficiency of the triply bonded Al atom.

[6] *L. Bán*, Planned Dissertation, Technische Hochschule Darmstadt; Nachr. Chem. Techn. *12*, 249 (1964); *Th. Kauffmann*, unpublished.

[7] *L. Birkofer* and *A. Ritter*, Angew. Chem. *77*, 414 (1965); Angew. Chem. internat. Edit. *4*, 417 (1965).

Preparation of Diammonium Tetraselenomolybdate

By *A. Müller*, *B. Krebs*, and *E. Diemann* [*]

If hydrogen selenide is passed into an ice-cold saturated solution of molybdenum trioxide in concentrated aqueous ammonia, initial yellow and red coloration of the solution is followed by precipitation of black, crystalline $(NH_4)_2MoSe_4$ *(1)*. Substance *(1)* was characterized by elemental analysis and by IR and electron absorption spectra. Solutions of *(1)*, and also the solid substance, decompose very rapidly in the presence of oxygen. Defined selenomolybdates have not been described previously [1].

The IR spectrum (NaCl and KBr region) shows only the vibrations of the NH_4^+ ion for the species F_2 ($\nu_4 \sim 3200$ cm^{-1}; $\nu_4 = 1395$ cm^{-1}). Absence of absorption in the region of the transition-metal-oxygen vibrations (for M—O π bonds $\approx$ 1100 to 800 cm^{-1}) excludes the occurrence of mixed oxoselenomolybdate anions. The fundamental vibrations of $MoSe_4^{2-}$ (IR active vibrations ν_3 (F_2) and ν_3 (F_2) with T_d symmetry) lie below the KBr region.

The electron absorption spectrum of the violet aqueous solution of *(1)* gives strong maxima at 17990 and 26040 cm^{-1} in the region between 10000 and 33000 cm^{-1}. Table 1 lists the absorption maxima of MoO_4^{2-} and MoS_4^{2-} for comparison. The band at 17990 cm^{-1} can be unambiguously assigned to

Table 1. Electron absorption maxima [ν_{max} (cm^{-1})] of MoO_4^{2-}, MoS_4^{2-}, and $MoSe_4^{2-}$ (cf. [2], [3]).

	$t_1 \rightarrow 2e$ ($^1A_1 \rightarrow {}^1T_2$)	$2t_2 \rightarrow 2e$ or $t_1 \rightarrow 3t_2$ ($^1A_1 \rightarrow T_2$)
MoO_4^{2-}	43200	48000
MoS_4^{2-}	21400	31500
$MoSe_4^{2-}$	17990	26040

the transition from the highest occupied molecular orbital of symmetry t_2 to the first unoccupied MO of symmetry 2e [ground state $(1a_1)^2(1t_2)^6(1e)^4(2t_2)^6(t_1)^6$; excited state ... $(2t_2)^6(t_1)^5(2e)^1$; for the MO scheme cf.[2], [3]]. Since the MO t_1 is centered on the ligands and 2e represents mainly a MO that is localized on the central atom, the course of the charge-transfer band $t_1 \rightarrow 2e$ of chalcogenomolybdates can be interpreted as in Table 1 (the ionization energy decreases from oxygen to selenium).

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[*] Dr. A. Müller, Dr. B. Krebs, and stud. chem. E. Diemann
Anorganisch-Chemisches Institut der Universität
Hospitalstr. 8–9
34 Göttingen (Germany)

[1] The compound described by *Wendhorst* (Z. anorg. allg. Chem. *173*, 268 (1928)) as red K_2MoSe_4 was, according to the conditions of preparation, probably KOH which was colored by mixed oxoselenomolybdates. Pure $(NH_4)_2MoSe_4$ could not be prepared or characterized.

[2] *A. Müller, W. Rittner,* and *G. Nagarajan,* Z. physik. Chem. N.F., in press.

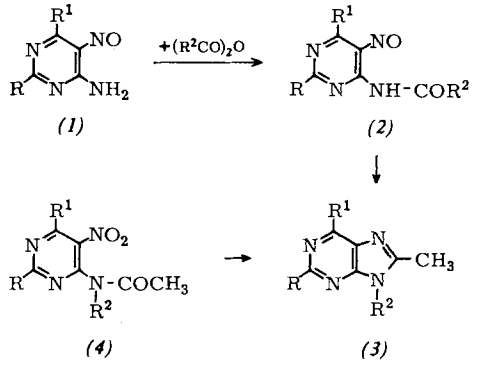
[3] *A. Müller, B.Krebs, W. Rittner,* and *M. Stockburger,* Ber. Bunsenges. physik. Chem., in press.

A New, Mild Purine Ring Closure [1]

By *F. E. Kempter, H. Rokos,* and *W. Pfleiderer* [*]

Most purines have been prepared by a modified Traube synthesis[2] involving cyclization of 4,5-diaminopyrimidines. Since it is always the 5-amino group that reacts in the first step, ring closure usually requires drastic conditions for the slightly nucleophilic 4-amino group.

We have now found that this imidazole ring closure can be achieved under much milder conditions from 4-acylamino-5-aminopyrimidines; starting materials are 4-amino-5-nitroso- and 4-amino-5-nitro-pyrimidines. If the acylation is carried out with anhydrides below 120 °C with short reaction times, 4-acylamino-5-nitrosoderivatives *(2)* can be obtained in good yields, and no rearrangement[3] to cyano-*s*-triazines occurs.



(1) *(2)* *(4)* *(3)*

	R	R¹	Anhydride	*T* (°C)	*t* (min)
(1a)	NH_2	OCH_3	Ac_2O	90	10
			$(C_6H_5CO)_2O$/DMF	120	20
			AcOCHO	40	5
			$(ClCH_2CO)_2O$	60	10
(1b)	SCH_3	NH_2	Ac_2O	120	10
(1c)	$(CH_3)_2N$	NH_2	Ac_2O	90	8
(1d)	NH_2	NH_2	Ac_2O	60	5
			Ac_2O/Pyridine	110	5
(1e)	$(CH_3)_2N$	OCH_3	Ac_2O	100	1

	R	R¹	R²	M.p. (°C)	Yield (%)
(2a)	NH_2	OCH_3	CH_3	220 (decomp.)	66
(2b)	NH_2	OCH_3	C_6H_5	211–213 (decomp.)	50
(2c)	NH_2	OCH_3	H	above 190 (decomp.)	63
(2d)	NH_2	OCH_3	CH_2Cl	140 (decomp.)	57
(2e)	CH_3S	NH_2	CH_3	184–185	56
(2f)	CH_3S	AcNH	CH_3	161–162	14
(2g)	$(CH_3)_2N$	AcNH	CH_3	205–206	70
(2h)	NH_2	AcNH	CH_3	200	87
(2i)	AcNH	AcNH	CH_3	217–218	20
(2k)	$(CH_3)_2N$	OCH_3	CH_3	183	95

Catalytic hydrogenation of 4-acylamino-5-nitrosopyrimidines[2] on Raney nickel or Pt affords first the 5-amino derivatives, which, however, are very unstable and, even at room temperature, are stabilized by nucleophilic attack of the 5-amino group on the 4-acylamino group and formation of the purine derivatives *(3)*. Hydrogenation of compound *(2)* with $R = NH_2$, $R^1 = OCH_2C_6H_5$, $R^2 = CH_3$ on Pd/C leads to 8-methylguanine *(3b)* by simultaneous debenzylation.

	R	R¹	R²	M.p. (°C)	Yield (%)
(3a)	NH_2	OCH_3	H	245–248 (decomp.)	33
(3b)	NH_2	OH	H	> 360	56
(3c)	CH_3S	NH_2	H	285–290	30
(3d)	NH_2	AcNH	H	204	40
(3e)	$(CH_3)_2N$	OCH_3	H	125	62
(3f)	H	$(CH_3)_2N$	CH_3	132	32
(3g)	$(CH_3)_2N$	H	H	245–249	11
(4a)	$(CH_3)_2N$	OCH_3	H	160–161	71
(4b)	$(CH_3)_2N$	OH	H	273–275 (decomp.)	21
(4c)	H	$(CH_3)_2N$	CH_3	100–101	77
(4d)	$(CH_3)_2N$	H	H	168	84
(4e)	OCH_3	NH_2	H	185–190	62

If 4-amino-5-nitropyrimidines are selected as starting materials, the acylation requires much more drastic conditions: good yields are obtained when *(4d)* or *(4e)* is boiled under reflux with acetic anhydride for a short time, but for *(4a)* to *(4c)* several hours' boiling is needed. The catalytic reductions proceed analogously to those of the 5-nitroso derivatives so that the purines *(3e)*, *(3f)*, and *(3g)* are formed at room temperature from *(4a)*, *(4c)*, and *(4d)*.

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[*] Dipl.-Chem. F. E. Kempter, Dipl.-Chem. H. Rokos, and Prof. Dr. W. Pfleiderer
Institut für Organische Chemie der Technischen Hochschule
Azenbergstr. 14/16
7 Stuttgart (Germany)

[1] Paper read to the 1st German Symposium on Heterocyclic Chemistry, Stuttgart, October 5–7, 1966.

[2] For a review, see *J. H. Lister,* Rev. pure appl. Chem. *11*, 178 (1961).

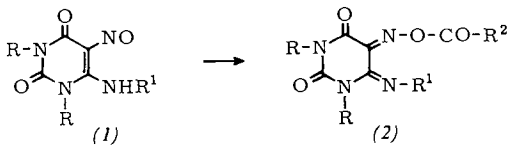
[3] *E. C. Taylor, C. W. Jefford,* and *C. C. Cheng,* J. Amer. chem. Soc. *83*, 1261 (1961); *E. C. Taylor* and *C. W. Jefford,* J. Amer. chem. Soc. *84*, 3744 (1962).

1,3-Disubstituted 5-Acyloxyimino-4-alkylimino-uracils as New "Activated Esters" [1]

By *W. Pfleiderer* and *F. E. Kempter* [*]

When carboxylic acid anhydrides react with 1,3-disubstituted 4-alkylamino-5-nitrosouracils *(1)* at *ca.* 20 to 60 °C (Method A), decoloration and monoacylation occur. This lightening of the color, the absence of a nucleophilic amino group in the

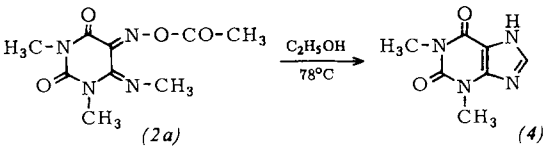
uracil system and the UV spectrum of the products (no uracil chromophore; only end absorption at 220 mμ) indicate clearly that acylation has occurred, not at the amino group[2], but at the nitroso group with formation of 1,3-disubstituted 5-acyloxyimino-4-alkyliminouracils *(2)*.



(1) *(2)*

The same products *(2)* are obtained if the anhydrides are replaced by aliphatic, aromatic, or heterocyclic carboxylic acids in the presence of dicyclohexylcarbodiimide in indifferent solvents such as tetrahydrofuran (method B). After the nitrosouracil color has disappeared, the dicyclohexylurea is filtered off and the reaction products, which are usually soluble, are isolated from the filtrate by evaporation to a small volume.

Moreover, reaction with acid chlorides and triethylamine (method C) leads also to products *(2)*.



(2a) *(4)*

In preliminary attempts to use these new types of "activated ester" *(2)* for peptide syntheses it was found that *N*-substituted amino acids such as *N*-(benzyloxycarbonyl)-DL-phenylalanine and *N*-phthaloyl-DL-phenylalanine can be converted into the activated esters *(2c)* and *(2d)* in high yield by method B. Their use for formation of the peptide link is under study.

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[*] Prof. Dr. W. Pfleiderer and Dipl.-Chem. F. E. Kempter
Institut für Organische Chemie der Technischen Hochschule
Azenbergstr. 14/16
7 Stuttgart (Germany)

[1] Paper read to the 1st German Symposium on Heterocyclic Chemistry, Stuttgart, October 5–7, 1966.

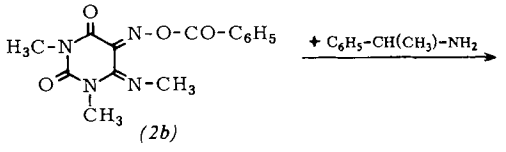
[2] *F. E. Kempter, H. Rokos*, and *W. Pfleiderer*, Angew. Chem. *79*, 233 (1967); Angew. Chem. internat. Edit. *6*, 258 (1967).

[3] *H. Goldner, G. Dietz*, and *E. Carstens*, Liebigs Ann. Chem. *691*, 142 (1966).

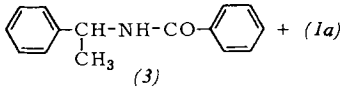
	R	R^1	Method		R^2	M.p. (°C)	Yield (%)	$\nu_{C=O}$ (cm^{-1})
(1a)	CH_3	CH_3	A; B	*(2a)*	CH_3	117	55; 70	1794
			B; C	*(2b)*	C_6H_5	above 120	75; 72	1772
			B	*(2c)*	DL-CH($CH_2C_6H_5$)-NH-$COOCH_2C_6H_5$	194–195	83	1706
			B	*(2d)*	DL-CH($CH_2C_6H_5$)-N-Phthaloyl	133–134	82	1803
			B	*(2e)*	C_6H_{11}	99–101	50	1786
			B	*(2f)*	CH=CH-C_6H_5	above 120	60	1772
			B	*(2g)*	2-Thienyl	above 120	65	1753
			B	*(2h)*	Isonicotinyl	137	69	1785
(1b)	CH_3	$CH(CH_3)_2$	B	*(2i)*	CH_3	64–65	40	1790
(1c)	C_6H_5	CH_3	A	*(2k)*	CH_3	172	53	1809

The 5-acyloxyimino compounds are derived from an isonitroso form; the first indication of this is the very high C=O frequency, between 1740 and 1810 cm^{-1} according to the nature of the group R^2.

Nucleophilic compounds are acylated by *(2)* even under the mildest conditions. For instance, *(2b)* reacts with α-methylbenzylamine in tetrahydrofuran at room temperature to give *N*-(α-methylbenzyl)benzamide*(3)* in 71% yield with regeneration of*(1a)*.The weaker nucleophile aniline gives an 80% yield



(2b)



(3)

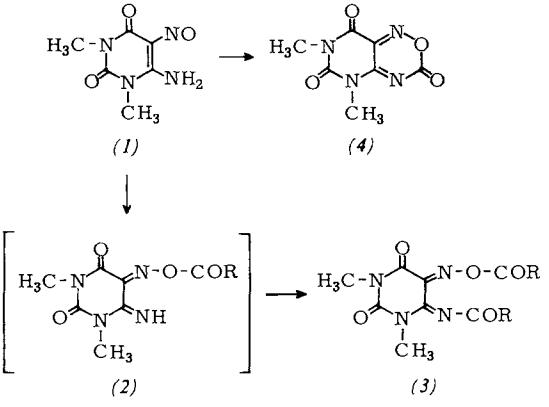
of benzanilide. The reaction of 5-isonicotinoyloxyimino-1,3-dimethyl-4-methyliminouracil *(2h)* with phenylhydrazine or aniline, to give the *N*-phenylhydrazide or anilide, respectively, of isonicotinic acid, emphasises the general applicability of the "activated esters" *(2)* for acyl transfer. Compounds *(2)* are rapidly hydrolysed by water at room temperature. The reaction with alcohols is very slow and incomplete at *ca.* 20 °C; at higher temperatures a competing reaction takes place, namely the imidazole ring formation that is known from the 4-alkylamino-1,3-dimethyl-5-nitrosouracil series[3]; thus theophylline *(4)* is formed from *(2a)*.

Syntheses and Reactions of 4-Acylimino-5-acyloxyiminopyrimidines [1]

By *W. Pfleiderer* and *F. E. Kempter* [*]

In acylations of 4-amino-5-nitrosopyrimidines the point of entry of the acyl group depends on the nature of the substituents in positions 2 and 6[2]. Acylation of 4-amino-1,3-dimethyl-5-nitrosouracil *(1)* at room temperature by carboxylic acids and dicyclohexylcarbodiimide in indifferent solvents (method A) or by acid chlorides and triethylamine (method B) leads to 4-acylimino-5-acyloxyimino-1,3-dimethyluracils *(3)*.

The stepwise acylation is doubtless initiated by attack on the nitroso group with formation first of the 5-acyloxyimino-4-imino derivative *(2)* (that cannot be isolated), whereby the



(1) *(4)*

(2) *(3)*

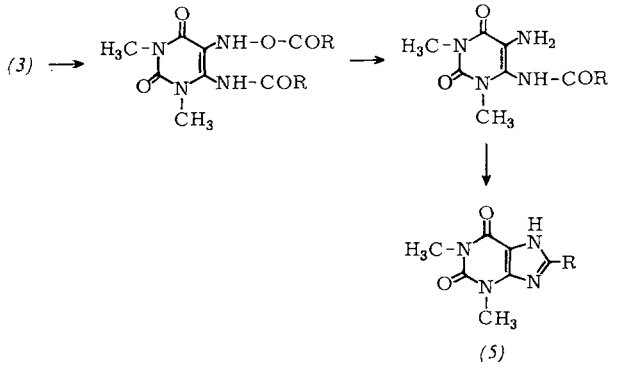
	R	Method	M.p. (°C)	Yield (%)	$\nu_{C=O}$ (cm^{-1})
(3a)	CH_3	A	176–177 (decomp.)	50	1806
(3b)	C_6H_{11}	A	155–156 (decomp.)	73	1790
(3c)	C_6H_5	A; B	191–193 (decomp.)	67	1782
(3d)	2-Furyl	A	188–190 (decomp.)	62	1779
(3e)	$C(CH_3)=CH_2$	A	181–182 (decomp.)	57	1773
(3f)	$CH=CH-C_6H_5$	B	181–182 (decomp.)	57	1757
(4)		B	218–220 (decomp.)	50	1779

relatively inert vinylogous acid amide group is modified and the nucleophilic imine group formed becomes susceptible to a further substitution.

Saturated or unsaturated aliphatic, aromatic, or heterocyclic carboxylic acids react without difficulty. Use of phosgene/triethylamine, or of phosgene alone in tetrahydrofuran, causes intramolecular cyclization with formation of an oxadiazinone ring, as in *(4)*.

4-Acylimino-5-acyloxyimino-1,3-dimethyluracils can be recognized as "activated esters" [2], as is evident from the high IR C=O frequencies. It is remarkable that not only the *O*-acyl group but also the *N*-acyl group is transferred to nucleophilic compounds; compound *(3c)* acylated α-methylbenzylamine (2 equivalents) giving *N*-(α-methylbenzyl)benzamide in 63% yield. It can be assumed that the *O*-benzoyl group acts first as acylating agent, giving 4-benzamido-1,3-dimethyl-5-nitrosouracil *(1)*, with $NHCOC_6H_5$ replacing NH_2, which has not yet been isolated but in turn acts as acetylating agent. Similarly, compound *(3a)* with phenylhydrazine or aniline in tetrahydrofuran at room temperature gives *N*-phenylacethydrazide in 76% yield or acetanilide in 85% yield, respectively.

The diacyl derivatives *(3)* can also be used for synthesis of purines. If *(3)* are hydrogenated catalytically with Raney nickel or Pt at room temperature, 2 equivalents of H_2 are absorbed and 8-substituted theophylline derivatives *(5)* are obtained. The reaction may involve first 1,4-addition, followed by hydrogenolysis of the 5-hydroxyamino derivative and finally nucleophilic attack of the basic 5-amino group on the partially activated 4-acylamino group.

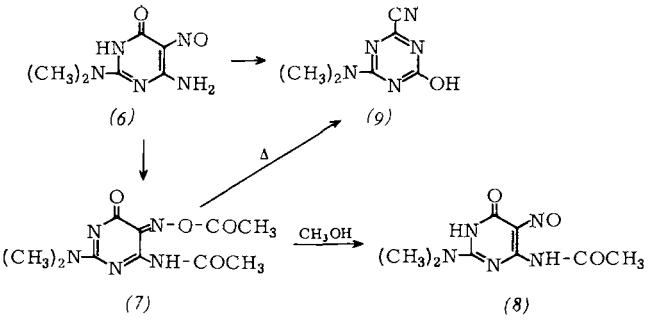


(5)

	R	M.p. (°C)	Yield (%)
(5a)	CH_3	333	74
(5b)	C_6H_{11}	268	57
(5c)	$C(CH_3)_3$	277–278	50

Another interesting diacyl derivative was obtained when 4-amino-2-dimethylamino-5-nitrosopyrimidin-6(1*H*)-one *(6)* was heated with acetic anhydride at 40 to 60 °C until dissolved.

Since there was no end absorption in the UV spectrum of the reaction product we assign to it the structure of a 5-acetamido-4-acetoxyimino-2-dimethylaminopyrimidin-6(4*H*)-one *(7)*. When kept in methanol, compound *(7)* passes into the monoacetyl derivative *(8)* (72% yield) and when heated alone it rearranges, at temperatures above 110 °C, to 4-cyano-6-dimethylamino-*s*-triazin-2-ol *(9)*. Thus compound



(6) *(9)* *(7)* *(8)*

(7) may be an intermediate in the *s*-triazine rearrangement that was first observed by *Taylor* [3] when boiling 4-amino-5-nitrosopyrimidines with acetic anhydride.

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[*] Prof. W. Pfleiderer and Dipl.-Chem. F. E. Kempter
Institut für Organische Chemie der Technischen Hochschule
Azenbergstr. 14/16
7 Stuttgart (Germany)

[1] Paper read to the 1st German Symposium on Heterocyclic Chemistry, Stuttgart, October 5–7, 1966.

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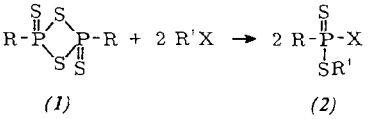
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A Simple Preparation of Dithiophosphonic Ester Halides and of the Novel 1-Thia-3-aza-2,4-diphospha^{V}cyclobutane *P,P*-Disulfide System

By *E. Fluck* and *H. Binder* [*]

Dithiophosphonic acid alkyl ester halides *(2)*, which have hitherto been obtained only by multistage processes [1], can be prepared directly by treating 1,3-dithia-2,4-diphospha^V-cyclobutane *P,P'*-disulfides *(1)* (*e.g.* R=C_6H_5, *p*-$CH_3O-C_6H_4$ or *p*-$C_2H_5O-C_6H_4$) with alkyl halides (R'X = CH_3Br, C_2H_5Br, or C_4H_9Cl).

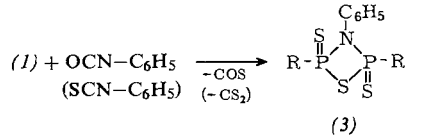
For example, when compound *(1)*, R = C_6H_5 (10 g), is heated with methyl bromide (27.6 g, 10 mol. equiv.) in a sealed tube for 48 h at 80 °C it affords methyl phenyldithiophosphonobromidate (95% yield; b.p. 175 °C/0.01 mm; chemical shift $\delta_P = -71.1$ ppm).



(1) *(2)*

Phenyl isocyanate or isothiocyanate reacts with 1,3-dithia-2,4-diphospha^{V}cyclobutane *P,P'*-disulfides *(1)* with elimination of COS or CS_2, respectively, whereby one sulfur atom of the ring system is replaced by a nitrogen atom and 1-thia-3-aza-2,4-diphospha^{V}cyclobutane disulfides *(3)* containing the hitherto unknown 1-thia-3-aza-2,4-diphospha^{V}cyclobutane ring are formed. Structure *(3)* is assigned because of the molecular weight (cryoscopically in benzene 386) and the NMR-spectroscopic equivalence of the two phosphorus atoms (a single ^{31}P–NMR line at $\delta_P = -61.0 \pm 1.0$ ppm with reference to 85% aqueous orthophosphoric acid).

The second sulfur atom of the ring system *(1)* has not yet been replaceable, even on use of a large excess of phenyl isocyanate or isothiocyanate.



(3)

Preparation of (3), R = C_6H_5: Compound *(1)* (5g) and phenyl isocyanate (2 g) are heated in xylene (50 ml) for 2 h and the xylene and excess of phenyl isocyanate are subsequently distilled off. The colorless substance that crystallizes is filtered off from the distillation residue and recrystallized from a little benzene (yield 4.3 g; m.p. 183 °C; chemical shift δ_P = 61.0 ppm).

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[*] Doz. Dr. E. Fluck and Dr. H. Binder
Anorganisch-Chemisches Institut der Universität
Tiergartenstrasse
69 Heidelberg (Germany)

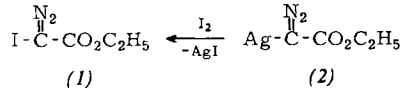
[1] *G. Schrader*, German Pat. 1104506 (April 13th, 1961); Chem. Abstr. *56*, 1482 (1961); Chem. Zbl. *1961*, 16253.

Diazocarboxylic Esters from Ethyl Argentodiazoacetate and Alkyl Halides

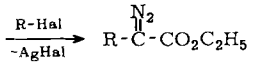
By *U. Schöllkopf* and *N. Rieber*[*]

Diazoacetic esters are of considerable importance in preparative organic chemistry[1]. Surprisingly, only a few members of the higher diazocarboxylic esters are known; possibly because the conventional synthetic route *via* α-amino carboxylic acid esters is either inconvenient or gives poor yields.

We have now found that higher ethyl diazocarboxylates *(3)* are relatively easily accessible by treating ethyl argentodiazoacetate *(2)* with S_N1 reactive alkyl bromides and iodides. The argento-ester is obtained from ethyl diazoacetate and silver oxide at 0 °C. This thermolabile compound has not yet been isolated, but its presence is shown by its characteristic IR absorption at 2040 cm^{-1} (N_2 group) and by its being trapped by iodine as ethyl diazoiodoacetate *(1)*[2].



(1) *(2)*



(3)

For example, we obtained ethyl 2-diazo-3-phenylpropionate *(3)* R = $C_6H_5CH_2$ [b.p. 95 C/1 mm (partial decomp. to ethyl cinnamate); IR bands at 2080 cm^{-1} and 1685 cm^{-1}; NMR signals (in CCl_4) at τ = 8.8 (t), 6.4 (s), 5.8 (q), 2.83 (m)] in *ca.* 60% yield when we stirred an ethereal suspension of *(2)* with benzyl bromide for 10 h at 0 to 20 °C. Analogously with crotyl bromide ethyl-2-diazo-4-hexenoate was obtained in about the same yield [b.p. 41 °C/0.1 mm; IR bands at 2080 cm^{-1} and 1680 cm^{-1}; NMR signals (in CCl_4) at τ = 8.75 (t), 8.33 (d), 5.84 (q), 4.5 (m)], accompanied by some ethyl-2-diazo-3-methyl-4-pentenoate.

When heated, ethyl 2-diazo-3-phenylpropionate gives a mixture of ethyl *trans*- and *cis*-cinnamate; this introduces the possibility of a new chain-lengthening synthesis of α,β-unsaturated carboxylic esters.

The existence of the argento derivative *(2)* is also interesting from a theoretical point of view: the role of the catalyst in the Ag_2O-catalysed Wolff rearrangement is still unknown[3]; according to our findings this role is very probably to convert the diazo ketone into its silver derivative, which then undergoes the shift.

Ethyl 2-diazo-4-pentenoate: Silver oxide (5.8 g, 0.025 mole) is added in 2 h in *ca.* 0.5 g portions, with stirring, to ethyl diazoacetate (5.7 g, 0.05 mole) with simultaneous dilution with ether (total 60 ml). After being stirred at 0 °C for 3 h, allyl iodide (12.6 g, 0.075 mole) is added dropwise with ice-cooling and the whole is stirred for a further 3 h at 0 °C. The mixture is then filtered, dried over Na_2SO_4, concentrated in a rotary evaporator (40 °C/13 mm), and fractionated. Yield of ethyl 2-diazo-4-pentenoate 4–5 g; b.p. 39–42 °C/0.5 mm; IR bands at 2080 cm^{-1}, 1685 cm^{-1}; NMR (in CCl_4), τ = 8.75 (t), 7.0 (d, some splitting), 5.8 (q), 4.85 (m), 4.3 (m).

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[*] Prof. Dr. U. Schöllkopf and Dr. N. Rieber
Organisch-Chemisches Institut der Universität
Windausweg 2
34 Göttingen (Germany)

[1] *R. Huisgen*, Angew. Chem. *67*, 439 (1955); *W. Ried* and *H. Mengler*, Fortschr. chem. Forsch. *5*, 1 (1965); *E. H. Rodd*: Chemistry of Carbon Compounds. Elsevier London 1952, Vol. I B, p. 855.

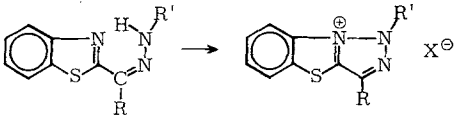
[2] *F. Gerhart, U. Schöllkopf*, and *H. Schumacher*, Angew. Chem. *79*, 50 (1967); Angew. Chem. internat. Edit. *6*, 74 (1967).

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Synthesis of 1,3-Triaryl[1,2,3]triazolo[5,1-*b*]-benzothiazolium and -benzimidazolium Salts, and of 1,3-Diphenyl[1,2,3]triazolo[1,5-*a*]benzimidazole[1]

By *A. Messmer* and *A. Gelléri*[*]

The hitherto recorded triazolium[2,3] and tetrazolium salts[4] have six-membered rings fused to them. We have found that benzothiazol-2-yl phenyl ketone phenylhydrazone *(1a)*, R = R′ = C_6H_5[5], is converted by 4 molar equivalents of *N*-bromosuccinimide in ethyl acetate at room temperature into 1,3-diphenyl[1,2,3]triazolo[5,1-*b*]benzothiazolium bromide *(2a)* with X = Br. A yellow, crystalline 1:1 complex (m.p. 152 °C) that contains *(2a)* X = Br, and *N*-bromosuccinimide is first deposited quantitatively from the solution; the salt *(2a)*, X = Br, is obtained from this complex by dissolution in acetone/methanol (5:1 v/v) and precipitation with ether. It is isolated as white crystals (m.p. 167 °C), which are converted into the excellently crystallizing tetrafluoroborate and perchlorate. The derivatives *(2b)* to *(2d)* are obtained analogously.



(1) *(2)*

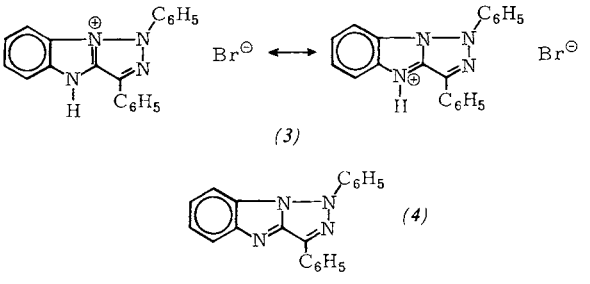
	R	R′	$X^{\ominus}=ClO_4^{\ominus}$ *(2)* M.p. (°C)	Yield (%)	$X^{\ominus}=BF_4^{\ominus}$ M.p. (°C)
(a)	C_6H_5	C_6H_5	193	69	185
(b)	C_6H_5	*m*-CH_3O—C_6H_4	204	58	187
(c)	Benzothiazol-2-yl	C_6H_5	230	54	—
(d)	Benzothiazol-2-yl	*p*-CH_3O—C_6H_4	207	54	199

The structure *(2)* is in accord with the elemental analysis and IR spectrum (no NH band). Alkaline $Na_2S_2O_4$ regenerates the hydrazone *(1)* from *(2)*.

In the case of benzoxazol-2-yl phenyl ketone phenylhydrazone, *(1a)* with O in place of S, m.p. 166 °C, cyclodehydrogenation does not occur under the above or under more drastic conditions (40–50 °C); the starting material is recovered in 70% yield.

However, benzimidazol-2-yl phenyl ketone phenylhydrazone[6], *(1a)* with NH in place of S, does undergo cyclode-

hydrogenation. Under the above conditions 1,3-diphenyl-[1,2,3]triazolo[5,1-*b*]benzimidazolium bromide *(3)*, m.p. 195 °C (corresponding $BF_4^{\ominus}$ salt, m.p. 190 °C), is at once precipitated in 72% yield after reaction with one equivalent of *N*-bromosuccinimide. Compound *(3)* can be considered, not only as a triazolium salt analogous to *(2)*, but also as a hydrobromide *(3')*. Thus, with aqueous pyridine it gives the white crystalline free base 1,3-diphenyl[1,2,3]triazolo[1,5-*a*]-benzimidazole *(4)*, m.p. 148 °C, in 88% yield.



(3)

(4)

The structures of compounds *(3)* and *(4)* have been proved by elemental analysis and IR spectra. The starting material, *(1a)* with NH in place of S, gives sharp NH bands at 3400 cm^{-1} and 3300 cm^{-1}, compound *(3)* gives an intense broad band at 2600 cm^{-1} characteristic of the $NH^{\oplus}$ group, but compound *(4)* gives no NH band. A remarkable property of the new ring system *(4)* is the intense blue fluorescence of its solutions.

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[*] Dr. A. Messmer and Dipl.-Chem. A. Gelléri
Central Institute for Chemistry Research of the
Hungarian Academy of Sciences
Pusztaszeri ut 57/69
Budapest II (Hungary)

[1] Part 3 of New Heteroaromatic Azolium Salts.-Part 2: [3].

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[3] *A. Messmer* and *O. Szimán*, Angew. Chem. *77*, 1077 (1965); Angew. Chem. internat. Edit. *4*, 1074 (1965).

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Carbamoyl Isothiocyanates

By *J. Goerdeler* and *D. Wobig* [*]

By reaction according to the scheme

$$R_2N{-}COCl + NaSCN \xrightarrow[80\,°C,\ 20min]{CH_3CN} R_2N{-}CO{-}NCS + NaCl$$

we have obtained compounds of type *(1)*, most of them as oils that are difficult to purify (R = CH_3, C_2H_5, allyl, n-C_4H_9, piperidino, or morpholino), but in one case as a crystalline solid (R = cyclohexyl; m.p. 101–102 °C).

The carbamoyl isothiocyanates *(1)* are in equilibrium with the corresponding thiocarbamoyl isocyanates *(2)* [1], as can be seen from the IR spectra and from chemical reactions.

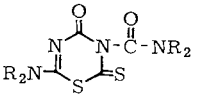
$$R_2N{-}CO{-}NCS \rightleftarrows R_2N{-}CS{-}NCO$$

(1) *(2)*

The isothiocyanate *(1)* predominates strongly in toluene at 20 °C (IR band at 1975–1985 cm^{-1}); the isocyanate component (IR band at 2220 cm^{-1}) is detectable only on use of thick layers (0.1 mm), but increases appreciably in a reversible reaction if the temperature is raised to 40–50 °C.

The chemical reactions are determined by this dualism. Thus rapid action of an excess of H_2O leads to derivatives ($R_2N{-}CO{-}NH_2$) of the isothiocyanate, but slow reaction (exposure to air) leads to derivatives ($R_2N{-}CS{-}NH_2$) of the isocyanate. Schiff bases react with *(2)* only (cycloaddition to give 2-amino-1,3,5-thiadiazin-4-ones). In most of the reactions, the isothiocyanate predominates *e.g.* in addition of benzylamine, aniline, or *p*-nitroaniline to give carbamoylthioureas, or of acetylacetone imine to give derivatives of 3-aminothiocrotonamide; 1,2-cycloaddition of diazomethane to give 1,2,3-thiadiazoles; 1,4-cycloaddition of $\Delta^{2,2'}$-bi(1,3-diphenylimidazolidine) or t-butyl, cyclohexyl, phenyl, or *p*-methoxyphenyl isocyanide to give derivatives of 1,3-oxazole-4-thione.

When kept for some time, some of the undiluted compounds *(1)* ⇄ *(2)* yield colorless, crystalline "dimers" *(3)* [*(3a)*



(3)

R = CH_3, m.p. 198–199 °C (decomp.); *(3b)* R = C_2H_5, m.p. 104 °C (decomp.)], probably by cycloaddition of one molecule each of *(1)* and *(2)*.

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[*] Prof. Dr. J. Goerdeler and Dipl.-Chem. D. Wobig
Organisch-Chemisches Institut der Universität
Meckenheimer Allee 168
53 Bonn (Germany)

[1] According to *J. Goerdeler*, *H. Schenk*, and *K. Jonas*, Chem. Ber. *98*, 2954 (1965); *99*, 3572 (1966), these can be prepared as metastable compounds by thermal cleavage of 2-aminothiazoline-4,5-diones.

Dithioacetylacetonatoiron Complexes [**]

By *K. Knauer*, *P. Hemmerich*, and *J. D. W. van Voorst* [*]

Stable iron mercaptide clusters as found in ESR- and redox-active nonheme iron proteins (*e.g.* ferredoxin [1] and Fe-flavoproteins [2] stimulate the search for model compounds which reflect the structure of FeS-, FeSS- and FeSSFe-groups as a function of the oxidation state and provide a basis for structural assignments of spectral data [3].

The iron-mercaptide system is defined by equation (a).

$$Fe^{3+} + SR^- \rightleftarrows \frac{1}{n}(Fe^{III}SR \leftrightarrow Fe^{II}\dot{S}R)_n^{2n+} \rightleftarrows Fe^{2+} + {}^1/_2\,(RS)_2 \quad (a)$$

Equilibrium positions, the value of *n*, kinetic stability, structure, and magnetochemistry of intermediates will be widely varying functions of the iron ligand fields and of the steric and electronic requirements inherent to R.

It has been shown earlier, that organic disulfides RSSR and Cu^I may react to give strongly colored CuSSCu-clusters [4]. A similar affinity for RSSR may be associated with low spin d^6-iron. Unfortunately, the two requirements of strong ligand field for preservation of spin state and binding of the relatively weak RSSR-ligand, seem to be mutually exclusive. We have found that a new stable FeSS-system is formed on reaction of dithioacetylacetone [5] *in statu nascendi* with Fe^{3+} according to equation (b).

$$2\ CH_3\text{-}CO\text{-}CH_2\text{-}CO\text{-}CH_3 + 4\ H_2S + 4\ Fe^{III}Cl_4^- \xrightarrow{75\%} Fe(C_5H_7S_2)_2Cl_4 + 3\ Fe^{II}Cl_4^{2-} + 2\ H_3O^+ + 2\ H_2O \quad \text{(b)}$$

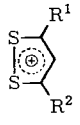
(1)

The violet crystals dissolve in water at pH ≤ 3 to give a colorless solution as described by equation (c).

$$Fe(C_5H_7S_2)_2Cl_4 \xrightarrow{H_2O} Fe^{2+} + 4\ Cl^- + 2\ (C_5H_7S_2)^+ \quad \text{(c)}$$

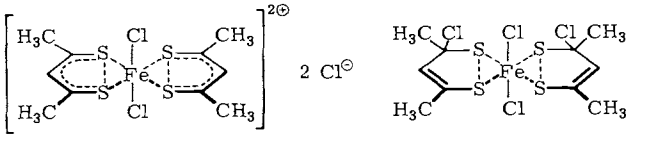
(1)

The Fe^{2+} formed was determined colorimetrically as the bipyridine complex, whereas $(C_5H_7S_2)^+$ was found to have the structure *(2)*, $R^1 = R^2 = CH_3$; the first stable dithiolium cation with only aliphatic substituents. It is stable towards hydrolysis at pH ≤ 4. Structure *(2)* is evidenced by ^1H–NMR-spectroscopy [2 peaks only, 8.4 and 3.1 ppm, of intensity ratio 1:6], by means of UV-spectra ($\lambda_{max} = 280$, 265 nm; $\varepsilon = 9300$, 7200 $mol^{-1}cm^{-1}$ compared to $\lambda_{max} = 356$, 287 nm; $\varepsilon = 19000$, 3800 $mol^{-1}cm^{-1}$ of the known *(2)*, $R^1 = C_6H_5$, $R^2 = H$)[6] and by isolation of the picrate $C_{11}H_9O_7N_3S_2$, m.p. 113 °C.



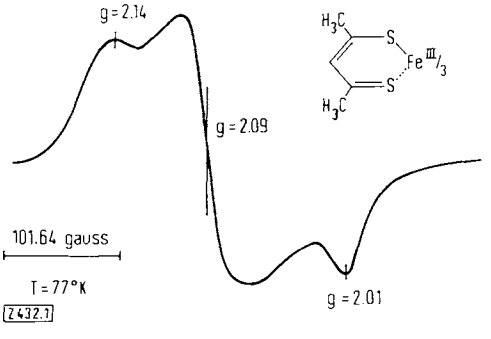
(2)

The complex *(1)* might have the structure $(C_5H_7S_2)_2[Fe^{II}Cl_4]$ which is in agreement with its elementary composition. Its very intense color, however, suggests Fe–SS-coordination, since $C_5H_7S_2^{\oplus}$ as well as the almost non-polarisable $FeCl_4^{2-}$ are colorless. Therefore, we propose the structures *(1a)* or *(1b)* as the most probable ones.



(1a) *(1b)*

If the colorless aqueous solution of *(1)* (cf. eq. (c)) is reduced by $Na_2S_2O_4$ or $NaBH_4$, red-brown crystalline $Fe^{III}(C_5H_7S_2)_3$ is obtained, which is soluble in $CHCl_3$ and may be further reduced by shaking with aqueous $Na_2S_2O_4$ to give the autoxidable $Fe^{II}(C_5H_7S_2)_2$. The compound $Fe^{III}(C_5H_7S_2)_3$ shows the ESR properties expected for an asymmetrical low spin d^5-octahedron (Fig. 1), while $Fe(C_5H_7S_2)_2$ and *(1)* do not show an ESR absorption at $T \geq 170$ °K.



The formal oxidation state of the iron is increased on reduction of complex *(1)*. This system may be a model for redox-active iron in proteins in which the ESR signals at $g < 2$ appear to belong to an "oxidized" d^5-state, even though they appear only on reduction of the complex. The electron balance of these reductions is thus determined not only by the central atom, but also by the acceptor ligand, a fact which should always be borne in mind when the stoichiometry of electron uptake by iron proteins is discussed.

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[*] Dipl.-Chem. K. Knauer and Doz. Dr. P. Hemmerich
Institut für anorganische Chemie der Universität
Spitalstraße 51
Basel (Switzerland)
Doz. Dr. J. D. W. van Voorst
Institute for Physical Chemistry of the University
Amsterdam (Netherlands)

[**] Financial support by the Swiss National Foundation for the Advancement of Natural Science as well as the Netherlands Organization for the Advancement of Pure Research (Z.W.O.). The elementary analyses are a generous contribution by the microanalytical laboratory CIBA Ltd., Basel (Dr. *W. Padowetz*).

[1] *E. Bayer* and *W. Parr*, Angew. Chem. *78*, 824 (1966); Angew. Chem. internat. Edit. *5*, 840 (1966); *B. B. Buchanon*: Structure and Bonding. Springer-Verlag, Berlin 1966. p. 109.

[2] Cf. *E. C. Slater*: Flavins and Flavoproteins. Elsevier, Amsterdam 1966, BBA-Library Vol. 8; *P. Hemmerich, C. Veeger*, and *H. C. S. Wood*, Angew. Chem. *77*, 699 (1965); Angew. Chem. internat. Edit. *4*, 671 (1965).

[3] *H. Brintzinger, G. Palmer*, and *R. H. Sands*, Proc. nat. Acad. Sci. USA *55*, 397 (1966); *J. D. W. van Voorst* and *P. Hemmerich* in "International Conference on Magnetic Resonance in Biological Systems", Stockholm 1966, Pergamon, in press.

[4] *P. Hemmerich, H. Beinert*, and *T. Vänngard*, Angew. Chem. *78*, 449 (1966); Angew. Chem. internat. Edit. *5*, 442 (1966); *P. Hemmerich* in *P. Aisen, W. E. Blumberg*, and *J. Peisack*, "Biochemistry of Copper". Academic Press, New York, 1966, p. 15.

[5] Dithioacetylacetone arises from acetylacetone and H_2S, but dimerizes instantaneously and irreversibly if not trapped as monomer by chelating metals. Chelates with other metals (Ni^{2+}, Co^{2+}, Pd^{2+}, Pt^{2+}) have been announced by *R. L. Martin* and *J. M. Stewart*, Nature (London) *210*, 522 (1966).

[6] *E. Klingsberg*, J. Amer. chem. Soc. *83*, 2934 (1961).

ESR Studies of Model Complexes for Non-Heme Iron Proteins

By *A. Röder* and *Ernst Bayer* [*]

It is difficult to decide the valence of the iron in redox-active non-heme iron proteins since the ligand, as well as the iron, is redox-active. In the reduced state many of these iron proteins have ESR spectra with g values below that of a free electron [1]. The ESR spectrum of reduced xanthine oxidase contains a broad signal with $g = 1.94$ (−175 °C) [1]; the g values for reduced ferredoxin from *Clostridium pasteurianum* are 1.89, 1.96, and 2.05 (15 °K) [2, 3]. Bonding of the iron to cysteinyl groups appears to be certain for ferredoxin [4]. Thus iron complexes of low molecular weight involving sulfur-containing ligands should also give g values below 2.0 at corresponding redox states, and it should be possible to determine the oxidation state of the active centre in the reduced non-heme iron.

Under the following conditions iron complexes of cysteine, cystine, and cysteamine gave g values at 1.94:

(a) Oxidation of the previously described [4] iron(II) complex of cysteine methyl ester:

1. 392 mg of Mohr's salt is added, under nitrogen, to a solution of 342 mg of cysteine methyl ester hydrochloride in 100 ml of 0.5 M tris-HCl buffer (pH = 7.0). The cysteine methyl ester-iron(II) complex that precipitates immediately is dissolved by the addition of 1 N NaOH (final pH = 9.5). The solution is shaken for 1 min with an equal volume of a 1 % solution of iodine in benzene in an ESR sample tube, then frozen and measured [**].

2. 227 mg of cysteamine and 392 mg of Mohr's salt are dissolved in 50 ml of 1 M tris-HCl buffer (pH = 7.0). The pH is then adjusted to 9.5 by 1 N NaOH, and a solution of 504 mg of the sodium salt of riboflavin monophosphate (FMN) in 25 ml of H_2O is added. After 5 minutes the mixture is transferred to an ESR sample tube, frozen, and measured. In this case absorption by the flavosemiquinone at $g = 2.00$ also occurs (see Fig. 1b).

(b) By oxidation of tricarbonyl(cystine dimethyl ester)-iron(0)[5]:

0.2 ml of a 10^{-2} M ethereal solution of the cystine dimethyl ester-iron(0) complex is treated in an ESR sample tube with 5 mg of solid iodine, frozen after 20-seconds' shaking, and measured.

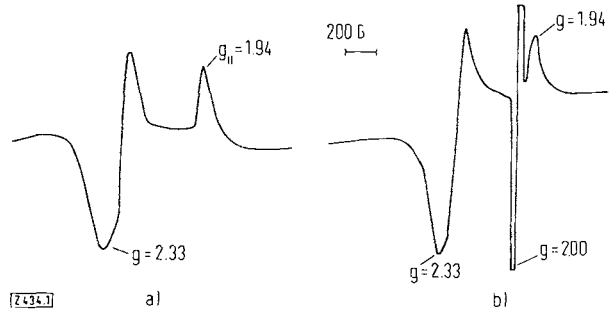
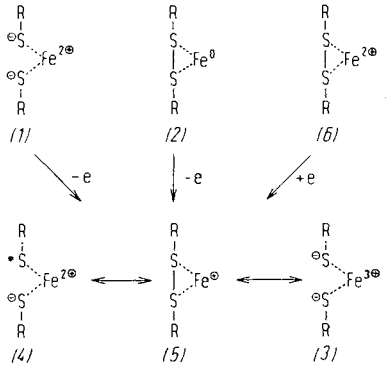


Fig. 1. a) ESR spectrum of the cysteine methyl ester iron(II) complex after oxidation by method (a)1, and of cysteine methyl ester after reaction with iron(III) chloride by method (c) (Mod. 1000, SL 1000, SR 200 gauss/min).

b) ESR spectrum of the radical complex ($g_{\parallel} = 1.94$; $g_{\perp} = 2.3$) obtained by method (a)2, and of the flavosemiquinone radical ($g = 2.00$) (Mod. 1000, Ampl. 1000, SR 250 gauss/min).

The ESR spectrum reproduced in Fig. 1a has the shape that, according to *Kneuenbühl*'s calculations[6], is characteristic of axial symmetry in complexes. A similar symmetry was observed with the reduced non-heme iron protein from *Azotobacter vinelandii*[1].

The oxidation states of the initial complexes used for (a) and (b) are given in the formulae *(1)* and *(2)*. The iron(II) complex *(1)* of cysteine methyl ester is equivalent to the tricarbonyliron(0) complex *(2)* of cystine dimethyl ester with respect to its total oxidation state when the oxidation states of the ligand and the central atom are considered together. Both complexes are converted into ESR-active substances on oxidation. In so far as oxidation involves a one-electron step the same ESR spectrum should result if the iron(III) salt is allowed to react with cysteine methyl ester; one can therefore formulate complex *(3)*.



(c) 80 mg of anhydrous iron(III) chloride is added, under nitrogen, to 100 ml of a 10^{-2} M solution of cysteine methyl ester in 0.5 M tris-HCl buffer (pH = 10.5). The pH value is then adjusted to 9.5 by addition of 1 N NaOH. After 10 min the mixture is transferred to an ESR sample tube, frozen at once, and measured. The same spectrum is obtained as under (a)1 (Fig. 1a).

The total oxidation state of the ESR-active complex is thus proved. The complex can be formulated as iron(III) mercaptide *(3)*, as iron(II) radical complex *(4)*, or as iron(I) complex of the disulfide *(5)*. The unpaired electron is delocalized over the central ion and the ligand. Neither the central ion nor the ligand can be assigned a specific oxidation state.

The similarity between the ESR spectra of reduced non-heme iron proteins and synthetic iron complexes makes it probable that formulations *(3)* to *(5)* can also be applied to reduced non-heme iron. This is supported by ESR-spectroscopic studies of bis(hexamethylbenzene)iron(I) tetrafluoroborate[7], of $Na_3[Fe(CN)_5NO]$[8], and of iron-oxygen-radical complexes[9]. The oxidized form of non-heme iron proteins is therefore described by structure *(6)* of an iron(II) complex of the disulfide; this is in agreement with results obtained by chemical methods.

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[*] Dipl.-Chem. A. Röder and Prof. Dr. Ernst Bayer
Chemisches Institut der Universität
Wilhelmstr. 33
74 Tübingen (Germany)

[1] *H. Beinert* in *A. San Pietro*: Non-Heme Iron Proteins. The Antioch Press, Yellow Springs, Ohio, 1965, p.23 and further literature cited.

[2] *G. Palmer, R. H. Sands*, and *L. E. Mortenson*, Biochem. biophys. Res. Commun. *23*, 357 (1966).

[3] *E. Bayer, W. Parr, G. Schwörer*, and *A. Röder*, unpublished.

[4] *E. Bayer, W. Parr*, and *B. Kazmaier*, Arch. Pharmaz., Ber. dtsch. pharmaz. Ges. *298*, 196 (1965); cf. also Angew. Chem. *78*, 824 (1966); Angew. Chem. internat. Edit. *5*, 840 (1966).

[**] All measurements at −170 °C (V-4540 variable temperature controller). Varian V-4502 X-Band spectrometer.

[5] *E. Bayer* and *A. Röder*, unpublished.

[6] *F. K. Kneuenbühl*, J. Chem. Physics *33*, 1074 (1960).

[7] *H. Brintzinger, G. Palmer*, and *R. H. Sands*, J. Amer. chem. Soc. *88*, 623 (1966).

[8] *H. Beinert, P. Hemmerich*, and *J. D. W. Van Voorst*, Biochim. biophysica Acta *96*, 530 (1965).

[9] *W. E. Blumberg* and *J. Peisach* in *A. San Pietro*: Non-Heme Iron Proteins. The Antioch Press, Yellow Springs, Ohio, 1965, p. 101.

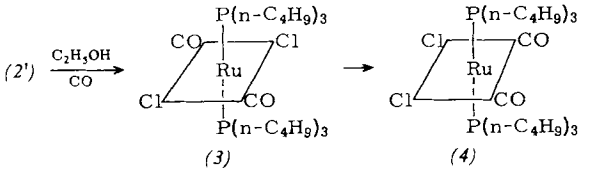
Ruthenium(II, III) Dimeric Complexes

By *J. K. Nicholson*[*][**]

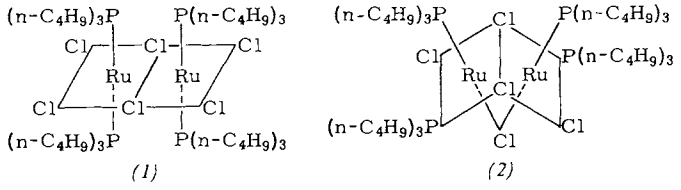
In certain dimeric carboxylate complexes of ruthenium the ruthenium atoms are formally in the oxidation states two and three. Their unexpectedly high magnetic moments have been ascribed to a spin free system[1]. We have now isolated a tri-n-butylphosphine complex of ruthenium, $[Ru_2(II,III)Cl_5\{P(n\text{-}Bu)_3\}_4]$[2] which has the expected magnetic moment for a spin paired dimer containing one unpaired electron per molecule. When a concentrated ethanolic solution of ruthenium trichloride and tri-n-butylphosphine (molar ratio 1:2.2) is allowed to stand at 20 °C under nitrogen for 72 h, a complex $[RuCl_3\{P(n\text{-}Bu)_3\}_2]_2$ *(1')*, dark red crystals, m.p. 132–134 °C, separates. After filtration in air, the mother liquor deposits $[Ru_2Cl_5\{P(n\text{-}Bu)_3\}_4]$ *(2')*, dark red crystals, m.p. 95.5–96 °C, over a period of 24 h.

Complex *(1')* has a magnetic moment of 1.93 B.M./Ru[3], as expected for a spin paired ruthenium(III) complex[4]. Molecular-weight determination (calculated 1224; found 1004; thermoelectric method of *Simon* and *Tomlinson*) suggests that, in dichloromethane solution, the complex *(1')* is largely dimeric. Complex *(2')* has a molecular weight of 1165 ± 24[5] (calc. 1189). The magnetic moment 0.75 B.M./Ru[3] indicates that there is one unpaired electron per molecule. The infrared spectrum exhibits no absorption bands in the region 4.0–6.0 μ (metal-hydride stretching frequency range). Complex *(2')* is formulated therefore with the ruthenium atoms formally in the oxidation states II and III. It is not

yet known whether the ruthenium atoms have similar ligand environments[6], but chemical evidence suggests this is so. Thus reaction of complex *(2')* with carbon monoxide in ethanol at 0 °C yields quantitatively *trans*-$[RuCl_2(CO)_2\{P(n\text{-}Bu)_3\}_2]$[3] *(3)*, and this rearranges in solution to the *cis* form *(4)*[7,8]. Complex *(1)* reacts similarly to give isomers *(3)* and then *(4)* as products.



At temperatures above 0 °C, the isomerization *(3)* → *(4)* is so fast that *(3)* cannot be isolated in a pure state. Complex *(1')* reacts similarly to *(3)* and *(4)*. Of the many possible ligand arrangements for complexes *(1')* and *(2')* the reactions with CO indicate that the following are the most likely.



The complexes $[RuCl_3(P\text{-}n\text{-}Pr_3)_2]_2$, *(1')* type, and $[Ru_2(II,III)Cl_5\{P(n\text{-}Pent)_3\}_4]$, *(2')* type, have also been isolated and shown to undergo the same reactions with carbon monoxide as the tributylphosphine complexes.

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[*] Dr. J. K. Nicholson
Monsanto Research S.A.
Binzstr. 39
CH-8045 Zürich (Switzerland)

[**] I wish to thank Mr. *G. Häusermann* for experimental assistance.

[1] *T. A. Stephenson* and *G. Wilkinson*, J. inorg. nuclear Chem. *28*, 2285 (1966).

[2] All the compounds reported gave satisfactory elemental analyses.

[3] Determined by Drs. *G. Olivé* and *S. Olivé* of MRSA Zürich, for tetrahydrofuran solutions, based on molecular weights of 1224.20 for complex (1) and 1188.78 for complex (2').

[4] *J. Lewis* and *B. N. Figgis* in: Prog. Inorg. Chem. *6*, 174 (1964).

[5] Determined by Dr. *P. J. Wheatley* of MRSA, by X-ray evaluation of cell constants and based on a density measured by flotation $d = 1.23 \pm 0.01$ g/cm³).

[6] An X-ray structure determination is being carried out in these laboratories.

[7] *J. Chatt* and *B. L. Shaw*, J. chem. Soc. *1964*, 3466.

[8] *J. M. Jenkins*, *M. S. Lupin*, and *B. L. Shaw*, J. chem. Soc. A *1966*, 1787.

CONFERENCE REPORTS

Swiss Chemical Society

The Summer Meeting of the *Schweizerische Chemische Gesellschaft* was held at Solothurn (Switzerland) on October 1st, 1966.

From the lectures:

Enthalpy and Entropy Changes on formation of Complexes

S. Ahrland, Zürich (Switzerland)

Enthalpy and entropy changes have been compiled for complexes formed between halide (or cyanide) ions and metal ion acceptors, ranging from typically class (a), or hard, to typically class (b), or soft[*]. The ligands have been chosen so that they should vary widely in softness while being as similar as possible in other respects. They become softer in the sequence $F^- < Cl^- < Br^- < I^- < CN^-$.

The stability of complexes between hard acceptors and hard ligands (*e.g.* F^-) is due exclusively to a large gain of entropy, while the enthalpy term as a rule even counteracts the complex formation (endothermic reaction). On the other hand, the stability of complexes between soft acceptors and very soft ligands (*e.g.* CN^-) is exclusively due to a large decrease of enthalpy (exothermic reaction), while the entropy term as a rule counteracts the reaction (which thus involves a loss of entropy). When the acceptor and/or ligand are of intermediate softness, intermediate cases occur where the enthalpy and the entropy terms both contribute to about the same extent towards the formation of the complex (*e.g.* $CdBr^+$, $HgCl^+$).

[*] For the terms "hard" and "soft" cf. *R. G. Pearson*, J. Amer. chem. Soc. *85*, 3533 (1963); *R. F. Hudson*, Chem. Engng. News *43*, No 22, p. 90 (1965).

The large entropy gain found for the fluoride complexes is certainly a combined effect of the breaking of acceptor-to-water and ligand-to-water hydrogen bonds. On the other hand, the softer ligands presumably disorder the solvent in a degree increasing with their softness. On complex formation, only the breakage of the acceptor-to-water bonds will thus involve a gain of entropy, while both the withdrawal of the ligand from its surrounding water molecules and the formation of the acceptor-to-ligand bond will cause entropy losses. For the diatomic cyanide ion, there is in addition a loss of rotational entropy.

Contrary to the electrostatic bonds formed between hard ligands and hard acceptors, the bonds formed between soft ligands and soft acceptors are best described as essentially covalent. The formation of such a covalent bond tends to make the total process of complex formation exothermic. In fact, the enthalpy change seems to be a fairly good measure of the strength of the covalent bonding.

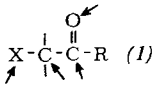
Reactions of Positive Halogen Organic Compounds with Phosphorus(III) Derivatives

P. A. Chopard, Cologny/Geneva (Switzerland)

The characteristic properties of halogeno-organic compounds are related to the "negative" nature of the halogens in comparison to carbon. This is typified by the inductive effect of the halogen which increases the acidity of protons on nearby carbon atoms, and the relatively easy ionization of the C–X bond to halide ions (S_N1 displacement reactions).

With a variety of polarizable nucleophiles, the halogen atom can also act as an electron acceptor, particularly in the cases where the halogeno compounds may form stable anions as leaving groups. Such nucleophiles are often

relatively deficient in non-bonding electrons and also preferably derived from elements of the second or higher periods. Because of their multiple positive centers, α-halogeno keto compounds *(1)* were chosen as model electrophiles and the results of their reactions with tertiary phosphines and phosphites as nucleophiles lead to the following observations:



(1)

a) Phosphines are better nucleophiles than phosphites with regard to displacement reactions and the order of reactivity follows the usual order I > Br > Cl.

b) The selectivity [*] for the reaction at halogen is greater than for the reaction at saturated carbon.

c) Phosphites react preferentially to phosphines at the carbonyl center.

The phosphines, having less non-bonded electrons than the phosphites, are more polarizable and softer than the phosphites. The greater selectivity for the reaction at halogen, with respect to the leaving groups, is interpreted as evidence for a high degree of bond formation in the transition state; this is compatible with a strong contribution of covalent bonding energy and a weak contribution of affinity and solvation energy. The great selectivity with respect to the electrophilic halogen (Br > Cl; $\Delta k \simeq 10^6$) is tentatively compared to the energy difference in the charge-transfer absorptions of complexes of tertiary amines with polyhalogenoalkanes. Support to this interpretation is given by the known light catalysis of some reactions of phosphites with alkyl polyhalides.

Compounds studied: Halogen substituted cyclohexanones, benzophenones, acetones, acetic acid, and esters.

Effect of Solvent Structure on Dissociation

R. Hümberlin, Basel (Switzerland)

When an ion pair dissociates, a void is created between them which remains until it is large enough to be occupied by a solvent molecule, the electrostatic energy required for this separation being about 50 kcal/mole. Interaction between such an intimate ion pair and water molecules is relatively small because the charge centers of the ion pair are close to each other and their effects almost cancel. The farther the two ions separate the stronger is the interaction with the solvent; the effective dissociation energy is thus reduced to about 5 kcal/mole.

An ion pair cannot dissociate spontaneously. There must be a vacant position in the solvent structure next to the departing ion; also a water molecule must be so situated with respect to the ion pair that it can occupy the resulting space as quickly as possible. The ions do not separate linearly – they move from one energetically favored position in the solvent structure to another. The rate and degree of dissociation are thus determined not merely by coulombic forces, but to a much greater extent by permanent and induced dipoles of the solvent molecule.

The potential energy-interionic distance function can be calculated from an electrostatic model, taking into account all the ion-dipole and dipole-dipole interactions. A maximum of about 5 kcal/mole is found when the distance between the electron shells of the ions is 1 Å. The activation energy is comparable with that of a rotation around a C–C-bond in saturated hydrocarbons. The intimate ion pair is thus a real compound but converts easily and reversibly into an ion pair separated by solvent molecules.

For quantitative treatment see: Chimia *18*, 335 (1964); *ibid 19*, 602 (1965).

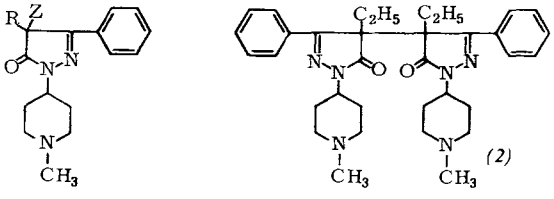
[*] $\ln k_1/k_2$ where k_1 and k_2 refer to two related reactions.

Transformation of Basically Substituted Pyrazolones

A. Vogel, Basel (Switzerland)

When an aqueous solution of 4-ethyl-1-(1-methyl-4-piperidyl)-3-phenyl-5-pyrazolone hydrogen maleate *(1a)* is kept in the air, the 4,4′-bipyrazolone *(2)* separates as bis(hydrogen maleate) after *ca.* 1 week. This product *(2)* presumably arises by dimerisation of the radical formed as primary product on autoxidation of the protonated molecule from *(1a)*. The structure of *(2)* was proved by elemental analysis and determination of the molecular weight and by comparison of the UV spectrum (ethanol; $\lambda_{max} = 299$ mμ, log ε = 4.26), the IR spectrum (Nujol or CH_2Cl_2; carbonyl bands at 1690 cm^{-1}), and the NMR spectrum with the spectra of compounds of similar structure (*e.g.* compound *(1a)* and the alkylation products 1-(*N*-methyl-4-piperidyl)-3-phenyl-4,4-diethylpyrazolin-5-one, 1-(*N*-methyl-4-piperidyl)-3-phenyl-4-ethyl-5-ethoxypyrazole and 1-(*N*-methyl-4-piperidyl)-2,4-diethyl-3-phenylpyrazolin-5-one.

The bipyrazolone *(2)* is also formed on oxidation of compound *(1a)* with ferric chloride; also by condensation of 4-bromo-4-ethyl-1-(1-methyl-4-piperidyl)-3-phenyl-5-pyrazolone with the sodium salt of *(1a)*.



(2)

(1a), *(1b)*, R = C_2H_5, CH_2-C_6H_5, Z = H

(3a), *(3b)*, R = C_2H_5, CH_2-C_6H_5, Z = HO_2C-CH-CH_2-CO_2H

Adducts *(3a)* and *(3b)* separated after several months when aqueous solutions of the hydrogen maleates of *(1a)* and *(1b)*, respectively, were allowed to stand under carbon dioxide in sealed ampoules. They are assumed to be formed by an ionic mechanism involving addition of the inner salts of *(1a)* or *(1b)* to maleic acid. The acids *(3a)* and *(3b)* were converted by diazomethane into their esters, which could also be prepared by Michael addition of *(1a)* or *(1b)* to dimethyl maleate. Hydrolysis of the esters with hydrochloric acid gave the hydrochlorides of *(3a)* and *(3b)*.

Matrix Spectroscopy

R. D. Werder, Zürich (Switzerland)

The first paper on matrix spectroscopy appeared in 1955. The principle of this technique is to embed a chemically active substance, preferably finely divided, in an inert solid matrix. Spectra obtained from such samples are similar to gas spectra but have certain advantages and certain disadvantages when compared with these. Advantages: substances of low vapor pressure can also be examined; there is no broadening of the absorption bands such as is caused by excitation to higher rotational energy levels. Disadvantages: the original absorption bands are generally shifted a few cm^{-1} to longer wavelengths.

Matrix spectroscopy is not merely a subsititute for gas spectroscopy, for the substance examined may also be an unstable radical or an easily polymerized monomer. At first, only such substances could be studied [1] as could be mixed in the gaseous state at room temperature with the matrix gas. In 1961 *Linevsky* [2] introduced a decisive innovation. By use of a Knudsen cell it was possible to study substances that had very small vapor pressures at room temperature.

[1] *G. C. Pimentel*, J. chem. Physics *25*, 224 (1956).

[2] *M. Linevsky*, J. chem. Physics *34*, 587 (1961).

The molecular beam issuing from the Knudsen cell was immediately condensed, together with the matrix gas, on the cold surface of a sample-container. Generally, neon, argon, krypton, or nitrogen are used as matrix-gas. The sample-container is placed in a low-temperature Dewar flask such that it can be rotated through 90° and the spectra of the sample directly recorded.

The matrix material must fulfill the following conditions: The matrix must be chemically inert and optically transparent, and have little tendency to scatter or to hinder diffusion. An important datum from matrix spectroscopy is the proportion of matrix molecules M to substances molecules A. The table shows the percentage of completely isolated molecules A with various M:A ratios and for various crystal lattices. (The calculation depends on the assumptions that the molecules A and M are of equal size and that there is no interaction between the molecules.) In our experience a ratio M:A = 100 to 1000 suffices to lead to "well isolated" spectra.

M:A	Simple cubic lattice	Body-centered cubic lattice	Face-centered cubic lattice
10000	99.9 %	99.9 %	99.9 %
1000	99.4 %	99.2 %	98.8 %
100	94.1 %	92.3 %	88.6 %
10	53.1 %	43.0 %	28.2 %

The first matrix spectra were taken in the infrared region; the method can, however, be used for recordings in the ultraviolet and visible regions as well as for electron spin resonance spectroscopy. With the aid of this technique we have examined metal halides which exist mainly as solid dimers or tetramers. It could be shown that $NbCl_5$ is monomeric in the gaseous phase, and is composed of dimeric units in the solid phase and in CCl_4 and cyclohexane solutions. [VB 31 IE]

German version: Angew. Chem. 79, 276 (1967)

Semiconductor Chemistry

The "Semiconductor Chemistry" Group of the *Gesellschaft Deutscher Chemiker* held a lecture meeting in Munich on October 18th and 19th, 1966.

From the lectures:

Pyrolytic Preparation of Boron Carbides

By *E. Amberger, M. Druminski,* and *W. Dietze*[*]

Pure boron triiodide is known to give red α-rhombohedral boron on pyrolysis on tantalum wire between 850 and 1100 °C. The great structural similarity between this boron modification and boron carbide, $B_{12}C_3$, prompted us to search for a carbon compound that could be pyrolysed under similar conditions. The preparation of pure boron carbide was then to be attempted by allowing boron and carbon to form simultaneously.

Carbon tetraiodide proved a suitable carbon component. This compound decomposes between 800 and 1050 °C to give pure carbon, particularly in the presence of boron and aluminium iodides.

BI_3 and CI_4 were simultaneously sublimed in a vacuum-tight borosilicate-glass apparatus and decomposed on tantalum wire at 900 to 1050 °C. Between 900 and 950 °C, boron and carbon are deposited together in varying ratios, depending on the ratio of the vapor pressures of the two components; the product is amorphous to X-rays. α- or β-Rhombohedral boron is also formed, depending on the experimental conditions. Above 1000 °C, however, the decomposition yields crystalline boron carbide, which could be unambiguously identified by X-ray analysis.

Pyrolytic Preparation of Silicon Borides

By *W. Dietze* and *E. Amberger*[**]

An apparatus was described for the pyrolytic decomposition of BI_3 and SiI_4, together or successively in any order, at various temperatures on tantalum wire.

The formation of silicon borides between 900 and 1250 °C by successive pyrolysis of BI_3 and SiI_4 was investigated. Below 1000 °C, finely crystalline silicon and amorphous boron, but not α-rhombohedral boron, were deposited; no silicon borides were formed. Above 1000 °C, however, the pyrolysis led to increasing formation of B_3Si at the interface between silicon and boron (which was still deposited only in the β-rhombohedral form).

The pyrolysis of BI_3 at 1200 °C on silicon that had previously been deposited by pyrolysis led to complete formation of B_3Si. An electron probe showed the presence of two boundary layers between the B_3Si and the silicon, one of which is possibly an unknown silicon-boron phase having the composition B_xSi, where $x \leq 1$. It was also found that the phase B_3Si can very widely in composition with no appreciable change in the lattice structure. Silicon diffuses only slowly into an existing deposit of β-rhombohedral boron.

Semiconductor Properties of Hexacyanobenzene

By *N. Karl*[*]

The most thoroughly investigated of the molecular crystals of small organic molecules having semiconductor properties is anthracene. However, this substance has properties which make it not very suitable as a model substance: low mechanical and thermal stability, low symmetry of the molecule and of the lattice, presence of pure σ bonds, presence of hydrogen atoms (possibility of protonic conduction).

Hexacyanobenzene[1] possesses an aromatic π-electron system, and might therefore be expected to exhibit semiconductor properties. The substance crystallizes in the cubic system[2]. It is thermally very stable (sublimation point 494–497 °C/760 mm) and can be obtained in good, relatively inert single crystals; furthermore it contains only nitrogen and carbon, and has at least one π-electron on each atom. Because of these features we decided to investigate it. Single crystals of hexacyanobenzene were prepared from chromatographically purified material in acetonitrile as pale yellow octahedra several millimeters long. In an electric field the crystals are easily polarized. (All measurements were carried out before an appreciable space charge had built up).

[*] Dr. E. Amberger
Dipl.-Chem. M. Druminski
Dr. W. Dietze
Institut für Anorganische Chemie der Universität
8 München 2 (Germany)

[**] Dr. E. Amberger
Dr. W. Dietze
Institut für Anorganische Chemie der Universität
8 München 2 (Germany)

[*] Dipl.-Chem. N. Karl
Physikalisch-chemisches Institut der Universität
78 Freiburg (Germany)

[1] *K. Wallenfels* and *K. Friedrich*, Tetrahedron Letters *19*, 1223 (1963).

[2] *W. Little* and *K. Wallenfels*, Tetrahedron Letters *38*, 3365 (1965).

With the electrodes short circuited these induced charges can be neutralized with white light.

The dark conductivity at 169 °C and at field strengths of 1 to 300 V/mm (crystal thickness 1 mm) accurately obeys Ohm's law. At 20 °C its value is 1×10^{-18} ohm^{-1} cm^{-1} and this increases on heating according to $\sigma = \sigma_0 e^{-E/2kT}$ (activation energy 2.0 eV from 20 to 169 °C).

The photoconductivity (side irradiation of the crystal carrying silver paint electrodes) is 2×10^{-13} ohm^{-1} cm^{-1} at 20 °C and at a photon flux density of about 8×10^{17} photons/cm^2 sec with a wavelength of between 300 and 582 mμ. A good linear relationship is again found between log σ and $1/T$, with an activation energy of 0.52 eV; the relationship is independent of the field strength (10, 30, 100, and 300 V/mm, measured between 20 and 97 °C). At higher temperatures the photocurrent is less than proportional to the applied voltage.

The photocurrent density j_{el} obeys the relationship $j_{el} \propto j_{hv}{}^{3/4}$ over three powers of ten, where j_{hv} is the photon flux density. The quantum yield of the photocurrent is constant for wavelengths between 314 and 582 mμ, and is equal to 5×10^{-9} electrons in the external circuit per photon falling on the crystal (± 10 %), at a photon flux density of 10^{16} photons/cm^2 sec. Like the optical absorption, it falls off rapidly towards greater wavelengths. Thus the optical absorption limit of the π-electrons, the onset of photoconduction, and the thermal activation energy of the dark conductivity all approximately coincide (≈ 2 eV).

Spectroscopic and Electrical Properties of Polymeric Donor-Acceptor Complexes

W. Klöpffer and *H. Rabenhorst*[*]

The spectroscopic and electrical properties of the complexes of poly-*p*-dimethylaminostyrene with the acceptors chloranil, tetracyanoquinodimethane, tetracyanoethylene, and dichloro dicyano-*p*-benzoquinone, the electron affinities of which are between 1.3 and 2.0 eV, were studied. The concentration of the acceptors was varied between 0.01 and 0.5 mole of acceptor/mole of the basic structural unit of the polymer. The ionization energy of the basic structural unit was found to be 7.2 eV.

Spectroscopic examination of the poly-*p*-dimethylaminostyrene/chloranil complex shows a charge-transfer band [(λ_{max} = 680 cm^{-1}) or: (ν'_{max} = 14700 cm^{-1})], while the stronger acceptors are partly to fully converted into radical-anions. No radical-cation derived from the polymer could be detected. Measurement of the Seebeck coefficient for the system poly-*p*-dimethylaminostyrene/tetracyanoquinodimethane showed that the charge carriers are electrons.

[*] Dr. W. Klöpffer
Dr. H. Rabenhorst
Battelle-Institut e.V.
6 Frankfurt (Germany)

It is shown that acceptors that form radical-anions considerably increase the conductivity of the poly-*p*-dimethylaminostyrene ($\sigma_{60\,°C}$ increases from $< 10^{-15}\,\Omega^{-1}$ cm^{-1} to about $10^{-10}\,\Omega^{-1}$ cm^{-1}). The fact that the conductivity of the samples increases rapidly with the acceptor concentration rules out the possibility of a band model for the explanation of the charge transport. The charge transport in these systems is due to electron jumps between radical-anions and neutral acceptor molecules over a potential barrier, the height of which gives the activation energy. A similar conduction mechanism occurs in the case of low temperature conductivity in doped germanium if the majority centers are partly compensated by minority centers.

Macromolecular Organic Semiconductors with Phthalocyanine Structures

G. Manecke, D. Woehrle, and *G. Kossmehl*[**]

Tetracyanothiophene *(1)*, tetracyanofuran *(2)*, and octacyanotriphenylphospholidine *(3)* were converted into polymers having phthalocyanine structures by reaction with various metal acetylacetonates. The reaction of *(1)*, *(2)*, and *(3)* with copper acetylacetonate in various molar ratios and with the addition of *o*-phthalodinitrile was studied.

The products are dark-colored to black, and are insoluble in organic solvents. They were characterized by elemental analysis, by their IR and ESR spectra, and by X-ray analysis.

The d.c. conductivity at a pressure of 1500 kg cm^{-2} was measured between 20 and 150 °C. The activation energy was determined from

$$\sigma = \sigma_0\, e^{-E/2kT}$$

The maximum conductivities at 300 °K are 5.7×10^{-5} for the copper chelate of *(1)*, 1.5×10^{-8} for that of *(2)*, and 2.2×10^{-9} ohm^{-1} cm^{-1} for that of *(3)*. The activation energies are between 0.36 and 1.29 eV. The conductivity increases with increasing pressure. For various metal chelates of *(1)*, there seems to be a relationship between the conductivity and the ionization potentials or the ionic radii of the metals.

Measurement of the thermal e.m.f. of the copper chelates of *(1)*, *(2)*, and *(3)* showed p conduction. Seebeck coefficients of +83 to +3160 μV/°C were obtained for the range 20 to 70 °C. [VB 34 IE]

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[**] Prof. Dr. G. Manecke
Dr. G. Kossmehl
Institut für Organische Chemie der Freien Universität
1 Berlin (Germany)
Dipl.-Chem. D. Woehrle
Fritz-Haber-Institut der Max-Planck-Gesellschaft
1 Berlin-Dahlem (Germany)

Reactor Chemistry

On October 3rd and 4th, 1966, the "Nuclear, Radio-, and Radiation Chemistry" Group of the *Gesellschaft Deutscher Chemiker* and the Kernforschungsanlage Jülich held a symposium on reactor chemistry at Jülich.

From the lectures:

Analytical Studies on Fuels Containing Plutonium

A. von Baeckmann, E. Mainka, and *L. Lindner*[*]

The methods used for the determination of the plutonium content in PuO_2 are as follows (all work with plutonium is carried out in gastight glove boxes, in which a vacuum of 20 mm H_2O is maintained):

1. *Cerimetric determination*[1]: Dissolution in 11 N HNO_3 and 0.05 N NH_4F, oxidation with AgO to PuO^{2+}, addition of NH_2SO_3H and Al^{3+}, reduction with Fe^{2+} to Pu^{4+}, oxidation of the excess Fe^{2+} with Ce^{4+}. (The end-point is determined

[*] Dr. A. von Baeckmann
Dr. E. Mainka
Dr. L. Lindner
Kernforschungszentrum
75 Karlsruhe (Germany)

[1] *J. Corpel* and *F. Regnaud*, Analytica chim. Acta *35*, 508 (1966).

potentiometrically with the Radiometer Titrigraph. The relative standard deviation is 0.2 %).

2. *Coulometric determination*[2]. Reduction to Pu^{3+} at a controlled-potential working electrode at +400 mV (against a saturated calomel electrode) followed by controlled oxidation to Pu^{4+} at +900 mV. (The Numec Electronic Controlled Potential Coulometric Titrator Model 600 is used. The relative standard deviation is 0.25 %).

As a check, the plutonium content is also determined gravimetrically by calcination at 1200 °C to obtain stoichiometric PuO_2. (The relative standard deviation is 0.1 %; on average, the results are 0.1 to 0.2 % higher than those obtained by oxidimetric determinations).

To determine other elements, the solution obtained after separation of the plutonium on ion exchangers (8 N HNO_3) is analysed by emission spectrography[3] for Al, B, Ca, Cr, Cu, Fe, Mg, Mn, Mo, Ni, Pb, and V. To determine traces of carbon, the samples are calcined in a current of oxygen at 1400 °C, and the CO_2 that escapes is determined coulometrically.

The plutonium content in UO_2/PuO_2 fuels is determined cerimetrically and coulometrically; the impurities are determined by emission spectrography. The uranium content is determined either from the sum of the uranium and plutonium[4] as determined by reduction to U^{4+} and Pu^{3+} with $TiCl_3$ and oxidation with Ce^{4+} with potentiometric end-point determination, or, after reduction of the UO_2^{2+} in approximately 60 % phosphoric acid with Fe^{2+} to U^{4+} and oxidation of the residual Fe^{2+} and dilution with 2 N H_2SO_4, by controlled oxidation of the U^{4+} with $Cr_2O_7^{2-}$ to UO_2^{2+}[5]. The end-point is determined with barium diphenylaminesulfonate. (The relative standard deviation for both methods is 0.3 %). For photometric analyses, a spectrophotometer (Zeiss PMQ II) was modified in such a way that the normal sample chamber was firmly attached to a glove box, so that it can be used for the examination of α-emitters. A second sample chamber was introduced between the light source and the monochromator for the analysis of inactive samples. The spectrophotometric determination of traces of boron, fluorine and nitrogen in PuO_2/UO_2 is being investigated.

Separation of Fission Products by Extraction Chromatography

R. Denig, N. Trautmann, and *G. Herrmann*[*]

Alkali metals, alkaline earths, and rare earth metals can be separated by elution chromatography on cation-exchange resins; other fission products as well as fissionable elements can be separated by extraction chromatography of solutions in hydrochloric acid. The extracting agent is adsorbed on a fine-grained support and packed into columns; the mixture is introduced and resolved by elution. Extracting agents tested include di(2-ethylhexyl)orthophosphoric acid (HDEHP), tri-n-butyl phosphate (TBP), tri-n-octylphosphine oxide (TOPO), and tri-n-octylamine (TOA), these agents being adsorbed on polytrifluoromonochloroethylene (Hostaflon C 2).

The partition coefficients of the elements Zn, As(III,IV), Sr, Zr, Nb, Mo, Tc, Ru(III,IV), Rh, Ag, Cd, In, Sn(IV), Sb(III,V), Te(IV), I, Cs, Ba, Ce, Tb, Th, Pa, U, Np(IV,VI) between the stationary phases and 0.1 to 12 N hydrochloric acid were determined. The elements behave towards TBP, TOPO, and TOA as towards anion-exchange resins, *i.e.* anionic complexes are extracted. HDEHP, on the other hand, preferentially extracts highly charged cations at low concentrations of hydrochloric acid, but also extracts anion complexes at high acid concentrations.

The separation scheme for the principal components is as follows:

1. Extraction with TBP from 8 M HNO_3 + $NaClO_3$ (Z_r, U, Np); elution with 8 M HNO_3 + SO_2 (Zr + Np) and water (U).
2. Extraction with HDEHP from 9 M HCl + $NaClO_3$ (Nb, Sb, I); elution with 0.1 M HCl (Sb, I; exchange of I on AgCl) and with 3 M HCl/0.4 M HF (Nb).
3. Extraction with HDEHP from 0.1 M HCl (Mo, rare earth metals); elution with 1.5 M HCl (rare earth metals) and 12 M HCl (Mo).
4. Extraction with TBP from 6 M HCl (Tc, Te); elution of both with 0.4 M HCl.

Sr, Ru, Rh, Cs, and Ba cannot be extracted. Ru is distilled after group 4. from perchloric acid; after the addition of a carrier, Rh is separated by precipitation with ammonia.

Decontamination of Radioactive Waste Water by Salts of Fatty Acids

By *L. von Erichsen*[*]

Many radioactive nuclides (with and without carriers) can be coprecipitated during the precipitation of calcium soaps by potassium salts of higher fatty acids. The decontamination is very nonspecific, calcium soaps being much more effective than Fe or Al salts of fatty acids. Potassium salts of mixtures of fatty acids are more effective than the salt of a single acid. If the calcium hardness of the water is not sufficiently high, Ca may be added in the form of gypsum solution.

The highest decontamination factors (about 12 to $\gg$ 100) are achieved with the alkaline earth and rare earth metals, actinides, and elements from Cr to Zn, while medium decontamination factors (about 10 to 65) are obtained with Y, PO_4, Sb, and Hg. No appreciable decontamination occurs with the alkali metals and halogens (as ions). Where a nuclide exists in several valence states, the decontamination factors for the various states can differ considerably (*e.g.* for Cr, Mn, Tc, I).

With substoichiometric precipitation ($<$ 50 % of the theoretical quantity of soap), the active calcium soaps coagulate well and can be satisfactorily filtered; when dry, they can be briquetted, and the fatty acid can be removed by ashing.

Since the salts of the higher fatty acids with various cations give large lattice constants on X-ray analysis, and since precipitates crystallize only slowly, the simultaneous incorporation of different types of cations (solid solution, adsorption, occlusion) becomes easier to understand. The calcium soaps exhibit lipophilic-polar characteristics and ion-exchanger properties. Moreover, free halogen adds to unsaturated fatty acids.

The process can probably be used for neutral or alkaline radioactive waste waters having wide ranges of activities.

Corrosion of Zirconium and Zirconium Alloys

By *K. H. Lieser*[**]

Radiochemical methods can be used to study the transfer of matter between the surface of a metal and a solution. Autoradiographs are particularly useful in this connection.

[2] *W. D. Shults*, Talanta *10*, 833 (1963).
[3] *A. W. Wenzel* and *C. E. Pietri*, Report NBL-215 (1964).
[4] *J. Corpel* and *F. Regnaud*, Analytica chim. Acta *27*, 36 (1962).
[5] *W. Davies* and *W. Gray*, Talanta *11*, 1203 (1964).

[*] Dipl.-Chem. R. Denig
Dipl.-Chem. N. Trautmann
Prof. Dr. G. Herrmann
Institut für Anorganische Chemie und Kernchemie der Universität
65 Mainz (Germany)

[*] Prof. Dr. L. von Erichsen
Institut für Physikalische Chemie der Universität
Abt. Kernchemie
53 Bonn (Germany)

[**] Prof. Dr. K. H. Lieser
Lehrstuhl für Kernchemie der Technischen Hochschule
61 Darmstadt (Germany)

When heated in an atmosphere of water vapor, zirconium at first shows a parabolic increase in mass with time. The break in the curve indicates the bursting of the oxide film, and the water vapor can then penetrate freely to the metal. Zirconium and zircaloy-2 are remarkably stable in electrolyte solutions, provided that no fluoride ions are present since these form complexes with the metal. Even in 6 N HCl, the average rate of dissolution at 97 °C is only about 0.2 $\mu g\ cm^{-2}\ h^{-1}$. No exchange is observed between labeled zirconium ions in solution and the metal. The labeled zirconium ions in the solution participate to a very small extent in the corrosion, which takes the form of pitting.

The corrosion becomes very much more pronounced in the presence of iron(III) or copper(II) salts. The experimental results obtained under various conditions are compared and discussed. The pitting can be detected even in the early stages by autoradiography. The alloying metals also appear in solution, the iron being present in relatively large amounts.

The behavior of zirconium in solutions with organic solvents, *e.g.* alcoholic hydrochloric acid, is quite different from its behavior in aqueous electrolyte solutions. If the water content is sufficiently low (less than about 1 %), the protective ZrO_2 film cannot be reformed, and the zirconium dissolves rapidly. In zircaloy-2, the alloying metals have a very unfavorable influence; the zirconium is completely corroded. A black residue containing zirconium hydride remains.

The experiments are significant in connection with the use of zirconium and zirconium alloys in reactors moderated with organic liquids. Here the protective ZrO_2 film is open to attack if there is no water present. The unfavorable influence of the alloying metals is probably due to the fact that the ZrO_2 film is no longer so inert when it contains other ions.

Radiometric Isotope-Frequency Analysis of $^{233}U/^{235}U$ Mixtures

By *E. Merz*[*]

Analysis of the fission products of nuclear fuels is generally carried out radiometrically after preliminary quantitative determination of one fission nuclide, *e.g.* ^{95}Zr, ^{137}Cs, or ^{144}Ce. However, this isotope-abundance analysis fails in cases where the two uranium isotopes ^{233}U and ^{235}U, which can both be fissioned by thermal neutrons, are present together, as can occur in thermal thorium breeder reactors.

However, the analysis can be carried out radiometrically by measurement of the neutron-induced radioactivity ratio of two fission nuclides whose fission yields for ^{233}U and ^{235}U are very different. The contents of ^{233}U and ^{235}U in the unknown sample can then be determined by comparison with pure ^{233}U and ^{235}U standards irradiated under identical conditions. Two pairs of nuclides, $^{103}Ru/^{89}Sr$ and $^{103}Ru/^{131}I$, are particularly suitable. The ^{238}U content can be simultaneously determined for the same sample by measurement of the (n,γ)-induced ^{239}Np γ-activity.

The Use of Boron Compounds in Gas-Cooled High-Temperature Reactors

H. Nickel[**]

Control elements containing boron or boron compounds have been considered for use in gas-cooled high-temperature reactors. This raises the important question of the stability of substances containing boron in a graphite matrix at high temperatures.

Emission-spectrographic measurements have shown that in graphite electrodes containing boron (carbon arc), the boron always diffuses towards the focus, *i.e.* towards the hot zone. The rate of this boron transport depends on the chemical nature of the boron compounds, the degree of graphitization, and the density of the graphite matrix. It is suggested that the diffusion mechanism is a combination of volume diffusion through lattice vacancy movement, and grain boundary diffusion.

Coated particles containing boron are suitable for use in the reactor (> 1000 °C) only if they contain a dense, isotropic high-temperature pyrocarbon layer. However, slight migration of the boron through the pyrocarbon layer into the surrounding graphite matrix cannot be completely avoided, even by prolonged heat treatment.

Radiochemical Determination of the Activities of Fission Products in Irradiated Fuel Elements

By *H. Wertenbach* and *A. von Baeckmann*[*]

In the radiochemical determination of the distribution of the various fission products in a fuel element after irradiation, very simple separation and measuring procedures have been developed for the nuclides Sr, Zr, Mo, Ru, Te, I, Cs, Ba, and Ce[1]. An accurately known quantity of an inactive carrier of the element to be determined is added to the solution of the fission products, care being taken to ensure homogeneous mixing of the carrier and the active component.

Precipitation and extraction operations for the isolation of the element in question in a radiochemically and chemically pure state were formerly followed by final precipitation, determination (generally gravimetric) of the chemical yield, and measurement of the activity. An appreciable simplification can be achieved by the addition of a known substoichiometric quantity of precipitant[2]. An accurately known constant proportion of the quantity of carrier added is now precipitated and it is ascertained whether the precipitation was substoichiometric. A separate determination of the chemical yield thus becomes unnecessary and the reproducibility and standard deviations (1–2.5 %) can be improved. The final precipitation is now carried out at boiling point in the following manner:

Sr is precipitated from ammoniacal solution (10 ml, 0.25 mmole of Sr carrier) with exactly 5 ml of 0.02 M oxalic acid. Zr is precipitated from 0.6 N HF solution (8 ml, 0.25 mmole of Zr carrier) with exactly 5 ml of 0.04 M $BaCl_2$ solution. The ratio Ba:Zr in the precipitate is constant (≈ 2.12). Mo is precipitated from phosphate-free acetic acid solution buffered with ammonium acetate (15 ml, 0.4 mmole of Mo carrier) with exactly 5 ml of 0.03 M of $Pb(CH_3COO)_2$ solution. The solution of tellurium(IV) in 3 N hydrochloric acid (10 ml, 0.3 mmole of Te carrier) is mixed with exactly 5 ml of 0.08 M $TiCl_3$ solution to reduce Te^{4+} to Te^0. I (carrier: 0.3 mmole of I) is precipitated from 25 ml of 0.5 N hydrochloric acid solution with exactly 5 ml of 0.01 M $PdCl_2$ solution. Cs (carrier: 0.5 mmole of Cs) is precipitated from acetic acid solution (40 ml) by the addition of exactly 10 ml of 0.0146 M sodium tetraphenylborate solution[2]. Ba is precipitated from weak hydrochloric acid solution (10 ml, 0.25 mmole of Ba carrier) with exactly 5 ml of 0.02 M H_2SO_4 solution. Ce (carrier: 0.25 mmole of Ce is precipitated from 0.02 N nitric acid solution (6 ml) with exactly 5 ml of a 0.025 M oxalic acid solution. [VB 35 IE]

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[*] Priv.-Doz. Dr. E. Merz
Kernforschungsanlage
517 Jülich (Germany)

[**] Dr. H. Nickel
Kernforschungsanlage
517 Jülich (Germany)

[*] Dr. H. Wertenbach
Dr. A. von Baeckmann
Kernforschungszentrum
75 Karlsruhe (Germany)

[1] *A. von Baeckmann, H. Schroeder, H.-H. Stamm,* and *H. Wertenbach,* Abtrennung und radiochemische Bestimmung von Spaltelementaktivitäten, Kernforschungszentrum Karlsruhe, Report No. 387 (1965).

[2] *A. von Baeckmann,* Z. analyt. Chem., *223,* 161 (1966).

The Influence of the Solvent on Coordination-Chemical Reactions

V. Gutmann [*]

Solvents can be classified as donor or acceptor solvents. Interaction of a covalent acceptor molecule and a donor solvent molecule (D) can be measured calorimetrically. The values of $-\Delta H$ (not ΔH^0) for the reaction

$$SbCl_5 \text{ (soln.)} + D \text{ (soln.)} \rightleftharpoons D{\cdot}SbCl_5 \text{ (soln.)}$$

are termed donor numbers, $DN(SbCl_5)$. They are proportional to the equilibrium constants K_1 and the $-\Delta H$ values of the corresponding reactions of the solvent with other acceptors, such as $SbCl_3$, $SbBr_3$, $(CH_3)_3SnCl$, I_2, and phenol.

Formation of a chloro complex on addition of chloride ions is considered as a ligand exchange:

$$D{\cdot}SbCl_5 \text{ (soln.)} + Cl^- \rightleftharpoons [SbCl_6]^- + D \text{ (soln.)}$$

The equilibrium constant is inversely proportional to the donor number of the solvent:

$$DN\ (SbCl_5) \cdot \log K_2 \sim \text{const.}$$

The donor number of a solvent determines its ability to dissolve ionic as well as covalent compounds, also the ionization of dissolved substances, the occurrence of autocomplex formation, and the tendency to formation of coordination compounds with other ligands (competing ligands).

The larger $DN(SbCl_5)$ is, the better is the dissolving power and the greater the ionization. Competing ligands give complexes if they are stronger complexing agents than the solvent. The smaller the donor number, the smaller is the dissolving power and the ionization; thus solvents with relatively small $DN(SbCl_5)$ must be used for reactions with weakly competing ligands. Autocomplex formation is to be expected when the coordination-chemical properties of the donor solvent and competing ligands are similar.

The dielectric constant is important only for ionic dissociation and thus for the electrochemical behavior of solutions.

Steric factors have more effect the higher the coordination number, the smaller the central ion, and the more bulky the solvent molecule.

Numerous examples in, particularly, acetonitrile (DN 15), propylene carbonate (DN 15), trimethyl phosphate (DN 23), and dimethyl sulfoxide (DN 30) are used to show that the donor number can be used to explain the varied behavior of one system, *e.g.* $Fe^{3+} + Cl^-$, in different solvents. Whereas in acetonitrile all the Cl^--coordination forms can be obtained, $FeCl_3$ undergoes autocomplex formation in trimethyl phosphate, and ionization occurs in dimethyl sulfoxide even in the presence of large concentrations of Cl^-:

$$FeCl_3 + 6\ DMSO \rightleftharpoons [Fe(DMSO)_6]^{3+} + 3\ Cl^-.$$

[VB 33 IE]

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[*] Dr. V. Gutmann
Institut für Anorganische und Allgemeine
Chemie der Technischen Hochschule
Getreidemarkt
Vienna VI (Austria)

Recent Studies of Optically Active Polymers

R. C. Schulz [*]

The rotatory dispersion of poly-L-lactide [1] can be described by the Moffit-Yang equation (a) or by the modified two-term Drude equation (b).

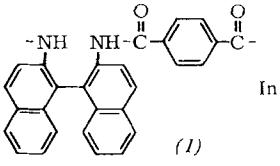
$$m' = a_0 \frac{\lambda_0^2}{\lambda^2-\lambda_0^2} + b_0 \frac{\lambda_0^4}{(\lambda^2-\lambda_0^2)^2} \quad \text{(a)}$$

$$m' = A_1 \frac{\lambda_1^2}{\lambda^2-\lambda_1^2} + A_2 \frac{\lambda_2^2}{\lambda^2-\lambda_2^2} \quad \text{(b)}$$

where m' = the reduced monomer unit rotation; the constants were calculated electronically: $\lambda_0 = 201$ mμ, $\lambda_1 = 225$ mμ, $\lambda_2 = 163$ mμ, for $CHCl_3$ $a_0 = -641$; $b_0 = 311$; $A_1 = 212$; $A_2 = -1402$.

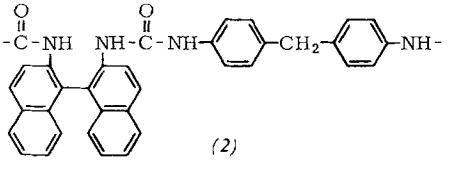
Copolymers of L-lactide with DL-lactide, glycollide, 6-hexanolactone, 3,3-bis(chloromethyl)oxetane, 3-propiolactone, epichlorohydrin, and 1,2-epoxy-4-vinylcyclohexane have been prepared and the influence of composition on the rotatory dispersion has been studied.

Racemisation of atropisomeric groups is much slower when they are present in polymer molecules than when they are present in model compounds of lower molecular weight [2]; but the viscosity of the medium has no influence on the rate of racemisation. Optically active polyamides *(1)* and polyureas *(2)* have been prepared from (+)-1,1′-binaphthalene-2,2′-diamine.



In THF, $[\alpha]_{589} = -20.4$
$[\alpha]_{353} = -2330$

(1)



(2)

On the basis of the helix structure assumed by *Freudenberg* [3] the familiar blue iodine-starch complex should show an induced Cotton effect; in fact, a maximum in the ORD curve occurs at 585 mμ; the circular dichroism is positive, with a maximum at 545 mμ. With a molar ratio I_2/glucose unit = 1:6, $[\alpha]_{580}^{25} = +4000$ (calc. per $C_6H_{10}O_5$). In contrast to the extinction ($\lambda_{max} = 565$ mμ), the rotation is approximately doubled in 40 hours. Factors that destroy the helix structure (heating, addition of urea or detergents) decrease the rotatory power. Addition of solvents (methanol, dimethyl sulfoxide, hexafluoroacetone hydrate) also alter the absorption and rotatory dispersion curves.

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[*] Dr. R. C. Schulz
Organisch-chemisches Institut der Universität
65 Mainz (Germany)

[1] *R. C. Schulz* and *J. Schwaab*, Makromolekulare Chem. *87*, 90 (1965).

[2] *R. C. Schulz* and *R. H. Jung*, Makromekulare Chem. *96*, 295 (1966).

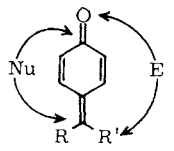
[3] *K. Freudenberg et al.* Naturwissenschaften *27*, 850 (1939); *F. Cramer* and *W. Herbst*, *ibid. 39*, 256 (1952).

Chemistry of Quinonemethides and Quinodimethanes

By *R. Gompper* [*]

ω,ω-Bis(alkylthio)quinomethides [1] *(1a)* and related compounds *(1b)* are ambifunctional nucleophiles and electrophiles.

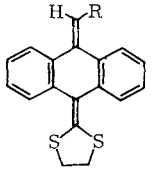
Typical reactions of *(1a)* with electrophiles include those with PCl_5 or $SOCl_2$, whereby, for instance, 4-chloroaryl 1,3-dithiolanium salts are formed. *o*- and *p*-Quinodimethides



(1a), R = R' = SR
(1b), R = R' = NR_2, OR, Hal

differ in their reactions with diphenylketene: whereas the *para*-compounds give diphenylquinodimethanes, dihydrocoumarins are formed from the *ortho*-isomers.

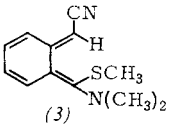
Reaction of *(1a)* with nucleophiles normally leads to removal of RSH, addition of amines gives, for instance, the product *(1b)* with R = R' = NR_2. The CO group is attacked only on interaction of Grignard compounds with compounds of type *(1a)* in the anthracene series; this yields *p*-quinodimethanes *(2)* that are characterized by halochromism (violet coloration). Synthesis of other *p*-quinodimethanes can be achieved (i) by heating phenylmalonodinitrile or related compounds with, *e.g.*, 1-methyl-2-methylthio-1,3-dithiolanium methyl sulfate[2] or (ii) by removal of HX from *N,N*-disubstituted *p*-cyanomethylthiobenzimidic ester salts. The color of quinodimethanes is strongly dependent on the extent of annelation. Some 2-aryl-1,3-dithiolanium salts of related structure were prepared by dehydration of the corresponding aldehyde



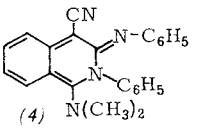
(2), R = Alkyl, C_6H_5

mercaptals, to serve as models for study of the relation between color and constitution.

Method (ii) was used in the first synthesis of an *o*-quinodimethane *(3)* that was stable at −40 to −20 °C, and in which valence isomerisation to the substituted bicyclo[4.2]octatetraene is apparently hindered. Compound *(3)* dimerises rapidly at room temperature to give a dibenzocyclooctate-



(3)



(4)

traene and reacts with acetylenedicarboxylic ester to give a naphthalene derivative. Heterocycles of *o*-quinodimethane structure, *e.g.* *(4)*, are obtained on treatment of *(3)* with diphenylcarbodiimide, phenyl isocyanate, phenyl isothiocyanate, or carbon disulfide. Substitution of *(3)* by 1-fluoro-2,4-dinitrobenzene affords an *o*-quinodimethane that is stable even at room temperature. [VB 40 IE]

German version: Angew. Chem. *79*, 279 (1967)
Lecture in Würzburg on November 18th, 1966

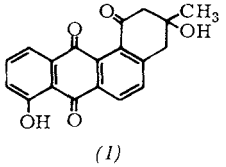
[*] Prof. Dr. R. Gompper
Institut für Organische Chemie der Universität
8 München (Germany)

[1] *R. Gompper, R. R. Schmidt,* and *E. Kutter,* Liebigs Ann. Chem. *684*, 37 (1965); Chem. Ber. *98*, 1374 (1965).

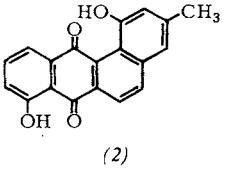
[2] *R. Gompper, E. Kutter,* and *H.-U. Wagner,* Angew. Chem. *78*, 545 (1966); Angew. Chem. internat. Edit. *5*, 517 (1966).

SELECTED ABSTRACTS

Tetrangomycin and tetrangulol, the first benz[*a*]anthraquinone derivatives obtained from natural sources, have been isolated by *M. P. Kunstmann* and *L. A. Mitscher* from *Streptomyces rimosus* cultures. 363 mg of tetrangomycin *(1)*, $[\alpha]_D^{25} = 41.8 \pm 3.5°$ (chloroform), yellow crystals, m.p. 182–184 °C, and



(1)

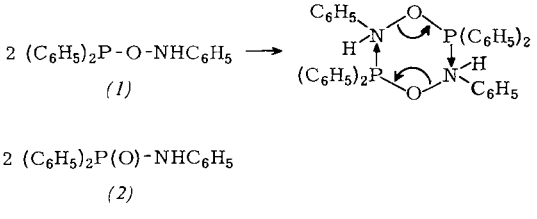


(2)

2.41 g of tetrangulol *(2)*, purple needles having m.p. 189 to 200 °C, were obtained from a 3000 l fermentation. Hydrocarbons with this ring system can act as carcinogens. / J. org. Chemistry *31*, 2920 (1966) / −De. [Rd 605 IE]

1,2-Azaboretidine *(1)* has been synthesized by *S. Åkerfeldt* and *M. Hellström* by the reaction of aziridine with sodium tetrahydridoborate in moist tetrahydrofuran, or in dry tetrahydrofuran with the addition of glacial acetic acid [*(1)*, m.p. 47–48 °C, yield 70 or 73%]. The compound is relatively toxic. Its structure was established from the NMR and IR spectra. / Acta. chem. scand. *20*, 1418 (1966) / −WG. [Rd 606 IE]

An Arbusov-type rearrangement of a >P−O−N grouping has been postulated for the first time by *B. J. W. F. Hibberd* and *B. L. Tonge.* For example, *N,P,P*-triphenyl-*O*-phosphinohydroxylamine *(1)*, which is prepared from equimolar amounts of chlorodiphenylphosphine and phenylhydroxylamine in benzene in the presence of triethylamine or pyridine at 5 °C, rearranges spontaneously and quantitatively to give *N,P,P*-triphenylphosphinamide *(2)*, probably by a six-center synchronous mechanism.



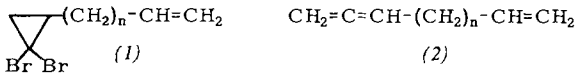
(1)

(2)

However, only compounds of the type $(RO)_2P-O-N<$ have so far been isolated, and not compounds of the type *(1)*. / Chem. and Ind. *1966*, 1599 / −Jg. [Rd 607 IE]

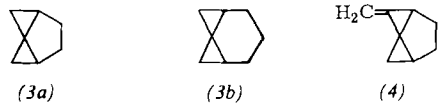
The separation of zirconium and hafnium with *o*-phenylenebis(dimethylarsine) in a single operation has been achieved by *R. J. H. Clark, W. Errington, J. Lewis,* and *R. S. Nyholm.* The rates of precipitation of the complexes $[MX_4 \cdot 2o\text{-}C_6H_4(As(CH_3)_2)_2]$ (M = Zr, Hf; X = Cl, Br) differ considerably. These complexes (coordination number 8, symmetry class D_{2d}) are obtained from the anhydrous tetrachlorides in anhydrous THF. Corresponding complexes can also be prepared with $TiCl_4$ and $TiBr_4$; with TiF_4 and TiI_4, however, the coordination number 8 is evidently no longer reached. The first fraction in the fractional precipitation of a mixture of zirconium and hafnium halides contains 35% of the zirconium used, but no hafnium. A disadvantage of the separation process is probably the need for complete exclusion of air and moisture. / J. chem. Soc. (London) A *1966*, 989 / −Bu. [Rd 617 IE]

Tricyclo[4.1.0.0.^{4,6}]heptane *(3)* **and tricyclo[5.1.0.0^{5,7}]octane** *(4)* have been synthesized by *L. Skatteböl.*

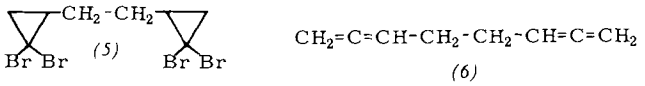


(1) *(2)*

(a): n = 2; *(b)*: n = 3; *(c)*: n = 1



(3a) *(3b)* *(4)*



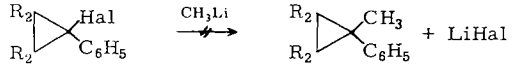
(5) *(6)*

(1a) reacts *e.g.* in ether solution with methyl-lithium to give *(2a)* (b.p. 104 °C, $\nu_{C=C=C}$ = 1950 cm^{-1}) and *(3a)* (b.p. 108 °C) in a total yield of 85%. Similarly, *(1b)* gives *(2b)* (b.p. 64 °C/100 mm, $\nu_{C=C=C}$ = 1950 cm^{-1}) and *(3b)* in 85% total yield, while *(1c)* gives only *(2c)* (b.p. 74 °C, $\nu_{C=C=C}$ = 1945 cm^{-1}) in 46% yield. Compounds such as *(5)* also give tricycloheptanes such as *(4)*, together with diallenes such as *(6)* (b.p. 48–50 °C/25 mm, $\nu_{C=C=C}$ = 1960 cm^{-1}). / J. org. Chemistry *31*, 2789 (1966) / –Bu. [Rd 618 IE]

The stereoselectivity of the addition of olefins to phenylhalocarbenoids (C_6H_5–$CHal_2M$) has been studied by *G. L. Closs* and *J. J. Coyle* and by *R. A. Moss* and *R. Gerstl.* Benzylidene chloride or bromide was allowed to react with strong bases such as potassium t-butoxide (at 25 to 70 °C) or methyl-lithium (at –40 °C) in the presence of olefins having neither a center of symmetry nor a mirror plane parallel to the π-electron cloud. The products are cyclopropanes in which the halogen atom is preferentially attached on the side carrying the largest number of methyl groups ("*anti* form" with regard to the phenyl group; individual phenyl and (to a greater extent) halogen substituents on the carbenoid carbon are *syn*-directing).

Olefin	*anti*/*syn* Ratio	
	(1a)	*(1b)*
2-Methyl-2-butene	1.5	1.28
cis-2-Butene	3.0	1.35
Cyclohexene	2.0	0.33
1-Butene	1.7	—

The *anti*/*syn* ratio does not depend on the base used. This is explained by assuming an interaction to take place between the alkyl groups of the olefin and the substituents on the carbenoid carbon before the formation of the three-membered ring. If methyl-lithium is used in excess, three-membered ring compounds *(2)*, as well as styrene and cumene, are formed in addition to *(1a)*. The ratio of these products depends on whether the methyl-lithium is prepared from CH_3Cl, CH_3Br, or CH_3I; the presence of I^- leads to higher yields.

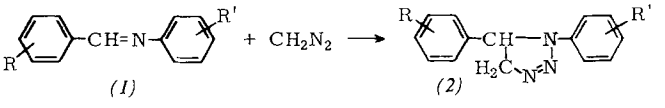


(1a) Hal = Cl *(2)*

(1b) Hal = Br

Reaction of *(1a)* with CH_3Li to give *(2)* could be ruled out. These findings can be explained without the assumption of a carbene intermediate. However, at present, stable carbenoids are known only with Li, and not with K. No stereospecificity is observed when cyclopropane derivatives such as *(2)* are produced from diazo compounds. / J. org. Chemistry *31*, 2759 (1966); Tetrahedron *22*, 2637 (1966) / –Bu. [Rd 619 IE]

The 1,3-dipolar addition of diazomethane to Schiff bases, previous attempts at which having met with little success, has now been achieved in aqueous solvents by *P. K. Kadaba.* This is the more remarkable in that kinetic measurements by the author indicate a one-step synchronous mechanism which is almost independent of the polarity of the solvent. This reaction can be used to obtain good yields of 1,2,3-triazolines *(2)*, which are analytically pure without recrystallization. The new method is far superior to the earlier process, in which *(2)* were prepared by 1,3-dipolar addition of azides to olefins.

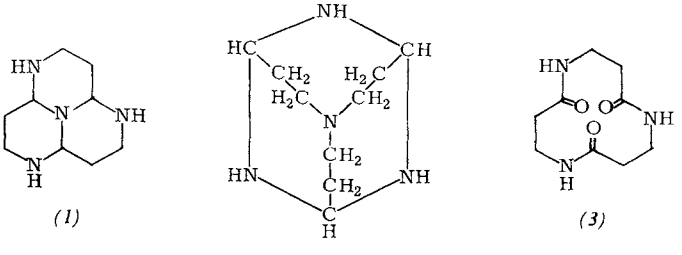


(1) *(2)*

(a) R = H; R' = *m*-Cl
(b) R = *o*-Cl; R' = *m*-NO_2

For example *(2a)*, m.p. 73–74.5 °C could be obtained in 59% yield from *(1a)* in aqueous dioxane after 4 days at 20 °C. Particularly high yields were obtained when R and/or R' = NO_2 [*e.g. (2b)*, m.p. 118–120 °C, 92%]. / Tetrahedron *22*, 2453 (1966) / –Bu. [Rd 620 IE]

Dodecahydro-1,4,7,9b-tetraazaphenalene *(1)* was obtained in 87% yield by *J. L. Van Winkle, J. D. McClure,* and *P. H. Williams* from acrolein and ammonia (molar ratio ≈ 1:10) in methanol at 150 °C and 105 atm.



(1) *(2)* *(3)*

Apart from polymers, only the 1:1 and 2:2 condensation products of acrolein and ammonia were hitherto known. The only way in which a decision could be made between *(1)* and *(2)* was by X-ray analysis of the trishydrochloride (by *A. E. Smith*) and by degradation. A C=N double bond could be introduced in the allyl position with respect to the central nitrogen (yield 44%, m.p. 118–120 °C) by oxidation with $Hg(ac)_2$, while oxidation with $KMnO_4$ gave 1,5,9-triazacyclododecane-4,8,12-trione *(3)* yield 11%, m.p. 300 °C). Hydrolysis of *(3)* gave a 90% yield of β-aminopropionic acid. *(3)* was also reduced with $LiAlH_4$ to 1,5,9-triazacyclododecane (b.p. 77–78 °C/3 mm). *(1)* (m.p. 118–120 °C, b.p. 117 °C/0.1 mm) reacts with HNO_2, H_2O_2, *etc.* as a secondary amine. pK_a values of *(1)* in aqueous solution: 7.6; 5.8; 3.3. Methacrolein and crotonaldehyde probably give homologous products. / J. org. Chemistry *31*, 3300 (1966) / –Bu. [Rd 624 IE]

The trimethylsilyl group can be used as a protective group for aromatic amines in organometallic syntheses. To introduce the protective group, the amines are selectively dimetalated at the nitrogen with C_2H_5MgBr and converted into the *N,N*-bistrimethylsilyl derivatives by treatment with trimethyl-

silane. After reaction, the trimethylsilyl groups can be removed from the nitrogen by refluxing with methanol. In this way, *D. R. M. Walton* converted *p*-bromoaniline into *N,N*-bis(trimethylsilyl)-*p*-bromoaniline (b.p. 106 °C/1.2 mm; n_D^{25} 1.5140); the lithium compound was then prepared by halogen/metal exchange with n-butyl-lithium. Reaction with $(CH_3)_3SiCl$, $(C_2H_5)_3GeBr$, or addition to benzophenone, followed by heating with methanol, gave *p*-trimethylsilylaniline (yield = 90%; b.p. 102 °C/6 mm Hg; n_D^{25} = 1.5348), *p*-triethylgermylaniline (yield = 96%; b.p. 94 °C/0.4 mm; n_D^{25} = 1.5487) or *p*-aminophenyldiphenylmethanol (yield = 76%; m.p. 120 to 121 °C). / J. chem. Soc. (London) C *1966*, 1706 / –Bu.

[Rd 627 IE]

Ag_2^+ ions are formed from silver atoms and silver(I) in γ-irradiated (^{60}Co) vitreous solutions of silver(I) salts, as has been shown ESR-spectroscopically by *L. Shields* and *M. C. R. Symons*. At low temperatures (*e.g.* 77 °K), silver atoms are formed during γ-irradiation; the ESR spectrum changes on slow warming; the new lines can be explained only by formation of Ag_2^+ ions. For further confirmation, similar experiments were carried out with silver salts enriched in ^{109}Ag. The formation of a silver-silver bond appears to be exothermic since all the silver atoms are converted into the dimeric species in the presence of an excess of Ag^+. At higher initial Ag^+ concentrations, the electrons for the formation of Ag^0 (and hence Ag_2^+) can be obtained not only from the solvent, but from Ag^+ ions; it is then also possible to detect Ag^{2+} ions. The Ag^+ ion may also play a part in the primary photographic process. / Molecular Physics *11*, 57 (1966) / –Hz.

[Rd 631 IE]

The states responsible for the photochemical decomposition of formaldehyde in the region of the $\pi^* \leftarrow n$ ($^1A_2 \leftarrow {}^1A_1$) absorption (2200–3700 Å) are described in MO schemes by *E. W. Abrahamson, J. C. F. Littler*, and *Kim-Phan Vo*. The decomposition takes place on occupation of one of the two CH_2-antibonding orbitals with an electron. One of these orbitals has H–H-bonding character ($^1A''$) and leads to decomposition into $CO + H_2$; the other CH_2-antibonding orbital ($^1A'$) also weakens the H–H "bond", and decomposition in this state yields H + HCO or 2H + CO. These two orbitals become occupied by radiationless transitions from the (n, π*) state, which, unlike the ground state (C_{2v} symmetry), has no planar nuclear skeleton (C_s symmetry; angle between CH_2 plane and CO axis: 20.7 °). The decomposition into $CO + H_2$ predominates in the range 3550 to 3700 Å with maximum quantum yields of 0.3. At shorter wavelengths the second type of decomposition becomes increasingly frequent, until at wavelengths lower than 3130 Å, it completely replaces the first type; the quantum yield of the latter type of decomposition is 0.4 to 0.5. / J. chem. Physics *44*, 4082 (1966) / –Hz.

[Rd 632 IE]

Ribosomes and aminoacyltransferase II interact with each other, according to *R. P. Sutter* and *K. Moldave*. The incorporation of amino acids from aminoacyl-tRNA into peptides requires the presence of the two aminoacyltransferases I and II, guanosine triphosphate (GTP), ammonium ions, and a thiol, as well as mRNA and ribosomes. The action of the thiol is based on the activation of the transferase II; the lag phase often observed in the incorporation of amino acids disappeared when transferase II and the thiol are preincubated together. The initial rate of incorporation is further increased when the ribosomes, transferase II, GTP, and ammonium ions are preincubated. mRNA and aminoacyl-tRNA need not be present during this preincubation, and these are added to start the reaction. The transferase II, which is very sensitive to oxidation *e.g.* by oxidized glutathione, is very much less susceptible to oxidation in the reaction product resulting from the preincubation. / J. biol. Chemistry *241*, 1698 (1966) / –Hö.

[Rd 579 IE]

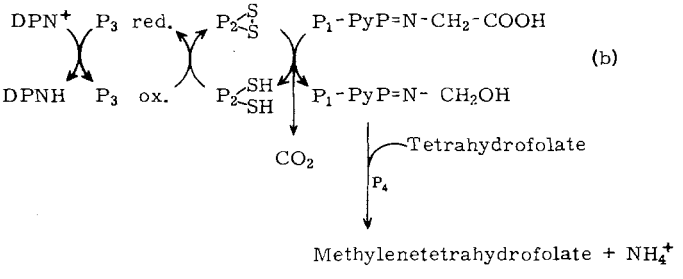
The regulation of the specificity of an enzyme has been observed by *W. S. Beck* and his co-workers. The cobamide-dependent ribonucleotide reductase from *Lactobacillus leichmannii* catalyses the reduction of ribonucleoside triphosphate, CTP, GTP, ATP, and UTP to the deoxyribonucleoside triphosphates by dihydrolipoic acid or by the system thioredoxin/thioredoxin reductase/TPNH. ATP and dATP stimulate the reduction of CTP, while dTTP stimulates that of GTP, dGTP that of ATP, and dCTP that of UTP. 8×10^{-3} M ATP, which acts catalytically (no degradation), is required in order to reduce the Michaelis constant for CTP by a factor of 6. dATP, dCTP, and dTTP inhibit the reduction of ATP, and dGTP inhibits the reduction of GTP. It is assumed that the regulation processes are based on an allosteric mechanism. / J. biol. Chemistry *241*, 2176 (1966) / –Hö.

[Rd 580 IE]

The oxidative decarboxylation of glycine [eq. (a)], according to *M. L. Baginsky* and *F. M. Huennekens*, involves an elec-

$$\text{Glycine} + \text{tetrahydrofolate} + DPN^{\oplus} \rightarrow 5,10\text{-Methylenetetrahydrofolate} + CO_2 + NH_4^{\oplus} + DPNH \quad \text{(a)}$$

tron-transferring protein. Four protein components are required for the reaction: P_1 is a pyridoxal phosphate (PyP) enzyme, P_2 is a small heat-resistant and acid-resistant protein having the properties of the thioredoxin found in *Escherichia coli*, P_3 is a flavoenzyme with the function of a thioredoxin reductase, and P_4 is presumably the catalyst for the formation of the methylenetetrahydrofolate. The roles of P_2 and P_3 are indicated by the following reactions: 1. Chemically reduced P_3 is readily oxidized by DPN. 2. DPN and P_3 can be replaced in the overall reaction by substrate amounts of 5,5'-dithiobis-2-nitrobenzoic acid (*Ellmann's*



reagent). 3. DPNH reduces *Ellmann's* reagent in the presence of P_2 and P_3. Scheme *(b)* is proposed for the decarboxylation of glycine in *Peptococcus glycinophilus*. / Biochem. biophysic. Res. Commun. *23*, 600 (1966) / –Hö.

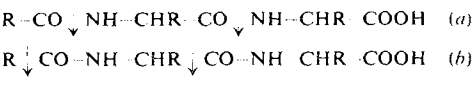
[Rd 581 IE]

Apoferredoxin has been reactivated by *R. Malkin* and *J. C. Rabinowitz*. The free thiol groups in crystallized ferredoxin from *Clostridium pasteurianum* were protected by blocking with Mersalyl (sodium *o*-[(3-hydroxymercuri-2-methoxypropyl)carbamoyl]phenoxyacetate), whereupon the brown color disappeared. The iron was then removed with the weak cation exchanger Chelex 100. The ferredoxin was regenerated with iron(II) salts and 2-mercaptoethanol. When the apoferredoxin was also filtered through Sephadex G25 to remove sulfide ions, renaturation was possible only in the presence of Na_2S. / Biochem. biophysic. res. Commun. *23*, 822 (1966) / –Hö.

[Rd 582 IE]

Methods for the automatic determination of amino acid sequences are reported by *M. Senn* and *F. W. McLafferty*. The determination is carried out by evaluation of mass spectra of peptides with the aid of computers. The peptide

is labeled at the amino end with a group X, so that *N*-terminal fragments can be easily identified. Suitable groups are the trifluoroacetyl, trideuteroacetyl, and CF_2BrCO derivatives, which permit an unambiguous assignment of the mass numbers, owing to the constant isotope ratio. The structure of a linear molecule is established when the fragments containing the introduced group, the possible mass numbers of which can be programmed, have been identified.



Depending on the peptide in question, the fragmentation proceeds almost exclusively in accordance with (*a*) or (*b*). / Biochem. biophysic. Res. Commun. *23*, 381 (1966) / –Hö.

[Rd 583 IE]

BOOK REVIEWS

Zahlentafeln zur Elementaranalyse (Tables for elementary analysis). By *G. Ege*. Verlag Chemie GmbH., Weinheim/Bergstr. 1966. 1st Edit., xxviii, 356 pp., plastic cover, DM 30.–.

The conversion of the percentages found in the elementary analysis of organic compounds into the empirical formula involves a relatively lengthy routine calculation. To avoid this, *Hatt et al.* published a reference work more than ten years ago (for nitrogen-free compounds up to C_{50}, atomic weight basis O=16). This work is now supplemented by *Ege*'s tables, which also cover compounds containing nitrogen.

Ege has used a new arrangement for the percentages (compounds up to C_{40}; basis: $^{12}C=12$), which greatly simplifies the work involved in searches; even in his first "emergency", the reviewer was able to find the correct formula immediately. Very well-chosen and well discussed examples in the "explanations" also provide for cases in which the indices of a formula have a common factor; such cases, as in *Hatt*'s book, are not given directly in the tables *i.e.* $C_{12}H_{18}O_3$ is found only under C_4H_6O, so that the molecular weight differs from that found from the mass spectrum or by titration. The use of other information, such as is often available in practice, is also discussed to enable the reader to make the maximum use of the data given.

A new feature is the inclusion of the *Beynon* unsaturation number R, which the computer has calculated from the H deficit and which gives the number of rings (and multiple bonds); this can be very useful in the establishment of possible structures.

Thus the new tables are found to be extremely useful; since the computer has expressed its results directly, the tables can claim to be "infallible". Mistakes of the kind that the reviewer found in another book of tables (*Stout*, Composition tables), namely, that all the values given for C_{84} to C_{120} are wrong since the computer found no position for the thousands digit and simply left it out, do not occur in *Ege*'s book.

F. Kuffner [NB 545 IE]

Anwendungen der kernmagnetischen Resonanz in der Organischen Chemie (Applications of Nuclear Magnetic Resonance in Organic Chemistry). By *H. Suhr*. Organische Chemie in Einzeldarstellungen (Organic Chemistry Monographs). Vol. 8. Springer-Verlag, Berlin-Heidelberg-New York 1965. 1st ed., viii, 424 pp., 123 illustrations, 110 tables, cloth DM 68.– (*ca.* $17.–).

This book starts with a simple introduction to NMR and is intended for those coming into contact with this method for the first time. It is also intended as a primer in the evaluation of spectra of organic compounds and presents comparative data for this purpose. Thus the author makes no attempt at a rigorous derivation of the observed patterns from theory; he touches only lightly on the technique of measurement and on the preparation of the sample, and he writes not so much for the physical chemist or spectroscopist as for the organic chemist who requires NMR for structural determinations, but cannot study it in full detail. For the last-named audience, this is an easy to follow and recommendable book.

The first 73 pages describe the main features of chemical shift and spin coupling. The two sections on the theory of τ and J values (p. 28 and p. 45) are kept qualitative, and fulfil their purpose admirably. The chapter on splittings of higher order should have explained in greater detail the practical procedure in the analysis of spectra. It is repeatedly suggested that theoretical spectra should be constructed with the aid of equations or tables. However, it is much less time-consuming to leave this work to a computer; a short description of the programs available for this purpose appears more to the point than the reproduction of rarely-used tables from the literature (27 pp.).

The special part of the book dealing with proton resonance (172 pp.) is arranged according to classes of compounds.

The considerable amount of experimental data and references collected makes this book an excellent source of quickly accessible reference values. However some of the many useful tables could have been improved with respect to the clarity and unambiguity of the data presented (*e.g.* p. 87, p. 93, and p. 134). A separate chapter (43 pp.) is devoted to nuclei other than the proton which are important in organic chemistry. The book closes with 77 pages describing a number of special application The topics discussed include solvent effects, hydrogen bonds, substituent effects, equilibria of all types, and conformation of cyclohexanes. The many references to methods of simplifying complicated spectra deserve special mention, since the success of structural determinations often depends on such simplifications.

The book contains many useful formulae and illustrations. The literature is covered up to the end of 1964, and in some cases to early 1965.

A. Mannschreck [NB 531 IE]

Fortschritte der Chemie organischer Naturstoffe (Progress in the chemistry of organic natural products). Edited by *L. Zechmeister*. Vol. 23. Springer-Verlag, Vienna-New York 1965. 1st Edit., viii, 397 pp., 58 figures, cloth DM 93.60.

Chemists interested in natural products will welcome the publication of any new volume of "Fortschritte", and Vol. 23 [*] certainly will be of great benefit to the reader.

In a survey of the polysaccharides of marine algae, *S. Peat* and *J. R. Turvey* discuss not only the chemistry of these compounds, but also their relation to the polysaccharides of higher plants. However, their biosynthesis is not mentioned. On the other hand, *H. Schlubach*'s contribution on carbohydrate metabolism in barley, oats, and millet deals not only with the constitution of the polyfructosans, but also with the enzymatic control of polyfructosan formation. It is interesting to note that the grains preferentially cultivated by man are those in which the amount of polyfructosans is greatest. *F. Schleuk* makes a successful attempt to explain the properties and functions of the biological sulfonium compounds on the basis of their reactions. The experiments, which show that, in some cases of transmethylation, only

[*] For a review of Vol. 22 see Angew. Chem. *78*, 554 (1966); Angew. Chem. internat. Edit. *5*, 529 (1966).

two protons of the *S*-methyl group of methionine appear in the methylation product, unfortunately could not be included.

A comprehensive review of chemical aspects and functions of human and animal hemoglobins is contributed by *W. A. Schrödinger* and *R.T. Jones*. A very original feature is the description of the construction of a paper model of the β-chain of hemoglobin A. The structure and metabolism of collagen are exhaustively discussed in a brilliant article by *W. Grassmann et al.* In the final chapter, *L. M. Jackmann* first presents a short but very informative introduction to nuclear magnetic resonance methods, and then with the aid of a number of typical examples, he discusses the application of NMR to the elucidation of the structures of natural products. Special attention is given to spin decoupling and the application of nuclear resonance to questions of stereochemistry. *H. Grisebach* [NB 547 IE]

ABC der Chemie (ABC of Chemistry) (2 volumes). Verlag Harri Deutsch, Frankfurt 1966. 1st Edit., 1590 pp., numerous illustrations, 40 tables, bound, total price DM 89.80 (about $ 23).

Good reference books are always welcome, and the present 2-volume work must be described as good. It contains some 12000 entries and 800 illustrations. For many of the entries one finds not only definitions, but descriptive articles which partly have the character of handbook articles. For example, under the entry "Lösungsmittel" (solvents) is given a 3½-page table listing 75 solvents with their densities, melting points, boiling points, flash points, methods of drying, and solvent powers. Similarly detailed information is given, *e.g.*, under "Nomenclature", "Coal", "Nuclear reactors", *etc.* The article on "Laboratory", which covers over six pages, unfortunately is rather inane, and the space could have been put to better use.

It is unlikely that everything in a reference work will be correct, but the number of serious errors here is small (*e.g.* adamantane is not a tetracyclic but a tricyclic hydrocarbon, and in the list of Nobel Laureates the merits of *Krebs* and *Lipmann* are interchanged). More often one finds information that is not strictly accurate: for example, in the article on enzymes, it is stated that " ... they enable reactions to proceed that would occur only under extreme conditions in the absence of the catalys "

Nevertheless, the work would have merited the grade "very good" were it not for the fact that the editors have adhered with Teutonic thoroughness to a spelling that is now considered archaic for technical literature. For example, they use "Azetyl-Koferment A" instead of "Acetyl-Coferment A" ("Coenzym" should be used rather than "Coferment" in any case), and "Azetonzyanhydrin" instead of "Acetoncyanhydrin"; one wonders why they did not have the courage to extrapolate to "Azetofenon". *H. Grünewald* [NB 543 IE]

Praktikum der makromolekularen organischen Chemie (Laboratory manual of macromolecular organic chemistry). Edited by *D. Braun, H. Cherdron*, and *W. Kern*. Dr. Alfred Hüthig-Verlag, Heidelberg 1966. 1st Edit., 250 pp., 25 figures, DM 26.—.

In view of the great importance of macromolecular organic chemistry, universities are showing a growing tendency to incorporate this important branch of organic chemistry into their curricula in the form of lectures and special courses. A handy primer corresponding to "Gattermann" for practical organic chemistry therefore has become a necessity. The present work is matched to the situation in Germany, and was produced with the support of the "Plastics and Rubber" Group of the *Gesellschaft-Deutscher Chemiker*.

Many companies have made tested laboratory procedures available to the compilers. The book gives not only a series of excellent and carefully selected examples of the preparation of the various types of polymers, but also a general picture of the precautions to be taken in laboratory preparations (choice of reaction conditions, purification and storage of monomers, temperature adjustment, control and termination of polymerizations, *etc.*). The theory of the macromolecular compounds is also clearly presented in the various experiments. The reviewer finds it rather disturbing that the examples begin with number 300 and that the decimal classification is used elsewhere.

As is only to be expected from these authors, the book is an excellent introduction to practical macromolecular chemistry and will certainly be warmly welcomed in all technical colleges. *H. Hopff* [NB 550 IE]

Physikalische Anorganische Chemie (Physical inorganic chemistry), by *M. D. Sienko* and *R. A. Plane*. Translated and enlarged by *F. Steinbach*. S. Hirzel, Stuttgart 1965. 1st Edit., 46 figures, 32 tables, 160 pp., paper DM 18.—.

One must be quite optimistic in order to believe that an understandable discussion of those fields of physical and theoretical chemistry with which inorganic chemists are currently involved can be treated in 169 small-format pages.

The abundance of material presented, the many useful tables, and the easy reading seems to make this book suitable for the beginner, who is less concerned with understanding and noting every detail, but rather with obtaining a general picture. Precision is not the strong point of the book, and one does not always gain the impression that the authors themselves fully understand what they are writing about, particularly in the chapters on atomic and molecular theory. This impression is probably more pronounced in the German translation than in the original. The German text is in fact clumsy in many places. Expressions translated too literally from the English version often do not correspond to German usage. For example, the correct German term for "normalization" should be "Normierung", rather than "Normalisierung", and "orbital quantum number" is not "Orbitalquantenzahl", but "Nebendnantenzahl". "Legendre polynomials" are not "Kugelfunktionen", "valence bond" is not normally rendered by "Valenzbindung", and hybridization and degeneracy are entirely different concepts. There is no "procedure called resonance". "Der Orbital" sounds odd when one is accustomed to "das Orbital". The reader is recommended to use in addition a more thorough treatment if he is interested in the theoretical part.

W. Kutzelnigg [NB 562 IE]

Kleine Quantenmechanik (Quantum mechanics in brief), by *W. Wessel*. Physik-Verlag GmbH., Mosbach/Baden 1966. 1st Edit., 161 pp., 46 figures, cloth DM 16.80.

As the author remarks in the introduction, he would like his book to appeal to that kind of non-physicist who might have been enthused in the 1920's by *Sommerfeld*'s "Atombau und Spektrallinien" (Atomic structure and spectral lines).

The particle-wave dualism and the particular role of probability statements in quantum theory are well presented. The author is wary of philosophical conclusions, despite his tendency towards belletristic insertions. The central theme of the book is guidance, as simply as this is possible, along the path that led *Heisenberg* to the development of matrix mechanics.

The subject matter is made somewhat difficult to follow by the fact that important and also secondary concepts and equations are simply pulled out of thin air without proof, or with the remark that their proof would be too difficult. Anyone who expects an introduction to the current formalism of quantum mechanics to enable him, for example, to obtain a better understanding of its chemical applications will be disappointed. However, for a theoretical chemist it

may be worth the experience to be presented the familiar one-dimensional free-electron model from quite a different point of view under the unusual name of "reflection oscillator".

W. Kutzelnigg [NB 563 IE]

Einführung in die Chromatographie (Introduction to Chromatography). By *H. Hrapia*. Wissenschaftliche Taschenbücher (Scientific Manuals), Vol. 30. Akademie-Verlag, Berlin 1965. 1st ed., 236 pp., 32 illustrations, 12 tables, paper \$ 8.00.

More or less comprehensive monographs on the various types of chromatography, *e.g.* paper, thin layer, and gas chromatography, already exist. However, until now there has been no German-language "Introduction to Chromatography", so that the 236-page book from the WTB series fills a gap. The author has a lucid style, and knows how to present even difficult ideas in a comprehensible manner. The subdivision is almost too rigid, so that the beginner may overlook the common feature of all these processes. However, a clearer separation of the actual types of chromatography from the numerous operating techniques is desirable. An introductory "Classification" is followed by a 44-page discussion of the theories of chromatography, the mathematical treatment of the plate theory being given more space than is necessary. The section on the "Practice of Column Chromatography" (45 pp.) is very successful. The next-largest section (37 pp.) is that on gas chromatography. A striking feature here is that details are given for the construction of detectors. 23 pages are devoted to paper chromatography, and 13 pages to thin-layer chromatography. Electrophoresis is discussed rather too briefly in 7 pages. References to companies are mainly confined to manufacturers in East Germany. For a second edition, the reviewer would like to see a more international character also in this respect.

On the whole, the book fully achieves its purpose, *i.e.* to introduce the beginner to the various and versatile possibilities of chromatography. It presents a good survey of the field. It can only be hoped that it will lead, not only to the use of one of these methods, but to their rational combination.

E. Stahl [NB 533 IE]

Synthetic Methods of Organic Chemistry, Vol. 20, by *W. Theilheimer*. Verlag S. Karger, Basel-New York 1966. 1st Edit., xiv, 740 pp., sFr 246.00.

The present volume of this well-known series [1] continues to report on modern synthetic reactions in the proven manner. 702 well-chosen articles from the period 1963–1965 cover the entire field of organic chemistry. In view of the growing importance of stereospecific reactions and photoreactions, more space is devoted to these topics. Numerous reactions for the synthesis of complicated isocyclic and heterocyclic ring systems are also included. To limit the volume to a reasonable size, synthetic work that has nothing new to offer with regard to method is omitted. However, the articles in earlier volumes are brought up to date by the list of "Supplementary references" (17 pages).

This comprehensive volume concludes the series 16–20, and accordingly contains all the references of volumes 16–19 in the text and in the index. This index (148 pages) will be welcomed by all who cannot become accustomed to the system of arrangement used throughout the series. The value of the collection is increased by the inclusion of new entries such as "prevention" and "retention" of functional groups. The four pages on important developments in organic chemistry in 1965–1966 are particularly useful.

This series, which was launched some time ago, no longer requires special recommendation. However, it occurs to the reviewer that the a supplementary peep-hole index might be a useful aid to the retrieval of the information collected in the 20 volumes of this work.

S. Hünig [NB 549 IE]

[1] Cf. Angew. Chem. *78*, 555 (1966); Angew. Chem. internat. Edit. *5*, 529 (1966).

The Penicillin Group of Drugs. By *G.T. Stewart*. Elsevier Publishing Company, Amsterdam 1965. 1st ed., xii, 212 pp., 11 illustrations, bound Dutch fl. 27.50 (*ca.* \$ 7.50).

Penicillin, originally the name of an active principle rather than of a definite substance, not only formed the starting point for antibiotics research in general, but also became a collective term for a group of drugs long after its first investigation. The author's description of this development in the first three chapters shows a great deal of detailed knowledge. This part of the book presents interesting information about the history of medicine, though it is not exhaustive, particularly in relation to non-British contributions.

The next five chapters deal with the semi-synthetic penicillins, mainly from the point of view of application. Chapter 9 discusses morphological and biochemical aspects of the mode of action, and the chemical aspects are discussed in Chapter 10. It would have been better if, *e.g.*, of the six structural formulae on page 100, at least one had been correct, and if C-2 of the penicillin skeleton had not been trivalent throughout the book. The general conclusions on the mode of action (Chapter 11) are very cautious. They are intended to show how far away we still are from an understanding of the relationships. Though the pharmacology and toxicology of some penicillins have already been considered, these and the problems of resistance and allergy are again discussed in three further chapters. The book closes with the epidemiologic importance of the penicillins and a brief discussion of the cephalosporins.

The book was not written for the organic chemist, but microbiologists, physicians, and pharmacists will find some fundamental information in it. Care has been taken with its presentation, and the index and reference lists are comprehensive.

H. A. Offe [NB 523 IE]

Théories moléculaires de la Résonance Magnétique Nucléaire. Applications à la chimie structurale. (Molecular Theories of Nuclear Magnetic Resonance. Applications to Structural Chemistry). By *G. Mavel*. Dunod, Paris 1966. 1st ed., x, 325 pp., 64 illustrations, 47 tables, paper F 78.– (*ca.* \$17.–).

In only a few years, high-resolution nuclear magnetic resonance gained an important place alongside other spectroscopic methods in chemistry. In the present book, *G. Mavel* reviews recent publications (subsequent to the book published in 1959 by *Pople, Schneider*, and *Bernstein*) dealing with the theoretical aspects of nuclear magnetic resonance with special reference to the electronic structure of organic molecules. The obvious aim of the author was to provide a bridge between theory and experiment in this rapidly developing field for the chemist who uses nuclear resonance as an aid in his work.

The two introductory chapters (20 pp.) on the interpretation of nuclear magnetic resonance on the basis of the Bloch equations and on the introduction of the chemical shift and nuclear spin coupling, consequently, are short. In the section on the chemical shift (60 pp.), the fundamental principles of the perturbation theory and of the variation method are first described, and the semi-empirical theories by means of which the empirical data have so far been interpreted are then discussed. A similar plan is followed in the chapter (34 pp.) on indirect spin coupling. Unfortunately, the recent development of the theory by the molecular orbital method (*Pople, Santry, Bothner-By*) is mentioned only briefly. The analysis of nuclear resonance spectra (72 pp.) is carried out explicitly for the simpler cases. Tables are given for a number of more complicated cases, and the moment method and iterative methods are mentioned. This chapter also contains a discussion (unfortunately very short) of the spectra of oriented molecules, which have recently attracted considerable attention. The book closes with chapters on multi-quantum transitions (10 pp.), the theoretical aspects of double reso-

nance (34 pp.), and the change in the spectra as a result of chemical exchange (8 pp.).

The book leans closely on the original literature, with the result that the mathematically more demanding chapters often make difficult reading for the beginner. However, as a guide to the growing literature (more than 1800 references are given) this book will be useful to anyone who is concerned with nuclear resonance. *H. Dreeskamp* [NB 524 IE]

Advances in Quantum Chemistry, Vol. 2. Edited by *P. O. Löwdin.* Academic Press, Inc.. New York-London 1965. 1st ed., xi, 372 pp., 79 figures, bound $ 14.50.

Like the first volume of the series, the present volume contains a collection of reviews on aspects of quantum chemistry ranging from general theory through *ab-initio* calculations to semiempirical applications. Strictly speaking, not all the articles are really reviews; for example, the contribution by *McWeeny* and *Steiner* on the theory of "pair-correlated wave functions" resembles more an original paper.

S. F. Boys and *P. Rajagopal*, in their article on "Quantum Calculations", deal with special problems in numerical *ab-initio* calculations for small molecules. *Inga Fischer-Hjalmars* reviews earlier work by other authors as well as her own more recent work on the justification for the neglect of differential overlap in the theory of π-electron systems. The theory of the hyperfine structure in atomic spectra (as well as in ions and complexes) is the subject of the article by *S. M. Blinder*, which includes a very extensive bibliography. *McWeeny* and *Steiner* discuss the theory of pair-correlated wave functions, as known from *Sinanoğlu*'s papers, but in a more rigorous manner within the framework of perturbation theory. In a detailed article on "Quantum Chemistry and Crystal Physics *L. Jansen* presents an absorbing illustration of the importance of short range interactions between three atoms or ions in the explanation of the relative stability of various crystal lattices of inert gases and alkali metal halides. *H. Jehlen* discusses the possible mechanisms for the interaction of large molecules under biological conditions.

Finally, more than one third of the book is taken up by an article by the editor, *P. O. Löwdin*, on "Quantum Genetics and the Aperiodic Solid", in which he presents his not undisputed views on the relationship between the tunneling of proteins in nucleic acids and special aspects of heredity.

W. Kutzelnigg [NB 568 IE]

Chemical Kinetics in Homogeneous Systems. *By M. Ritchie,* Vol. 2 of the Series "University Chemical Texts". Edited by *T. L. Cottrell.* Oliver & Boyd. Edinburgh-London 1966. 1st Edit., viii, 115 pp., 9 figures. 21 s (Paper 13s6d).

After a short introductory passage on experimental methods for the determination of reaction orders, simple reactions, and the temperature-dependence of reaction rates, the author discusses numerous examples of complex reactions, radiation and photochemical reactions, and acid and base catalysis in aqueous solutions. The greatest space is devoted to photochemical reactions. Unfortunately the modern methods for the investigation of fast reactions and the results of these investigations are hardly mentioned. The author has attempted to give the mechanisms deduced for the various reactions from the kinetic measurements. It should be remembered, however, that the reaction mechanisms are only an interpretation of the kinetic measurements, and that the mechanisms are by no means proved by these measurements.

The intention of the author is that this book should occupy a position midway between a chapter in a general textbook of physical chemistry and a detailed monograph on kinetics. This aim is achieved, but little more.

U. Schindewolf [NB 552 IE]

Mathematics for Quantum Chemistry. By *J. M. Anderson.* W. A. Benjamin, Inc., New York-Amsterdam 1966. 1st ed., x, 154 pp., several illustrations, $6.00.

A deep understanding of the quantum-mechanical principles underlying the approximation methods of quantum chemistry requires a familiarity with mathematical techniques and concepts that is generally quite difficult to acquire for the chemist who has not specialized in theoretical chemistry. *Anderson*'s "Mathematics for Quantum Chemistry" is a successful attempt to tackle these difficulties. This short introduction to the mathematical apparatus that is essential for the proper application of quantum mechanics to problems of chemistry is based on a course of lectures intended as a preliminary to a course in quantum mechanics. The book deals with "orthogonal functions" including Fourier series and the special functions of physics (*e.g.* spherical harmonics), "linear algebra" including linear operators and their matrix representation, and contains in a chapter on "classical mechanics", the Lagrangian and Hamiltonian formulations with brief examples of their applications to molecular vibrations and rotations.

The presentation is lively and readily comprehensible, and is supplemented by well-chosen exercises. The occasional reference to detailed textbooks is entirely in line with the aim of this book, *i.e.* to make the abstract world of pure mathematics more accessible to the chemist. The book can be strongly recommended as a stimulating introduction to anyone who wishes to use the methods of quantum mechanics beyond the stage of simple Hückel calculations.

M. Klessinger [NB 532 IE]

The Chemistry of Open-Chain Organic Nitrogen Compounds. By *P. A. S. Smith.* W. A. Benjamin, Inc., New York-Amsterdam. 1st Edit., Vol. 1, 1965; xi, 356 pp., $ 21.45; Vol. 2, 1966: xii, 531 pp., $ 37.50.

Organic nitrogen compounds are treated in textbooks partly as functional derivatives of inorganic nitrogen compounds, *e.g.* amines as substitution products of ammonia, and partly as derivatives of alcohols, aldehydes, ketones, and carboxylic acids (*e.g.* hydrazines, hydrazones, acid hydrazides).

In the present work, the former method of classification is followed throughout. The members of the various classes of compounds appear as derivatives of ammonia, hydrazine, hydroxylamine, *etc.*; this is an unusual approach from the structural point of view, and has the advantage that the organic chemist can see familiar classes of compounds in a new light.

The first of the fifteen chapters presents a brief survey of the inorganic nitrogen compounds on which the organic derivatives discussed are based. The next six chapters deal with ammonia derivatives: aliphatic amines, aromatic amines, amides, nitriles and isonitriles, *N*-derivatives of carbonic acid, and ammonia derivatives of aldehydes and ketones.

The second volume begins with hydroxylamine derivatives, including the amine oxides; this is followed by hydrazine derivatives, azides and diazo compounds, diazonium, azo, and azoxy compounds, substances having chains of three or more nitrogen atoms, *C* nitroso compounds, *C*-nitro compounds, and finally in the last chapter, the esters and amides of the oxo acids of nitrogen.

The various chapters are similar in structure. They start with a discussion of nomenclature, followed by a summary of physical properties, and the main part of each chapter is formed by a clear and systematic treatment of the reactions of the functional group in question. The most important syntheses are given at the end of each section.

In scope and structure, this work is a textbook on organic nitrogen compounds; with its extensive bibliography, which covers the literature up to the beginning of 1965 (some 2560 references), it offers all the comprehensiveness of a handbook. It enables one to obtain a very quick and thorough

grounding on a given class of substances. As can be seen from the contents, the work is intended for the advanced reader, so that the discussion of general problems could well have been shortened as *e.g.* in the case of deamination (Vol.1, p. 36) or the nitration mechanism (Vol. 2, p. 436). Instead, the author might profitably have provided an introductory chapter on bond lengths, energy relationships, hybridization, *etc.* in nitrogen compounds.

The printing errors, which are particularly common in the first volume, should be corrected in future editions. With a little effort it should also be possible to present many of the structural formulae in a clearer form.

Apart from these small defects, the author has succeeded in presenting a comprehensive survey of the chemistry of open-chain organic nitrogen compounds that restricts itself to the description of the functional groups containing nitrogen. It is to be hoped that the work will find a wide audience.

F. Effenberger [NB 548 IE]

Transition Metal Chemistry. Edited by *R. L. Carlin.* Vol. 1 Marcel Dekker, Inc., New York 1966. 1st Edit., xi, 307 pp., numerous figures and tables, cloth $ 12.75.

The present volume begins what should become a very useful series of short monographs on current problems in the field of transition metals. As is shown by a preview of the contents of future volumes, recognized experts will report not only on questions concerned purely with coordination chemistry, but also on special physical and biological results in connection with the transition metals.

In the first chapter (*R. L. Carlin*, 32 pp.) of the present work, the electronic configuration and molecular geometry of a wide range of Co(II) complexes are discussed on the basis of the ligand field theory and with the aid of spectroscopic and magnetochemical results. A well written section by *H. B. Gray* (49 pp.) deals with the electronic structure of square-planar metal complexes from a similar point of view. After an introduction on bonding mechanism and electronic spectra in simple complexes of the type $[M^{II}L_4]^{2-}$, the section deals in particular with the recently discovered systems having bidentate ligands containing sulfur and which are stabilized in a rigidly planar conformation.

Another article (*J. E. Earley* and *R. D. Cannon*, 77 pp.) is concerned with the coordination chemistry of the Cr(III) ion in aqueous systems. Finally, special mention should be made of the excellent section on "Hydrido complexes of transition metals" (*A. P. Grinsberg*, 127 pp.), which presents a systematic survey of practically all molecules and ions of the type $H_iM_jL_k$ (L = any ligand, $k \geq 0$) known up to February 1965 that contain a direct M–H bond. In accordance with the definition, for $k = 0$ the section only deals with ions of the general formula $[M_jH_i]$. In addition to preparative techniques, the author presents a particularly critical discussion o the structure of these complex hydrides and the M–H interaction.

The volume is richly provided with references, and has a good author- but a rather poor subject-index. It is not only a progress report, but also can be recommended to anyone who is interested in modern inorganic chemistry, both as an introduction and for further study. *Th. Kruck* [NB 546 IE]

Advances in Chromatography, Vol. 1. Edited by *J. C. Giddings* and *R. A. Keller.* Marcel Dekker, Inc., New York 1965. 1st ed., xiv, 368 pp., numerous illustrations, bound $14.50.

Modern analysis makes wide use of physical methods. The physical effects on which these methods are based are so numerous that there is a considerable need for textbooks, monographs, or reviews. However, textbooks in particular satisfy only in part the readers information requirements. Though they generally describe the theoretical basis of the method and the principle of the apparatus used, too little space is given to applications to the various classes of substances and to the discussion of special techniques. Finally, most textbooks are outdated by the time they are read, and owing to their limited scope, fail to give the reader the answers to the very questions in which he is interested.

The "Advances in Chromatography", the first volume of which contains four contributions on liquid-phase chromatography and six on gas chromatography, do not exhibit these disadvantages to the same extent as conventional textbooks. Specialists were asked to write on narrowly limited topics in the hope that the authors would give a picture, even subjective, of the current state of development. Accordingly, nearly all the chapters in the first volume are interesting and stimulating. The content of new information of practical value is high. The theoretical and practical aspects of the techniques under discussion are well presented by the authors. Thus the reader of the Advances" is spared the complete study of the original literature, and is nevertheless acquainted with the latest position and the trend of the development of the methods in question. The fact that the individual articles bear little relation to one another detracts little from the value of the book. However, the reader of the chapters on gas chromatography will generally not be so interested in those on liquid chromatography, and *vice versa*. The editors are to be congratulated on their project and the authors on the articles in the first volume, and it is to be hoped that future volumes can also do justice to the editors' intentions.

G. Schomburg [NB 528 IE]

Dynamics of Chromatography. Part 1. Principles and Theory. By *J. C. Giddings.* Series of monographs: Chromatographic Science, Vol. 1. Marcel Dekker, Inc., New York 1965. 1st ed., xii, 323 pp., numerous illustrations, bound $11.50.

The first six chapters present a step-by-step build-up of the general dynamic theory of chromatography as applied to the behavior of the zones, and in particular to the changes in the zone profiles in column chromatography. The seventh chapter alone is devoted to the problems of the actual separation. The author never fails to indicate the relationships between theory and experiment.

The formulae are carefully chosen and clearly listed at the end of the book. One defect, which could easily be rectified in a later edition, is the absence of section numbers at the top of each page. A pleasing feature of the book is the extensive list of references at the end of each chapter, though it must be admitted that practically no recent German-language literature is included.

This book, like the other well-known works on the fundamentals of chromatography, is indispensable to anyone who wishes to penetrate more deeply into this field and who seeks a new approach. It is outstanding for its lucidity of expression and its accurate mathematical formulations without making too heavy demands on the reader's mathematical knowledge.

There are so many elementary physical processes underlying the chromatographic procedures that it seems hopeless to build up a theory that offers a quantitative approach to all chromatographic phenomena which can be utilized in practice. Of the various theoretical models. the conventional "discontinuous plate model is not acceptable in the author's view. The author is not entirely consistent, since he nevertheless regards the conventional concept of plate height, which is used to characterize the chromatographic separating power, as indispensable. In the reviewer's opinon, this inconsistency is one shortcoming of this book, but probably the only one.

On the whole, this is a thorough and interesting treatment of general chromatography; we must therefore wait expectantly to find what results will be achieved by its application to gas chromatography (Vol. 2) and to liquid-phase chromatography (Vol. 3). *E. Palm* [NB 535 IE]

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New Methods of Preparative Organic Chemistry VI[**]

Syntheses of Thiocarbamates

BY W. WALTER AND K.-D. BODE[*]

The methods suitable for the preparation of thiocarbamates are described and illustrated by examples and procedures. They are grouped under the following headings:

1. Addition of Alcohols and Thiols to Isothiocyanates
2. Thioacylation of Amines
   a) with chlorothioformates
   b) with *O,S*-diesters of dithiocarbonic acid
   c) with trithiocarbonates
3. Thioacylation of Alcohols, Phenols, and Thiols
   a) with thiocarbamoyl chlorides
   b) with *N,N*-dialkylmercaptochloroformimidium chlorides
   c) with *N,N'*-thiocarbonyldiimidazole
4. Reaction of Thiocyanates and Cyanates with Hydrogen Sulfide
5. Alkylation of Metal Dithiocarbamates
6. Additions to Thiocyanic Acid

A. Introduction

Following the discovery that thiocarbamates exert many biological actions, ranging from hypnotic, analgesic, and anesthetic to fungicidal, bactericidal, and tuberculostatic activity, these compounds have been investigated by many research groups [1–12b]. The biocidal properties are particularly pronounced in thiocarbamates which can liberate isothiocyanates, as was shown by *Rieche* [7] and *O.-E. Schultz* [8]. *Kreutzkamp et al.* [11] confirmed this observation, and also studied other compounds that can release isothiocyanates, such as cyanothioformamides, dialkylphosphorylthioformamides, and the alkali metal salts of monosubstituted thioformamidosulfonic acids.

However, the activity of many thiocarbamates is not entirely due to this decomposition, since disubstituted compounds of this class, which cannot release isothiocyanates in an organism, are frequently also biologically active. For example, dithiocarbamates of the

[*] Prof. Dr. W. Walter
Chemisches Staatsinstitut,
Institut für organische Chemie der Universität
Papendamm 6
2 Hamburg 13, (Germany)
Dr. K.-D. Bode
present address:
Farbenfabriken Bayer AG
Wissenschaftliches Hauptlaboratorium
509 Leverkusen-Bayerwerk (Germany)

[**] The articles of the first four series have been published by Verlag Chemie Weinheim/Bergstr. English edition: Academic Press, New York-London. Vol. V is in preparation. This article will appear in Vol. VI of the series.

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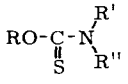
type *(1)* have relatively high fungicidal activities [12]. This is evidently because of the ability of these compounds to react with nucleophiles *(2)* in accordance with equation (a).

$$R_2N{-}CS{-}SCH_2NR_2 \rightleftharpoons \underset{(1)}{R_2N{-}CS{-}S^{\ominus}} + [\overset{\oplus}{C}H_2{-}NR_2 \leftrightarrow CH_2{=}\overset{\oplus}{N}R_2]$$

$$R_2N{-}CS{-}S^{\ominus} + CH_2{=}\overset{\oplus}{N}R_2 + R'^{\ominus} \quad (2)$$

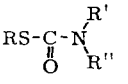
$$\rightarrow R_2N{-}CS{-}S^{\ominus} + R'{-}CH_2{-}NR_2 \qquad (a)$$

The thiocarbamates can be divided into three classes [*(3a)*, *(3b)*, and *(3c)*]. The names primary, secondary,



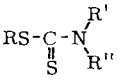
(3a)

O-Alkyl thiocarbamates (*O*-Alkylthiourethanes)



(3b)

S-Alkyl thiocarbamates (*S*-Alkylthiourethanes)



(3c)

Dithiocarbamates (Dithiourethanes)

and tertiary thiocarbamates refer to the substitution of the amino groups. We have investigated only dithiocarbamates and thiocarbamates containing the thioamide group $-C(S)-NR_2$, the oxidation of which was of interest to us [14]. Substances in which the thiocarbamate structure forms part of a ring system or is joined to hetero atoms such as phosphorus and silicon were not considered (see [13, 15, 16]).

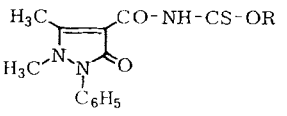
B. Methods

1. Addition of Alcohols or Thiols to Isothiocyanates

Aliphatic alcohols add to isothiocyanates to form secondary thiocarbamates [17–19]:

$$ROH + R'N{=}C{=}S \rightarrow R'NH{-}CS{-}OR$$

The isothiocyanate is usually refluxed for 10–20 hours with a large excess of the alcohol [20–27a]. On the other hand, when the more strongly nucleophilic alkoxide anions are used, the reaction is complete in 10 min. *Kaufmann* and *Lüthje* [27b] obtained *N*-(2,3-dimethyl-5-oxo-1-phenyl-3-pyrazolin-4-yl)carbonylthiocarbamates *(4)* in good yields from the acyl isothiocyanates and alcohols in only 15 min.



(4), R = Alkyl

Göckeritz and *Pohloudek-Fabini* [28] recommend a reaction time of 2 h for the reaction of aliphatic alcohols with aromatic isothiocyanates; the thiocarbamates are obtained in yields of between 40 and 80% (for procedure see Section C, Method 1).

Favorable results are obtained by the addition of aliphatic alcohols to aryl isothiocyanates in dimethyl sulfoxide or dimethylformamide. *N*-Alkyl isothiocyanates react under these conditions on the introduction of potassium t-butoxide [28b].

Table 1. Preparation of secondary thiocarbamates and dithiocarbamates according to $R{-}C_6H_4{-}N{=}C{=}S + R'XH \rightarrow R{-}C_6H_4{-}NH{-}CS{-}XR'$ *(5)*.

Compound	R	R'	X	M.p. (°C)	Ref.	Yield (%)
a	F	CH_3	O	64–65	[28a]	[a]
b	Cl	CH_3	O	92–93	[28a]	[a]
c	Br	CH_3	O	102	[28a]	[a]
d	I	CH_3	O	112–113	[28a]	[a]
e	SCN	CH_3	O	137–138	[28a]	[a]
f	C_2H_5O	*p*-$C_2H_5O{-}C_6H_4$	S	127–128	[25]	60
g	Cl	*p*-$Cl{-}C_6H_4$	S	126–127	[25]	55
h	$(CH_3)_2N$	*p*-$C_4H_9O{-}C_6H_4$	S	146–149	[25]	84
i	C_4H_9O	*p*-$C_4H_9O{-}C_6H_4$	S	88	[25]	85.5
j	$(CH_3)_2N$	*p*-$(CH_3)_2N{-}C_6H_4$	S	151	[25]	57
k	2-CH_3	C_6H_5	S	123–123.5	[28c]	69 [b]
l	2,6-$(CH_3)_2$	C_6H_5	S	114–116	[28c]	90 [b]
m	2,6-$(C_2H_5)_2$	C_6H_5	S	117–118	[28c]	39 [b]
n	2,6-$(CH_3)_2$	3-$C_6H_5{-}C_6H_4$	S	104–105	[28c]	75 [b]

[a] The yields are between 40 and 80%. For other compounds of this type see [28].
[b] Triethylamine considerably accelerates the reaction.

The reactants used in this synthesis may be varied widely; as well as the saturated aliphatic alcohols mentioned above, unsaturated compounds such as β-

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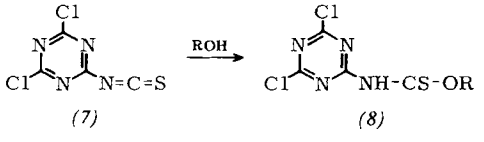
iodopropargyl alcohol [29], pyridols [29a], and quinolinols [29b] may also be used for the preparation of pharmaceutically valuable *O*-alkyl thiocarbamates. On the other hand, various types of isothiocyanates have also been used. Thus *Goerdeler* and *Schenk* obtained *e.g.* the *O*-alkyl thiocarbamate *(6)* from diphenylcarbamoyl isothiocyanate and ethanol [29c]:

$(C_6H_5)_2N-CO-NH-CS-OC_2H_5$

(6)

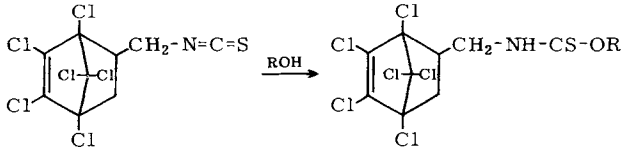
Substituted benzenesulfonyl isothiocyanates react with aliphatic alcohols to give *O*-alkyl thiocarbamates in quantitative yield [29d]. Very reactive members of this class, *e.g. (8)*, which are used as fungicides and herbicides, are obtained by the addition of alcohols to dichlorotriazinyl isothiocyanates *(7)* [30].

Hexachlorobicycloheptenylmethyl isothiocyanate *(7a)* reacts with aliphatic alcohols to form *O*-alkyl thiocarbamates *(8a)*, which are effective fungicides [30a].



(7) *(8)*

R = CH_3, C_2H_5, C_4H_9, $C_6H_5CH_2$

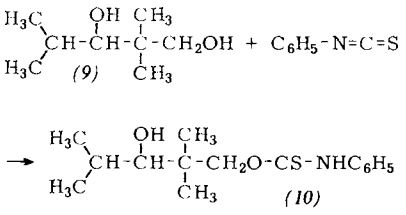


(7a) *(8a)*

R = CH_3, C_2H_5, C_3H_7, i-C_3H_7, n-C_4H_9, i-C_4H_9, sec-C_4H_9

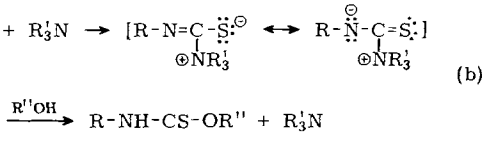
Cherbuliez et al. [30b] studied the addition of diols to phenyl isothiocyanate, which lead to crystalline *O*-alkylthiocarbamates. In the presence of pyridine at 65 to 140 °C, 1,3- to 1,10-diols always give bis (*O*-alkyl thiocarbamates), occasionally together with low yields of *O*-alkyl monothiocarbamates. On the other hand, the reaction of 2,2,4-trimethyl-1,3-pentanediol *(9)* leads only to the formation of the *O*-alkyl monothiocarbamate *(10)*, the structure of which has been verified by NMR spectra.

Under these conditions ethylene glycol gave *N,N'*-diphenylthiourea and by-products, but no *O*-alkyl thiocarbamate. The bis(*O*-alkyl thiocarbamates) obtained from 1,3-propanediols influence the clotting of blood [30c].



(9) *(10)*

The addition of alcohols to isothiocyanates is a second-order reaction [31]. Since the nucleophilic character of aliphatic alocohols decreases with increasing chain length, their reactivity is low, therefore it is recommended that the more strongly nucleophilic alkoxide ions should be used [2, 27, 32–35]. The reaction can also be accelerated by the addition of catalytic quantities of triethylamine [31, 36], diethylamine, or pyridine [30b, 37], as shown in equation (b).



(b)

The reactivities of *m*- and *p*-substituted phenyl isothiocyanates with hydroxide ions [37a, 37b] obey the Hammett equation. The rate of reaction increases with decreasing π-electron density on the C atom of the NCS group (Table 2). The rate is increased by sub-

Table 2. Rate constants for the addition of hydroxide ions to aryl isothiocyanates Ar—N=C=S [37a, 37b].

Ar	k (30 °C) (l·mol·min^{-1})	Ar	k (30 °C) (l·mol·min^{-1})
C_6H_5	7.51 ± 0.20	α-$C_{10}H_7$	6.13 ± 0.27
4-Cl—C_6H_4	40.4 ± 1.4	β-$C_{10}H_7$	11.6 ± 0.6
4-Br—C_6H_4	36.4 ± 1.0	4-Br-α-Naphthyl	23.0 ± 0.4
4-I—C_6H_4	37.1 ± 1.1	1-Br-β-Naphthyl	16.5 ± 2.1
3-Cl—C_6H_4	63.9 ± 3.6	Acridin-2-yl	84.5 ± 7.4
3-Br—C_6H_4	54.7 ± 1.5	Acridin-3-yl	53.6 ± 2.4
3-I—C_6H_4	56.2 ± 1.6	Acridin-4-yl	54.1 ± 1.8
4-HOOC—C_6H_4	14.0 ± 0.7	Acridin-5-yl	100
3-HOOC—C_6H_4	5.76 ± 0.21		
4-C_2H_5OOC—C_6H_4	84.0 ± 2.4		
4-$(CH_3)_2N$—C_6H_4	1.70 ± 0.05		
3-$(CH_3)_2N$—C_6H_4	4.05 ± 0.26		
3-NC—C_6H_4	154 ± 5.6		
2,4-Cl_2—C_6H_4	77.5 ± 2.3		

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[29c] *J. Goerdeler* and *H. Schenk,* Chem. Ber. *98*, 2954 (1965).

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stituents having a –I effect, the values for *m*-cyanophenyl and 5-acridinyl isothiocyanates being particularly high. *o*-Substituted aryl isothiocyanates frequently react more slowly than would be expected from the substituent; this is due to the steric influence of the *o*-substituent, which is even more pronounced in the 2,6-disubstituted aryl isothiocyanates [37].

The increased reactivity of halogenated phenyl isothiocyanates has been utilized for the paper-chromatographic separation and identification of aliphatic alcohols [28].

The literature contains contradictory reports on the reaction of isothiocyanates with thiols. Since the resulting secondary dithiocarbamates readily decompose into the starting substances [38,39], this method was regarded as unsuitable for the preparation of dithiocarbamates; on the other hand, aromatic dithiocarbamates prepared in this way have been described [25]. We have found that the method gives dithiocarbamates in good yields, which are analytically pure and are therefore not susceptible to decomposition during purification [28c] (see Table 1). *Asinger* and *Gentz* [39a] recently obtained the compounds *(12)* and *(14)* in very good yields by the reaction of phenyl isothiocyanate with 4,4-dimethyl-3-mercapto-2-pentanone *(11)* and 4,4-dimethyl-1-mercapto-2-pentanone *(13)* respectively; it must be assumed that the sterically hindered mercapto group in *(11)* is activated by the adjacent acyl group.

$$\underset{(11)}{CH_3\text{-}CO\text{-}CHSH\text{-}C(CH_3)_3} + C_6H_5NCS \rightarrow \underset{(12)}{CH_3\text{-}CO\text{-}\overset{\displaystyle S\text{-}CS\text{-}NHC_6H_5}{\overset{|}{C}}H\text{-}C(CH_3)_3}$$

$$\underset{(13)}{(CH_3)_3C\text{-}CH_2\text{-}CO\text{-}CH_2SH} + C_6H_5NCS \rightarrow \underset{(14)}{(CH_3)_3C\text{-}CH_2\text{-}CO\text{-}CH_2\text{-}S\text{-}CS\text{-}NHC_6H_5}$$

Triphenylmethyl isothiocyanate *(15)* differs appreciably from the other isothiocyanates in its chemical behavior. With nucleophilic reagents for example, it can undergo not only addition [eq. (c)], but also substitution [eq. (d)] [39b,39c].

$$(C_6H_5)_3C\text{–}N{=}C{=}S + ROH \rightarrow (C_6H_5)_3C\text{–}NH\text{–}CS\text{–}OR \quad (c)$$

$$(C_6H_5)_3C^{\oplus} + NCS^{\ominus} + ROH \rightarrow (C_6H_5)_3COR + NCS^{\ominus} + H^{\oplus} \quad (d)$$

The reactions with methanol and ethanol lead to ether formation, whereas 2-propanol, cyclohexanol, and cyclopentanol give ketones [39d].

$$\underset{(15)}{(C_6H_5)_3C\text{–}N{=}C{=}S} + RR'CHOH \rightarrow (C_6H_5)_3CH + NCS^{\ominus} + RR'CO + H^{\oplus}.$$

The addition of alcohols to *(15)* as indicated in equation (c) can be achieved by the use of the alkoxides in a suspension in xylene at room temperature [39c]. The reactivity of the alcohols in this addition reaction decreases in the following order:

$$C_2H_5 > i\text{-}C_3H_7 \approx C_6H_{11} > CH_3.$$

The addition of alcohols or thiols to isothiocyanates (Method 1) is best suited for the preparation of *N*-aryl-*O*-alkyl thiocarbamates. Phenols give unsatisfactory results [40], and *O*-aryl thiocarbamates are better prepared by the following method (Method 2a).

2. Thioacylation of Amines

a) With Chlorothioformates

Alkali metal salts of alcohols [21], phenols [14,41–43], and thiols [3,44,45] react with thiophosgene under mild conditions to form the easily handled chlorothioformates or chlordithioformates:

$$RX^{\ominus}Na^{\oplus} + CSCl_2 \rightarrow RX\text{–}CS\text{–}Cl + NaCl$$

X = O, S

R = Alkyl, aryl

The reaction with enols, on the other hand, has so far been unsatisfactory [11], presumably because *C*-thioacylation occurs as well as the desired *O*-thioacylation.

The chlorothioformates and chlorodithioformates, which are often obtained in yields of more than 90%, are very suitable agents for the thioacylation of ammonia, primary and secondary aliphatic amines, and aromatic amines, as well as for hydroxylamines [1,3,4,14,21,42,45a,46–52d].

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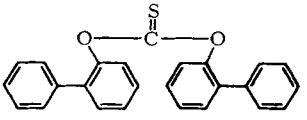
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$$R{-}X{-}CS{-}Cl + 2\ R'_2NH \rightarrow R{-}X{-}CS{-}NR'_2 + R'_2NH{\cdot}HCl$$

X = O, S
R′ = H, alkyl, aryl

Triethylamine, sodium hydrogen carbonate, or alkali metal hydroxides may also be used as acid acceptors instead of the amine undergoing thioacylation. It is interesting to note, however, that the reaction of 2-biphenylyl chlorothioformate with 2,6-dialkylanilines in the presence of triethylamine leads not to the expected thiocarbamate, but to *O,O′*-di-2-biphenylyl thiocarbonate *(16)* [53]:

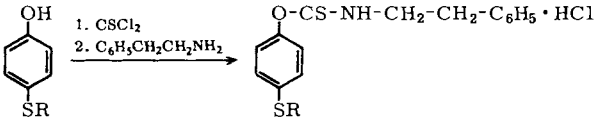


(16)

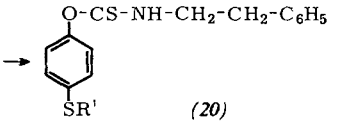
Similarly, the reaction of aryl chlorodithioformates with aromatic amines yields trithiocarbamates as well as the corresponding thioureas [53a].

However, this method normally gives good results, which cannot be achieved by any other method in the case of secondary and tertiary thiocarbamates (for procedure see Section C, Method 2a).

The versatility of the method is illustrated by the synthesis of the water-soluble thiocarbamate *(20)*: *Rieche et al.* [1] treated the thioglucoside *(18)* with thiophosgene to form the chlorothioformate, which was converted into the thiocarbamate *(19)* by reaction with phenylethylamine without prior isolation. Deacetylation of *(19)* yields the water-soluble compound *(20)*.



(18) *(19)*



(20)

R = Tetraacetyl-β-D-glucosyl R′ = β-D-Glucosyl

b) Thioacylation with *O,S*-Diesters of Dithiocarbonic Acid (Xanthates)

Alcohols react with carbon disulfide and bases to form salts of xanthic acid, which can be *S*-alkylated to form esters [53b].

$$ROH + CS_2 + NaOH \rightarrow RO{-}CS{-}S^{\ominus}Na^{\oplus}$$
$$RO{-}CS{-}S^{\ominus}Na^{\oplus} + R'I \rightarrow RO{-}CS{-}SR' \quad (21)$$

These esters react with ammonia to give moderate yields of thiocarbamates [54–67]. Better results can be

Table 3. Thiocarbamates and dithiocarbamates by thioacylation of ammonia or amines with chlorothioformates RX—CS—NRR′ *(17)*.

Compound	R	R′	R″	X	M.p. (°C)	Yield (%)	Ref.
a	C_6H_5	H	H	O	132 [a]	51	[14]
b	*o*-CH_3—C_6H_4	H	H	O	155—156.5 [a]	49	[14]
c	2,6-$(CH_3)_2C_6H_3$	H	H	O	171—172 [a]	31	[14]
d	2,6-$(C_2H_5)_2C_6H_3$	H	H	O	156.5—158 [a]	35	[42]
e	2,6-$(i\text{-}C_3H_7)_2C_6H_3$	H	H	O	230—231 [a, b]	30	[42]
f	C_6H_5	C_6H_5	H	O	143 [c]	90	[4]
g	C_6H_5	*p*-Cl—C_6H_4	H	O	130 [c]	91	[4]
h	*p*-CH_3O—C_6H_4	$C_6H_5CH_2CH_2$	H	O	107 [c]	84	[4]
i	C_2H_5	*p*-H_2NSO_2—C_6H_4	H	O	182 [d]	80—90 [i]	[2]
j	C_6H_5	*p*-H_2NSO_2—C_6H_4	H	O	180—182 [e]	80—90 [i]	[2]
k	C_6H_5	*o*-CH_3—C_6H_4	H	O	109.5—111.5 [a]	73	[14]
l	C_6H_5	2,6-$(CH_3)_2C_6H_3$	H	O	102.5—103 [c]	61	[14]
m	2,6-$(CH_3)_2C_6H_3$	C_6H_5	H	O	169—169.5 [a]	65	[14]
n	*o*-C_6H_5—C_6H_4	2,6-$(CH_3)_2C_6H_3$	H	O	134—135 [c]	68	[53]
o	*o*-C_6H_5—C_6H_4	2,6-$(C_2H_5)_2C_6H_3$	H	O	97—99 [f]	49	[53]
p	C_6H_5	*c*-C_6H_{11}	*c*-C_6H_{11}	O	128 [c]	81	[4]
q	C_6H_5	$C_6H_5CH_2$	H	S	67—68 [g]	61 [j]	[3]
r	*p*-Cl—C_6H_4	$C_6H_5CH_2$	H	S	90—91 [g]	66 [j]	[3]
s	*p*-CH_3—C_6H_4	$C_6H_5CH_2$	H	S	86—87 [h]	75 [j]	[3]
t	C_6H_5	$C_6H_5CH_2CH_2$	H	S	73—74 [h]	76 [j]	[3]
u	C_6H_5	C_6H_5	H	S	124—127 [h, b]	53	[53a]
v	C_6H_5	*o*-CH_3—C_6H_4	H	S	115—117 [k]	21	[53a]

[a] From benzene. [b] Measured in a sealed tube. [c] From benzene/petroleum ether. [d] From ethanol. [e] From acetone. [f] From methylcyclohexane. [g] From ethanol/petroleum. [h] From petroleum. [i] Yields from several experiments. [j] Crude yields. [k] From chloroform/petroleum ether.

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obtained with aliphatic amines, alkyl dithiocarbonates [*(21)*, R = R′ = alkyl] having proved particularly suitable as the xanthate component [68–71].

$$RO{-}CS{-}SR' + R''NH_2 \rightarrow RO{-}CS{-}NHR'' + R'SH$$
(21)

(Alkoxythiocarbonylthio)acetic acids *(21a)*, which are obtained by reaction of alkali metal xanthates with sodium chloroacetate, react with primary and secondary amines to form thiocarbamates in good yield, with liberation of thioglycolic acid *(22)* [35,55,57,72].

$$RO{-}CS{-}SCH_2CO_2H + R'NH_2 \rightarrow RO{-}CS{-}NHR' + HSCH_2CO_2H$$
(21a) *(22)*

This method is particularly suitable for the preparation of primary aliphatic thiocarbamates, which are difficult to obtain by other methods. The reaction of the dithiocarbonates *(21a)* with glycine leads to good yields of thiocarbamate derivatives. An example of this interesting group of compounds is *N*-ethoxythiocarbonylglycine, the synthesis of which is described in Section C, Method 2b.

Replacement of the alkoxy group in compounds of the type *(21a)* by an alkylthio group leads to the trithiocarbonates, which react with amines to form dithiocarbamates.

c) Thioacylation of Amines with Trithiocarbonates

Diesters *(23)* of trithiocarbonic acid can be prepared from thiols and thiophosgene (for procedure see Section C).

$$2\,ArSH + Cl{-}CS{-}Cl \xrightarrow{NaOH} ArS{-}CS{-}SAr + NaCl$$
(23)

These compounds (also with heterocycles as "Ar") may be used for the thioacylation of amines, particularly piperidine [70,74,74a]. *N*-Ethylaniline and diphenylamine do not react. Primary amines are also unsuitable, since the monosubstituted dithiocarbamates *(24)* decompose under the conditions of the reaction to form thiols and isothiocyanates, which can then react further to give thioureas [75]:

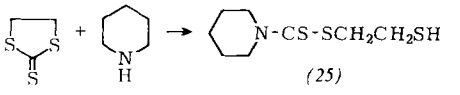
$$ArS{-}CS{-}SAr + RNH_2 \rightarrow ArS{-}CS{-}NHR$$
(23) *(24)*

$$ArS{-}CS{-}NHR \rightleftharpoons ArSH + RNCS$$
(24)

$$RNCS + RNH_2 \rightarrow RNH{-}CS{-}NHR$$

As can be seen from Table 4, tertiary dithiocarbamates can be obtained in very good yields by this method, provided that the above limitations are borne in mind. However, this method is of no great preparative importance, since the alkylation of metal dithiocarbamates (see Sections B.5 and C, Method 5) using more readily obtainable starting materials is preferable.

An interesting example of the use of the reaction is the synthesis of the very sensitive *S*-(β-mercaptoethyl)dithiocarbamate *(25)* [74a,76]:



(25)

Table 4. Dithiocarbamates by thioacylation of amines with trithiocarbonates [75] [solvent ethanol; ether for *(26g)*].

Compound	ArS–CS–NR$_2$ *(26)* Ar	R_2	M.p. (°C)	Yield (%)
a	*p*-CH_3–C_6H_4	$(CH_2)_5$	121–121.5	95
b	*p*-CH_3O–C_6H_4	$(CH_2)_5$	107.5–108.5	93
c	2,4-Cl_2–C_6H_3	$(CH_2)_5$	94.5–95.5	90
d	4-Cl-α-Naphthyl	$(CH_2)_5$	128.5–129.5	91
e	*p*-Br–C_6H_4	$(CH_2)_5$	120.5–121.5	96
f	2,5-Br_2–C_6H_3	$(CH_2)_5$	117.5–118.5	98
g	2-Benzo[1,3]thiazolyl	$(C_2H_5)_2$	80	97
h	4-Phenyl[1,3]thiazolyl	$(C_2H_5)_2$	94–95	90

Tertiary thiocarbamates have been obtained by the reaction of diaryl thiocarbonates with secondary aliphatic amines [76a].

3. Thioacylation of Alcohols, Phenols, and Thiols

a) With Thiocarbamoyl Chlorides

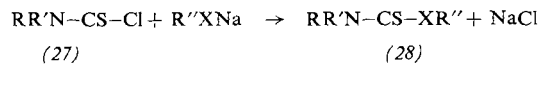
Thiocarbamoyl chlorides (chlorothioformamides) *(27)* are obtained by chlorolysis of thiuram disulfides [78] or better, by reaction of amines with thiophosgene [79].

$$R_2N{-}CS{-}S{-}S{-}CS{-}NR_2 + Cl_2 \rightarrow 2\,R_2N{-}CS{-}Cl + 2\,S$$
(27)

$$2\,R_2NH + Cl{-}CS{-}Cl \rightarrow (27) + R_2NH{\cdot}HCl$$

Alcohols, phenols, and thiols (frequently used as the alkali metal salts) react with the compounds *(27)* to form thiocarbamates or dithiocarbamates in good yields.

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[73] *E. B. Knott*, US-Pat. 2691581 (Oct. 12th 1954), Eastman Kodak; Chem. Abstr. *49*, 83 (1955).
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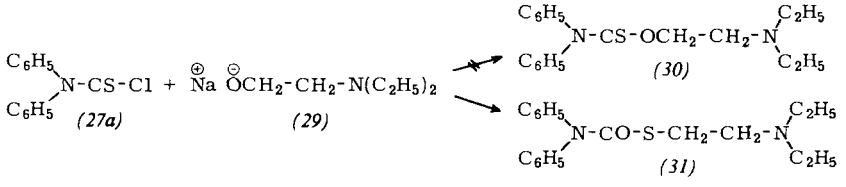


(27) (28)

X = O, S

Since the primary and particularly the secondary thiocarbamoyl chlorides *(27)* are not very stable, this reaction is used almost exclusively for the synthesis of tertiary thiocarbamates[14,21,48,80,81] and dithiocarbamates[41,82–85c] (see Table 5 and procedure for *(28a)* in Section C). *Battegay* and *Hégazi*[86] have used this method for the preparation of primary thiocarbamates, though these are better prepared by other methods. Primary and secondary thiocarbamoyl chlorides *(27)* are of little interest in this connection because of their low stability and sensitivity to moisture[87]; a number of disubstituted thiocarbamoyl chlorides also decompose readily. Thus *N*-t-butyl-*N*-ethylthiocarbamoyl chloride decomposes even during distillation, with formation of ethyl isothiocyanate and probably isobutylene[88].

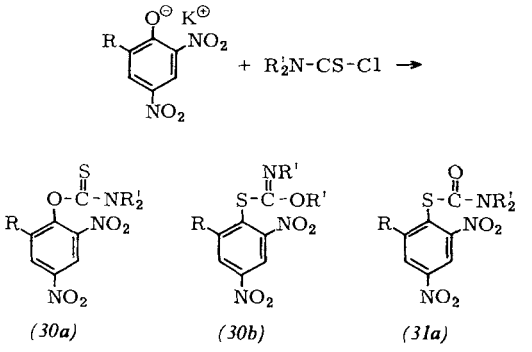
It should also be noted that in these syntheses, rearrangement to form *S*-alkyl thiocarbamates *(31)* frequently occurs[89]. For example, the reaction of diphenylthiocarbamoyl chloride *(27a)* with the sodium salt of *N,N*-diethylaminoethanol *(29)* yields not the expected *O*-substituted thiocarbamate *(30)*, but the *S*-substituted compound *(31)*.



(27a) (29) (30) (31)

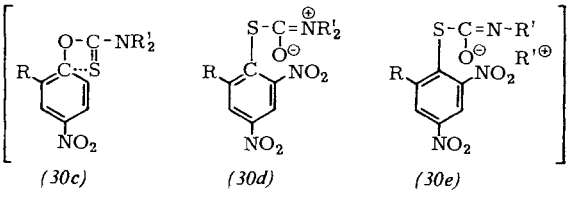
This rearrangement depends on the substitution of the thiocarbamoyl chloride; *N*-phenyl-*N*-ethylthiocarbamoyl chloride gives the expected *O*-substituted thiocarbamate. The nucleophilic component also plays a part, since this abnormal reaction behavior is observed particularly with amino alcohols of the type *(29)*.

Edwards and *Pianka*[89a] recently reported similar observations in the reaction of *o*-substituted 2,4-dinitrophenoxides with aliphatic thiocarbamoyl chlorides. Depending on the substituent R and on the reaction conditions, these authors obtained an *O*-aryl thiocarbamate *(30a)*, an *O*-alkyl alkylimidothiocarbonate *(30b)*, or an *S*-aryl thiocarbamate *(31a)*.



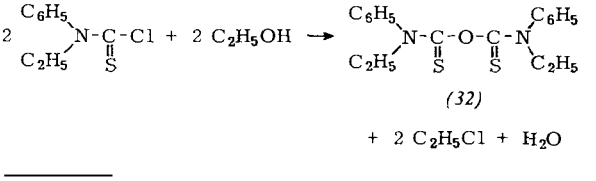
(30a) (30b) (31a)

The *O*-aryl thiocarbamates *(30a)* are formed at high temperatures when R = t-butyl; *O*-alkyl alkylimidothiocarbonates *(30b)* are formed as by-products, whereas *(30b)* are the only products at room temperature. When R = s-butyl, on the other hand, the *O*-aryl thiocarbamates and the *O*-alkyl alkylimidothiocarbonates *(30b)* rearrange to form the *S*-aryl thiocarbamates *(31a)*. The authors explain this difference as resulting from the weaker +I effect of the s-butyl group and its smaller bulk. They propose the transition states *(30c)* and *(30e)*, the most important step being assumed to be an attack of the nucleophilic sulfur on the phenolic carbon atom.



(30c) (30d) (30e)

Kwart and *Evans*[89b] and *Newman* and *Karnes*[89c] have developed the thermal rearrangement of thiocarbamates into a preparatively useful method for the conversion of phenols into thiophenols that are otherwise difficult to obtain. In the reaction of free alcohols with thiocarbamoyl chlorides, the alcohols are not thioacylated, but halogenated, a thiocarbamic anhydride *(32)* being formed also[90].



(32)

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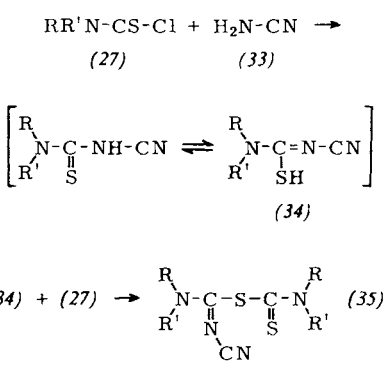
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[90] *O. Billeter*, Ber. dtsch. chem. Ges. *20*, 1629 (1887).

A new type of disubstituted dithiocarbamate *(35)* was obtained by *Davidson* and *Peak* [91] by the thioacylation of cyanamide *(33)*.

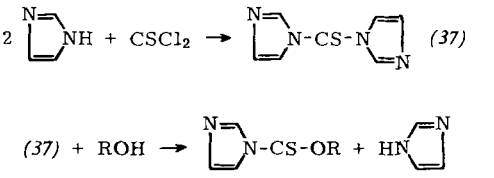


Some examples of tertiary thiocarbamates and dithiocarbamates are shown in Table 5.

c) Thioacylation with *N,N'*-Thiocarbonyldiimidazole

Thioacylation with *N,N'*-thiocarbonyldiimidazole *(37)* [93] is of little general interest, since it leads only to the thiocarbamate derivatives of imidazole.

Thiophosgene reacts with imidazole to form the compound *(37)*, which transfers its thioacyl group to alcohols and phenols.



(38a), R = C_2H_5, yield 76%
(38b), R = C_6H_5, yield 78%
(38c), R = β-naphthyl, yield 74%

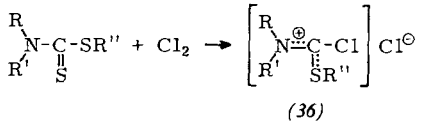
Table 5. Thiocarbamates and dithiocarbamates by thioacylation of nucleophilic compounds with thiocarbamoyl chlorides RR'N–CS–XR'' *(28)*.

Compound	R	R'	R''	X	M.p. (°C)	Yield (%)	Ref.
a	CH_3	CH_3	*o*-NO_2–C_6H_4	O	126.5–128	57	[14]
b	CH_3	C_6H_5	β-$C_{10}H_7$	O	131–132	88	[81]
c	CH_2=CH–CH_2	C_6H_5	β-$C_{10}H_7$	O	106–107	[a]	[81]
d	n-$C_{10}H_{21}$	C_6H_5	β-$C_{10}H_7$	O	92.5–94	[a]	[81]
e	CH_3	α-$C_{10}H_7$	*p*-Cl–C_6H_4	O	115.1–116	[a]	[81]
f	CH_3	CH_3	2,4,5-$Cl_3C_6H_2$	S	133–134	77	[83]
g	C_2H_5	C_2H_5	2,4,5-$Cl_3C_6H_2$	S	64–65	73	[83]
h	CH_3	CH_3	C_6Cl_5	S	195–196	60	[83]
i	C_2H_5	C_2H_5	C_6Cl_5	S	185–187 (decomp.)	53	[83]
j	C_2H_5	C_2H_5	4-Phenyl-5-thioxo[1,3,4]-2-thiadiazolin-2-yl	S	114.5–116	[a]	[84]
k	CH_3	CH_3	2-Benzo[1,3]thiazolyl	S	120–123	[a]	[85]

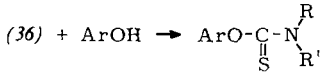
[a] Not given in the literature.

b) Thioacylation with *N,N*-Dialkylmercaptochloroformimidium Chlorides

Very little investigation has been carried out as yet on the reaction with *N,N*-dialkylmercaptochloroformimidium chlorides *(36)*, which can be obtained by chlorination or phosgenation of disubstituted dithiocarbamates [92].



(36)



Though this synthesis has so far been studied for only two examples (β-naphthol and 2-hydroxyanthraquinone), it is expected to become very important for the preparation of tertiary thiocarbamates, since the dithiocarbamates required are very readily obtainable from cheap starting materials, as described in Section C, Method 5.

The thioacylation of thiols by this method apparently has not been studied; the reaction with enols and oximes is also unknown at present.

4. Reaction of Thiocyanates and Cyanates with Hydrogen Sulfide

Nitriles add on hydrogen sulfide to form thioamides. This reaction [94] has also been applied to the preparation of thiocarbamates (from thiocyanates and hydrogen sulfide) [95–98]; the addition of H_2S under increased pressure has proved particularly favorable [99]. The thiocyanates may also be prepared from ammonium thiocyanate and alkyl halide, and can then be treated with hydrogen sulfide without first being isolated [100]. *Wheeler* and *Johnson* [100a] obtained acyldithiocarba-

[91] *J. S. Davidson* and *D. A. Peak*, J. chem. Soc. (London), *1963*, 3327.

[92] *H. Eilingsfeld* and *L. Möbius*, Chem. Ber. *98*, 1293 (1965).

[93] *H. A. Staab* and *G. Walther*, Liebigs Ann. Chem. *657*, 98 (1962).

[94] *W. Walter* and *K.-D. Bode*, Angew. Chem. *78*, 517 (1966); Angew. Chem. internat. Edit. *5*, 447 (1966).

[95] *F. Jeanjean*, Procés verbaux des Séances de l'Académie de Montpellier 1863, 12, 26.

[96] *J. v. Braun*, Ber. dtsch. chem. Ges. *35*, 3368 (1902).

[97] *R. Conrad* and *F. Salomon*, J. prakt. Chem. [2], *10*, 28 (1874).

[98] *G. Gerlich*, Liebigs Ann. Chem. *178*, 80 (1875).

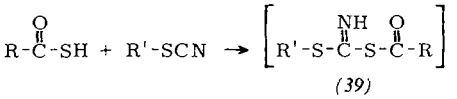
[99] *M. T. Bogert*, J. Amer. chem. Soc. *25*, 289 (1903).

[100] *M. Delépine*, Bull. Soc. chim. France [3], *29*, 48 (1903).

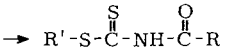
[100a] *H. L. Wheeler* and *T. B. Johnson*, Amer. chem. J. *26*, 185 (1901).

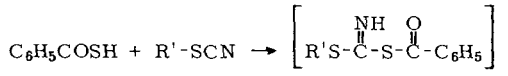
mates by the addition of thiocarboxylic acids to thiocyanates. This reaction is assumed to proceed *via (39)* [100b].

v. Braun and *Lemke* [100c] later obtained unsubstituted dithiocarbamates with thiobenzoic acid; the dibenzoyl sulfide expected as a by-product could not be detected.

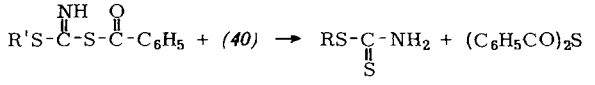


(39)





(40)



On the other hand, the synthesis of thiocarbamates from thio acids and cyanates had not previously been known, since the required cyanates have only recently become available [101–104]. For the preparation of primary thiocarbamates, it is of interest to observe that cyanates can be obtained from phenoxides and cyanogen halides [101, 102, 105, 106], whereas the synthesis of the cyanates *via* the chlorothioformates [103, 104] is of no interest since thiocarbamates can be prepared directly from chlorothioformates (see Method 2a, Sections B 2a and C).

The addition of hydrogen sulfide to cyanates proceeds in good yield in the presence of triethylamine (see *e.g.* synthesis of 2,6-di-t-butyl-4-alkylphenyl thiocarbamate in Section C) [14, 107]. *Jensen* and *Holm* [103] used this synthesis to prove the structure of the alkyl cyanates, which they had prepared for the first time. *Grigat* and *Pütter* have shown that thioureas (see *e.g.* procedure for *p*-tolyl thiocarbamate in Section C) [108], thiocarboxylic acids [108a, 109], and thioamides [109] may be used as sources of H_2S, the products in every case being very pure primary thiocarbamates (see *e.g.* procedure for 2,4-dimethylphenyl thiocarbamate in Section C).

A particularly convenient method is the reaction with sodium thiosulfate in acidic solution, which also gives very good yields [109a]. Thus this synthesis was found to be the best method for the preparation of primary thiocarbamates (see Table 6). Method 5 (see Section B 5 and C) is generally more suitable for the preparation of dithiocarbamates.

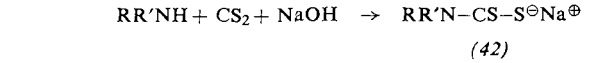
Table 6. Preparation of primary thiocarbamates from cyanates and hydrogen sulfide, RO–CS–NH_2 *(41)*.

Compound	R	M. p. (°C)	Yield (%)	Ref.
a	CH_3	39–41	55	[110]
b	C_2H_5	40–41	39	[103]
c	n-C_3H_7	35	31	[110a]
d	i-C_3H_7	81	47	[110a]
e	n-C_4H_9	19–21	56	[110a]
f	i-C_4H_9	36	84	[110a]
g	s-C_4H_9	39–39.5	94	[110a]
h	Cl_3C-CH_2	101	100	[107]
i	C_6H_5	134	98	[107]
j	2,4-$(CH_3)_2C_6H_3$	140	99	[107]
k	4-$CH_3-C_6H_4$	153	87	[107]
l	3-Cl–C_6H_4	122	93	[107]
m	2-$CH_3O-C_6H_4$	141(decomp.)	82	[107]
n	2,6-(t-C_4H_9)-4-$(CH_2=CH-CH_2)-C_6H_2$	190–190.5	87	[14]
o	2,6-(t-C_4H_9)-4-(CH_3)-C_6H_2	252 [a]	60	[42]

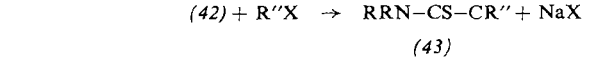
[a] Measured in a sealed tube.

5. Alkylation of Metal Dithiocarbamates

Amines react with carbon disulfide and alkali metal hydroxides to form salts *(42)* of dithiocarbamic acids, which are strongly nucleophilic and react with many electrophiles to give dithiocarbamates *(43)* [111, 112, 96].

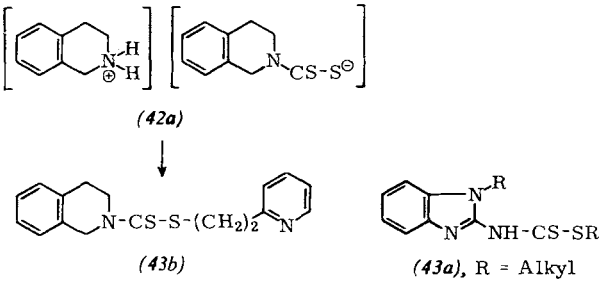


(42)



(43)

This method can be used for the preparation of 2-benzimidazolyl-dithiocarbamates *(43a)*, which are used as anthelmintics [112a].



(42a)

(43b) *(43a)*, R = Alkyl

[100b] *H. Busse*, Dissertation, Universität Hamburg, 1966.

[100c] *J. v. Braun* and *G. Lemke*, Ber. dtsch. chem. Ges. *55*, 3536 (1922).

[101] *R. Stroh* and *H. Gerber*, Angew. Chem. *72*, 1000 (1960).

[102] *E. Grigat* and *R. Pütter*, Chem. Ber. *97*, 3012 (1964).

[103] *K. A. Jensen* and *A. Holm*, Acta chem. scand. *18*, 826 (1964).

[104] *D. Martin*, Angew. Chem. *76*, 303 (1964); Angew. Chem. internat. Edit. *3*, 311 (1964).

[105] *M. Hedayatullah* and *L. Denivelle*, C. R. hebd. Séances Acad. Sci. *256*, 4029 (1963).

[106] *J. C. Kauer*, and *W. W. Henderson*, J. Amer. chem. Soc. *86*, 4732 (1964).

[107] *E. Grigat* and *R. Pütter*, Chem. Ber. *97*, 3022 (1964).

[108] *E. Grigat* and *R. Pütter*, Chem. Ber. *98*, 1168 (1965).

[108a] *D. Martin*, GDR-Pat. 42176 (Nov. 5th 1965).

[109] *E. Grigat* and *R. Pütter*, Chem. Ber. *98*, 1359 (1965); Belg. Pat. 665682 (June 21st, 1965), Farbenfabr. Bayer.

[109a] *E. Grigat*, *R. Pütter*, and *E. Mühlbauer*, Chem. Ber. *98*, 3777 (1965).

[110] *D. Martin* and *W. Mucke*, Chem. Ber. *98*, 2059 (1965).

[110a] *K. A. Jensen*, *M. Due*, and *A. Holm*, Acta chem. scand. *19*, 438 (1965).

[111] *S. M. Losanitsch*, Ber. dtsch. chem. Ges. *24*, 3021 (1891).

[112] *M. Delépine*, Bull. Soc. chim. France [3], *27*, 585 (1902).

[112a] *Ph. P. Actor* and *J. F. Pagano*, Belg. Pat. 666795 (Jan. 13th, 1966), Smith, Kline and French Lab.

The compound *(42a)*, which can be obtained by the reaction of 1,2,3,4-tetrahydroisoquinoline with carbon disulfide, reacts with 2-vinylpyridine to form the dithiocarbamate *(43b)*; 1-aminoisoquinoline does not react in this way [112b].

A survey of the possible applications of this very versatile method is given in Table 7.

An interesting reaction is that of metal dithiocarbamates *(42)* with diazonium salts *(44)*, since *S*-aryl compounds can also be obtained in this way [3] (see also Section C).

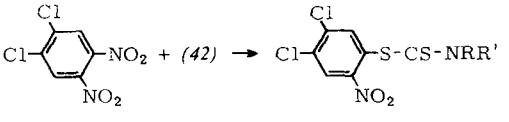
$$\underset{(42)}{RR'N-CS-S^{\ominus}Na^{\oplus}} + [C_6H_5N{\equiv}N]^{\oplus}Cl^{\ominus} \rightarrow \underset{(44)}{RR'N-CS-SC_6H_5} + N_2 + NaCl$$

Table 7. Dithiocarbamates by addition of dithiocarbamate ions to electrophiles RR'N–CS–SR'' *(43)*; R = R' = Alkyl or aryl.

R''	Electrophilic component	Ref.
Alkyl	Alkyl halides	[3, 14, 96, 113–116b]
Alkyl	Dimethyl propynylphosphonate	[116c]
$CH_2{=}CH{-}CH_2$	Allyl halides	[117–119]
$CH_2{-}CH_2OH$	β-Chloroethanol	[120]
Aryl	Aryldiazonium salts	[3, 121, 122]
$CH_2{-}CH_2SH$	β-Chloroethylthiol	[74]
$CH_2{-}CN$	α-Halogenonitriles	[123]
$CH_2{-}OR$	ω-Halogeno ethers	[124]
Alkyl	Olefins	[3, 9, 10, 125, 128, 128a]
$CH_2{-}NR_2$	α-Halogenoamines	[11, 126]
4,6-Dichloro[1,3,5]triazin-2-yl	Cyanuryl chloride	[127]
$(CH_2)_n{-}COOH$	ω-Halogenocarboxylic acid	[126, 126a, 129]
$(CH_2)_n{-}CONR_2$	Amides of ω-halogenocarboxylic acids	[130, 131]
$(CH_2)_n{-}CSNR_2$	Thioamides of ω-halogenocarboxylic acids	[132]
$CH_2{-}O{-}CO{-}CH_2C_6H_5$	Chloromethyl phenylacetate	[133]
$C_6H_5{-}CH\langle$	Benzylidene chloride	[133a, 133b]
CN [a]	Cyanogen halides	[134]
Thenyl	Thenyl chloride	[134a]

[a] In compounds of this type, the thiocyanate group is readily replaced by thiolate ions with formation of dithiocarbamates [134].

The reaction of activated aromatic compounds, such as 2-nitrochlorobenzene and 2,6-dinitrochlorobenzene, with sodium dithiocarbamates of heterocyclic amines leads, with substitution of hydrogen directly to the corresponding esters of dithiocarbamic acid [134b]; in more activated molecules nitro groups are substituted nucleophilically and aromatic esters of dithiocarbamic



R and/or R' = CH_3, C_2H_5, C_3H_7
RR' = Morpholino, piperidino

[112b] *G. Buchmann* and *L. Kahnert*, J. prakt. Chem. [4], *30*, 241 (1965).

[113] *M. Delépine*, Bull. Soc. chim. France [3], *29*, 48 (1903).

[114] *M. Kulka*, Canad. J. Chem. *34*, 1093 (1956).

[115] *J. v. Braun*, Ber. dtsch. chem. Ges. *42*, 4568 (1909).

[116] *J. C. Thomas*, US-Pat. 2384577 (Sept. 11th, 1945), du Pont; Chem. Abstr. *40*, 177 (1946).

[116a] *A. A. Shamshurin* and *M. Z. Krimer*, Izvest. Akad. Nauk Moldarsk. SSR Ser. Estestv. i Techn-Nauk *9*, 108 (1963); Chem. Abstr. *63*, 13070 (1965).

[116b] *R. O. Zerbe* and *J. J. D'Amico*, US-Pat. 3224866 (Dec. 21st, 1965).

[116c] *G. Schrader* and *R. Schliebs*, German Publ. Pat. Appl. 123390 (Feb. 2nd, 1967), Farbenfabriken Bayer.

[117] *J. v. Braun* and *R. Murjahn*, Ber. dtsch. chem. Ges. *59*, 1202 (1926).

[118] *J. J. D'Amico*, US-Pat. 3161496 (Dec. 15th, 1964), Monsanto; Chem. Abstr. *62*, 7683 (1965).

[119] *R. O. Zerbe* and *J. J. D'Amico*, US-Pat. 3152163 (Oct. 6th, 1964), Monsanto; Chem. Abstr. *62*, 454 (1965).

[120] *G. Nachmias*, Ann. Chim. [12], *7*, 584 (1952); Chem. Abstr. *48*, 597 (1954).

[121] *A. M. Clifford* and *J. G. Lichty*, J. Amer. chem. Soc. *54*, 1163 (1932).

[122] *A. Rieche*, *G. Hilgetag*, *D. Martin*, and *J. Kreyzi*, German Pat. 1177141 (Sept. 3rd, 1964), Dtsch. Akad. Wiss. Berlin.

[123] *P. Chabrier* and *G. Nachmias*, C.R. hebd. Séances Acad. Sci. *233*, 57 (1951).

[124] *A. Frank*, *F. Grewe*, and *H. Kaspers*, German Pat. 1178416 (Sept. 24th, 1964), Farbenfabr. Bayer; Chem. Abstr. *62*, 16070 (1965).

[125] *E. Kühle*, *B. Homeyer*, and *E. Urbschat*, German Pat. 1178417 (Sept. 24th, 1964), Farbenfabr. Bayer; Chem. Abstr. *62*, 454 (1965).

[126] *I. J. Posstovski*, *N. F. Kasarinova*, *G. B. Afanassyeva*, and *N. I. Latosch*, Doklady Akad. Nauk SSSR *132*, 141 (1960); Chem. Zbl. *1962*, 11175.

[126a] *V. R. Mamdapur*, *A. S. U. Choughuley*, and *M. S. Chadha*, J. Indian chem. Soc. *43*, 37 (1966).

[127] *L. G. Valenzan*, US-Pat. 3139350 (June 30th, 1964); Chem. Abstr. *61*, 8324 (1964).

[128] *R. Delaby*, *R. Damiens*, and *R. Seyden-Penne*, C.R. hebd. Séances Acad. Sci. *238*, 121 (1954); *242*, 910, 1482 (1956).

[128a] *J. E. Jansen* and *R. A. Mathes*, J. Amer. chem. Soc. *77*, 2866 (1955).

[129] *J. L. Garraway*, J. chem. Soc. (London) *1962*, 4072, 4077.

[130] *J. Metivier*, French Pat. 1274421 (Feb. 28th, 1962), Rhône-Poulenc; Chem. Abstr. *57*, 7170 (1962).

[131] *J. G. Lichty*, US-Pat. 2247917 (July 1st, 1941), Wingfoot Co.; Chem. Abstr. *35*, 6836 (1941).

[132] *H.-G. Schicke* and *G. Schrader*, German Pat. 1129949 (May 24th, 1962), Farbenfabr. Bayer; Chem. Abstr. *57*, 13626 (1962).

[133] *G. Rossi*, French Pat. 1277960 (June 4th, 1963), Montecatini.

[133a] *Sidney M. Cadwell*, US-Pat. 1726647 (Sept. 3rd, 1929), Naugatuck Chem. Co.; Chem. Zbl. 1929, II 2938.

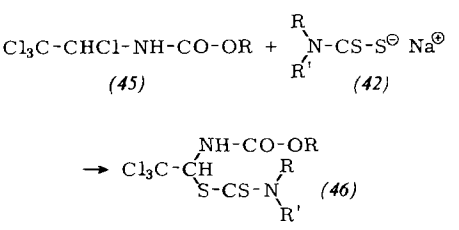
[133b] *M. A. Gradsten*, US-Pat. 3257441 (June 21st, 1966), Tenneco Chem.; US-Pat. 3266882 (Aug. 16th, 1966).

[134] French Pat. 789500 (Oct. 29th, 1935), Soc. An. des Matières Colorantes et Produits Chimiques de Saint-Denis; Chem. Zbl. *1936*, I 2828.

[134a] *B. P. Fedorov*, *G. I. Gorushkina*, and *Y. L. Gol'dfarb*, Ž. org. Chim. *1*, 777 (1965); Chem. Abstr. *63*, 5580 (1965).

[134b] *S. Prakasch Gupta* and *D. Mohan Lal Garg*, J. Indian chem. Soc. *42*, 412 (1965); Chem. Abstr. *63*, 11562 (1965); *D. Mohan Lal Garg*, J. Indian chem. Soc. *42*, 415 (1965); Chem. Abstr. *64*, 11562 (1965).

acid result in yields of 72–92% [134c]. The strongly fungicidal compounds *(46)* have been obtained from halogenated carbamates of the type *(45)* [134d].



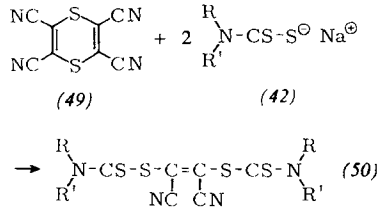
Another synthesis of dithiocarbamates is based on the reaction of acyl chlorides *(47)* with paraformaldehyde and salts of dithiocarbamic acid *(42)* [134e].

$$RR'\text{–}CS\text{–}S^{\ominus}Na^{\oplus} + R''COCl \xrightarrow{CH_2O} RR'N\text{–}CS\text{–}SCH_2OCOR''$$

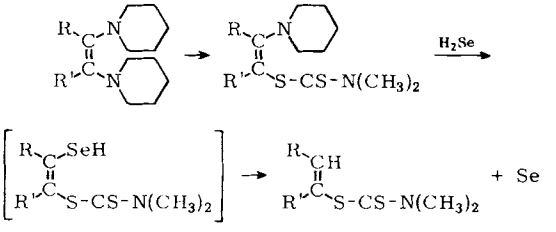
(42) *(47)* *(48)*

R,R′ = Alkyl, aryl; R″ = Alkyl, aralkyl, aryl

Dithiocarbamates containing sulfo groups are prepared by the reaction of alkali metal dithiocarbamates with sultones [134f]. Whereas the compounds described here are "true" dithiocarbamates, those described below can only be formally regarded as such. For example, *Vest* [134g] has described the cleavage of tetracyanodithiin *(49)* by sodium dithiocarbamate to form a bis-dithiocarbamate *(50)*.



Alkenyldithiocarbamates are obtained by the reaction of enamines with tetramethylthiuram disulfide followed by treatment with hydrogen selenide [134h]



On the basis of their chemical behavior, the *S*-acyl dithiocarbamates *(51)* [135, 136] must be regarded as mixed anhydrides.

$$Ar\text{–}CO\text{–}S\text{–}CS\text{–}NRR'$$

(51)

Finally, mention should also be made of the *S*-aminoalkyl dithiocarbamates *(53)*, which behave as aminoalkylating agents. *Kreutzkamp et al.* have synthesized these compounds from alkali metal dithiocarbamates, formaldehyde, and amines [11, 135a].

$$R_2N\text{–}CS\text{–}S^{\ominus}Na^{\oplus} + CH_2O \xrightarrow{H^{\oplus}} R_2N\text{–}CS\text{–}SCH_2OH$$

(42) *(52)*

$$(52) + R_2'NH \rightarrow R_2N\text{–}CS\text{–}SCH_2NR_2'$$

(53)

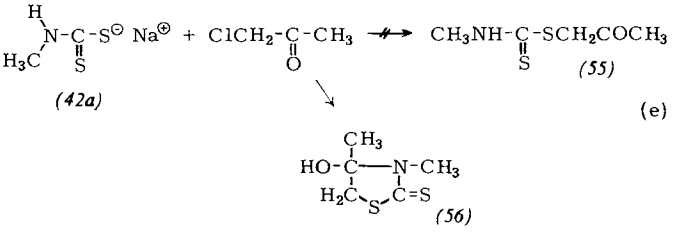
Another possibility is the reaction of aminals *(54)* or Mannich bases, *e.g.* gramine, with carbon disulfide [135a, 135b].

$$R_2N\text{–}CH_2\text{–}NR_2' + CS_2 \rightarrow R_2N\text{–}CS\text{–}SCH_2NR_2'$$

(54) *(53)*

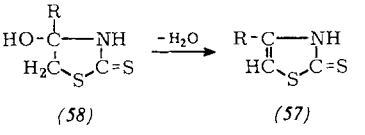
This reaction, which may be regarded as an insertion of carbon disulfide, finds a parallel in the reaction of olefins with amines and carbon disulfide, leading to the formation of true dithiocarbamates (see Table 7).

The alkylation of metal dithiocarbamates has sometimes been misinterpreted in the past. As early as 1955, *Hirano* [136a] reported, that the reaction of sodium *N*-methyldithiocarbamate *(42a)* with chloroacetone leads, not to the expected dithiocarbamate *(55)*, but to the thiazolidinethione *(56)* [*].



(e)

This was confirmed by *Humphlett* and *Lamon* [137] in analogous investigations on the reactions of ammonium dithiocarbamate with chloroacetaldehyde, chloroacetone, ethyl chloroacetate, and phenacyl bromide. These reactions again lead, not to the primary dithiocarbamates, as had previously been assumed [138–140], but to the 4-hydroxythiazolidinethiones *(58)*, which lose water within a few days to form thiazoline-2-thiones *(57)*.



These results, which are based on IR investigations, were confirmed by *Humphlett* and *Lamon* by the preparation of stable 4-hydroxythiazolidine-2-thiones of the type *(58a)*, R = CH_2–SO_2–C_2H_5 [141].

[134c] *J. Krsek* and *Z. Stota*, Czech. Pat. 117428 (Feb. 15th, 1966); Chem. Abstr. *65*, 20059 1966; see also *J. J. d'Amico*, Belg. Pat. 670434 (April 1st, 1966), Monsanto.

[134d] *M. Pianka* and *J. D. Edwards*, Brit. Pat. 993051 (May 26th, 1965), Murphy Chem. Co.; Chem. Abstr. *63*, 9822, (1965).

[134e] *H. Pianka* and *J. D. Edwards*, Brit. Pat. 993053 (May 26th, 1965), Murphy Chem. Co.; Chem. Abstr. *63*, 8212 (1965).

[134f] Brit. Pat. 1030566 (May 25th, 1966), Deutsche Hydrierwerke.

[134g] *R. D. Vest*, US-Pat. 3197472 (July 27th, 1965), du Pont; Chem. Abstr. *63*, 11576 (1965).

[134h] *E. Fanghänel*, Z. Chem. *6*, 395 (1966) Conference report.

[135] *J. v. Braun*, Ber. dtsch. chem. Ges. *36*, 3520 (and p. 3527) (1903).

[135a] *N. Kreutzkamp* and *H. Y. Oei*, Arch. Pharmaz. *299*, 906 (1966).

[135b] *R. A. Donia, J. A. Shotton, L. O. Bentz*, and *G. E. P. Smith jr.*, J. org. Chemistry *14*, 952 (1949).

[136] *D. S. Tarbell* and *R. P. F. Scharrer*, J. org. Chemistry *27*, 1972 (1962).

[136a] *H. Hirano*, J. pharmac. Soc. Japan (Yakugakuzasshi) *75*, 244 (1955); Chem. Abstr. *50*, 1830 (1956).

[*] *Schultz* and *Gleixner* have described reactions in accordance with equation (e) [8]. They formulated the reaction products as *(55)*, without discussing the work of *Hirano*. The products are probably again compounds of the type *(56)*.

[137] *W. J. Humphlett* and *R. W. Lamon*, J. org. Chemistry *29*, 2146 (1964).

[138] *R. A. Mathes* and *A. J. Beber*, J. Amer. chem. Soc. *70*, 1451 (1948).

[139] *T. G. Levi*, Gazz. chim. ital. *61*, 719 (1931).

[140] *I. Ubaldini* and *A. Fiorenza*, Gazz. chim. ital. *73*, 169 (1943).

[141] *W. J. Humphlett* and *R. W. Lamon*, J. org. Chemistry *29*, 2148 (1964).

In a variant of this synthesis[142], sulfonamides *(59)* are treated with carbon disulfide and sodium hydroxide solution. Subsequent alkylation yields *N*-sulfonyldithiocarbamates *(61)*.

$$\underset{(59)}{RSO_2NH_2} + CS_2 + 2\,NaOH \rightarrow \underset{(60)}{RSO_2N{=}C(S^{\ominus}Na^{\oplus})_2}$$

$$(60) \xrightarrow[2.\ HCl]{1.\ R'X} \underset{(61)}{RSO_2NH{-}CS{-}SR'}$$

The analogous reaction with α-halogensulfonamides *(62)* leads to the sodium salt of Δ^2-3-mercapto[1,2,4]dithiazoline 1,1-dioxide *(63)* [142a].

$$\underset{(62)}{ClCH_2SO_2NH_2} + NaOH + CS_2 \rightarrow \underset{(63)}{\text{sodium salt of } \Delta^2\text{-3-mercapto[1,2,4]dithiazoline 1,1-dioxide}}$$

6. Addition to Thiocyanic Acid

The reactions of thiocyanic acid described in this section are not very important. However, they should be mentioned, since the starting materials are readily available and the low yields are consequently not significant. *Blankenhorn* [143] and *Rathke* [144] observed the formation of *O*-ethyl thiocarbamate *(41b)* in the reaction of ammonium thiocyanate with concentrated hydrochloric acid in ethanolic suspension. It must be assumed that the alcohol adds to the free thiocyanic acid *(64)*.

$$\underset{(64)}{[H{-}N{=}C{=}S]} + C_2H_5OH \rightarrow \underset{(41b)}{C_2H_5O{-}CS{-}NH_2}$$

The analogous reaction with ethyl chloroformate *(65)* [145–148] proceeds in very good yields with formation of *O*-alkyl thiocarbamates of the type *(67)*. This reaction evidently proceeds by initial formation of ethyl isothiocyanoformate *(66)*.

$$KSCN + Cl{-}CO{-}OC_2H_5 \rightarrow \underset{(66)}{[C_2H_5O{-}CO{-}NCS]}$$

$$(66) + C_2H_5OH \rightarrow \underset{(67)}{C_2H_5O{-}CO{-}NH{-}CS{-}OC_2H_5}$$

This synthesis was used by *Skinner* and *Vogt* [149] for the preparation of *O*-ethyl-*N*-benzoyl-thiocarbamate *(68)* from benzoyl chloride *(69)*, potassium thiocyanate, and ethanol, but the yield obtained is low.

$$\underset{(69)}{C_6H_5COCl} + KSCN \rightarrow \underset{(70)}{[C_6H_5{-}CO{-}NCS]}$$

$$(70) + C_2H_5OH \rightarrow \underset{(68)}{C_6H_5CONH{-}CS{-}OC_2H_5}$$

7. Concluding Remarks

The present survey has been deliberately confined to reactions having some preparative importance. However, mention should also be made of the conversion of thioureas into thiocarbamates by the action of an excess of alcohol in the presence of acidic catalysts, as described in the literature (see *e.g.* [150]). This synthesis could become industrially important, since the starting materials are relatively easily obtainable. The comparison of the various methods in each section is intended as an aid to the choice of the best method. Finally, the choice of method should also be facilitated by the following procedures, nearly all of which have been checked in our laboratory.

C. Procedures

Method 1 [28]

0.01 mole of the isothiocyanate is refluxed with 0.1 mole of the alcohol for 2 hours. The thiocarbamate precipitates when the reaction mixture is cooled in an ice/salt bath. To remove any isothiocyanate that may be present, the product is recrystallized either from the alcohol used in the reaction and water, or from petroleum ether (Yield 40–80%; see also Table 1).

Method 2a

0.2 mole of the primary or secondary amine is dissolved in carbon tetrachloride and cooled to 0 °C. A solution of 0.1 mole of the chlorothioformate in carbon tetrachloride is added slowly to the above solution. After 24–48 hours, the amine hydrochloride that has precipitated is filtered off and the filtrate is evaporated to dryness under vacuum. The residue crystallizes immediately or within a few days (see Table 3).

Preparation of Chlorothioformates and Chlorodithioformates

0.1 mole of thiophosgene and 0.1 mole of the phenol or thiophenol are dissolved in dichloromethane and cooled to about 0 °C. A solution of 5.6 g of KOH in 100 ml of water is added dropwise with stirring, the temperature not being allowed to rise above 10 °C. When the addition is complete, stirring is continued for 1 hour, and the reaction mixture is then poured into ice/water. The organic phase is separated and washed with water. The solution is dried over sodium sulfate and then evaporated to dryness. The resulting orange oil is distilled under vacuum.

[142] *R. Gompper* and *W. Hägele*, Angew. Chem. *74*, 753 (1962); Angew. Chem. internat. Edit. *1*, 553 (1962); Chem. Ber. *99*, 2885 (1966).

[142a] *K. Dickoré*, *R. Wegler*, and *K. Sasse*, Angew. Chem. *74*, 874 (1962); Angew. Chem. internat. Edit. *1*, 594 (1962).

[143] *E. Blankenhorn*, J. prakt. Chem. [2], *16*, 358 (1877).

[144] *B. Rathke*, Ber. dtsch. chem. Ges. *18*, 3102 (1885).

[145] *G. Delitsch*, J. prakt. Chem. [2], *10*, 116 (1874).

[146] *R. E. Doran*, J. chem. Soc. (London) *69*, 324 (1896).

[147] *P. C. Guha*, *G. Rao*, and *A. Saletore*, J. Indian chem. Soc. *6*, 565 (1929).

[148] *H. L. Wheeler*, *W. H. Saunders*, and *B. Barnes*, J. Amer. chem. Soc. *22*, 366 (and p. 377) (1900).

[149] *G. S. Skinner* and *H. C. Vogt*, J. Amer. chem. Soc. *77*, 5440 (1955).

[150] *J. Nishimura*, Sci. Pap. Inst. physic. chem. Res. (Tokyo) *40*, 181 (1942); Chem. Abstr. *41*, 6214 (1947).

Method 2b: N-Ethoxythiocarbonylglycine [73]

1 mole of ethanol is shaken with 250 ml of carbon disulfide and 1 mole of potassium hydroxide until the hydroxide dissolves and a crystalline substance separates. The mixture is cooled in ice to complete the precipitation, and is then filtered. The crude potassium ethyl xanthate is introduced into 200 ml of methanol and refluxed for 30 min with 1 mole of ethyl bromide. The solution is diluted with 200 ml of water and extracted twice with ether. Evaporation of the ether leaves a yellow oil, which is heated for 24 hours on a boiling water bath with a solution of 1 mole of glycine and 1 mole of potassium hydroxide in 200 ml of 50% ethanol. The solution is condensed under vacuum to about 100 ml, dissolved in an equal volume of water, and slowly acidified with concentrated hydrochloric acid, whereupon the desired product is precipitated. Recrystallization from water gives 77% of *N*-ethoxythiocarbonylglycine (*N*-carboxymethyl-*O*-ethylthiocarbamate), m.p. 186 °C.

Method 2c [77]

A large excess of pyridine or diethylaniline (about 1 mole) is added to 0.1 mole of a diester of trithiocarbonic acid in the absence of solvent. The reaction begins immediately with strong evolution of heat, and the ester dissolves. The clear solution is heated for a further 15 min on a boiling water-bath, and is then diluted with a large quantity of water. When the solution is cooled, the dithiocarbamate often separates as an oil, but this soon crystallizes (for examples see Table 4).

Preparation of Diester of Trithiocarbonic Acid [77]

1 mole of a heterocyclic thiol is dissolved in 10% sodium hydroxide solution under nitrogen, and 0.5 mole of thiophosgene is added slowly with vigorous stirring. After the addition, stirring is continued until the solution is clear and the ester separates as an oil. (This can be best seen if stirring is interrupted for a short time). Water is added dropwise to complete the separation of the ester. The oil solidifies after a short time and is recrystallized from benzene/methanol (yields: 60–98%).

Method 3a:
N,N-Dimethyl-O-(2-nitrophenyl)thiocarbamate (28a)

8.7 g of sodium 2-nitrophenoxide is dissolved in 80 ml of water, and 10.0 g (approx. 50% excess) of *N,N*-dimethylthiocarbamoyl chloride in 50 ml of chloroform is added. The mixture is shaken vigorously until the dark red color disappears and a light yellow organic phase is obtained. The organic phase is separated, washed with $NaHSO_3$ solution and water, and dried with sodium sulfate. On evaporation to dryness under vacuum, a yellow crystalline product is obtained. M.p. 126.5–128 °C (from benzene/petroleum ether), yield 6.9 g (57%).

Method 4:
2,6-Di-t-butyl-4-allylphenylthiocarbamate [14]

5 g of 2,6-di-t-butyl-4-allylphenyl cyanate [101] is dissolved in 80 ml of dry benzene. After the addition of 0.1 ml of triethylamine, a vigorous current of H_2S is passed through the solution for 50 min, and the reaction mixture is allowed to stand overnight in the closed vessel at room temperature. The solvent is evaporated under vacuum, and the residue is recrystallized from benzene. Yield 4.4 g (78%), m.p. 190 to 190.5 °C.

2,4-Dimethylphenylthiocarbamate [109]

7.35 g (50 mmole) of 2,4-dimethylphenyl cyanate is added dropwise at room temperature to a suspension of 6.85 g (50 mmole) of thiobenzamide in 100 ml of petroleum ether. The solution becomes slightly warm. After 24 hours, the pure thiocarbamate is filtered off. Yield 8.8 g (97%), m.p. 138 to 139 °C.

p-Tolylthiocarbamate [108]

5.2 g (0.05 mole) of *N,N*-dimethylthiourea and 6.7 g (0.05 mole) of *p*-tolyl cyanate in 20 ml of acetone are refluxed for one hour. The solvent is distilled off under vacuum, and the dimethylcyanamide is filtered off from the thiocarbamate, which is recrystallized from toluene. Yield 7.5 g (90%), m.p. 153 °C.

Thiourea, *N*-methylthiourea, and *N*-phenylthiourea have also been used as thiourea components.

Method 5:
Arylation of Metal Dithiocarbamates with Diazonium Salts [3, 121]

0.1 mole of sodium dithiocarbamate is dissolved in 250 ml of water, and a diazonium salt solution, freshly prepared from 0.1 mole of amine, is added at 25–35 °C (the temperature must not be allowed to rise higher) with vigorous stirring. An orange oil separates out within an hour and nitrogen is liberated. The oil crystallizes after a short time. Yields 25 to 90%.

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The Action of Carbon Disulfide and Sulfur on Enamines, Ketimines, and CH Acids [1]

BY ROLAND MAYER AND K. GEWALD [*]

The reaction of sulfur, carbon disulfide, and enamines at room temperature leads mainly or exclusively to 3H-1,2-dithiole-3-thiones; these are occasionally accompanied by 2H-1,3-dithiole-2-thiones, which can also be prepared by a modified procedure. Many enamines react with sulfur at room temperature to form thioamides. At about 50 °C, enamines of acetophenone give 2-benzylidene-4-phenyl-2H-1,3-dithiol. The action of isothiocyanates and sulfur on enamines leads to the formation of thiazolidine-2-thiones. 2H-Thiopyran-2-thiones can be prepared from enamines or dienamines with carbon disulfide at room temperature. The reaction of ketimines (Schiff bases) with carbon disulfide and sulfur yields 3H-1,2-dithiole-3-thiones or isothiazoline-5-thiones. The reaction of alkynes with sulfur and carbon disulfide leads to 2H-1,3-dithiole-2-thiones. Nitriles containing active methylene groups react with carbon disulfide and sulfur to form 5-amino-3H-1,2-dithiole-3-thiones. When isothiocyanates are used instead of CS_2, the reaction leads to Δ^4-4-amino-thiazoline-2-thiones.

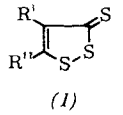
I. Introduction

In our investigations on organic sulfur compounds [1] and CH-acid nitriles [2], we tried to find a generally applicable and efficient synthesis of 3*H*-1,2-dithiole-3-thiones *(1)*, preferably proceeding at atmospheric pressure and at room temperature.

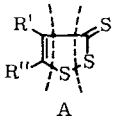
This class of compounds, which was already well known [3], had attracted renewed interest on theoretical and practical grounds. In the course of this work we found simple routes to other, new sulfur heterocycles, as well as new and efficient methods for the preparation of known classes of compounds.

The present paper deals particularly with preparatively useful syntheses of 3*H*-1,2-dithiole-3-thiones, 2*H*-1,3-dithiole-2-thiones, Δ^3-isothiazoline-5-thiones, 2*H*-thiopyran-2-thiones, thioamides, and thiophene derivatives.

In order to synthesise the dithiolthiones *(1)*, we decided to adopt the approach indicated in A. A sufficiently active two-carbon system was therefore required



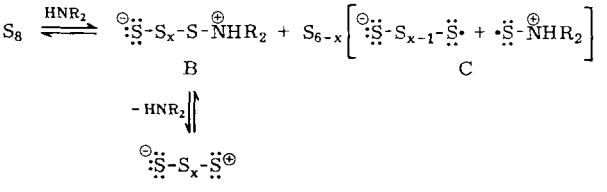
(1)



A

that would react directly with elementary sulfur and carbon disulfide under the required conditions to give *(1)*.

Elementary sulfur (S_8) is activated on nucleophilic attack by a base (*e.g.* an amine). (Investigations are being carried out at present to determine whether the activated complex B exists (*e.g.* in the form C at room temperature.)



In addition to amines [4], which activate sulfur at about 10 °C, the S_8 ring can also be attacked by other bases of corresponding nucleophilic strength, including bases formed during sulfurization, such as sulfide, polysulfides, and sulfite [5–7].

Little is known [5–11] about the mechanism of thiolation reactions [9], particularly the action of sulfur on compounds containing nucleophilic C atoms. Thus, it is not even always clear whether the sulfur is attacked directly by the C base and transferred to the substrate as "activated" sulfur. However,

[*] Prof. Dr. Roland Mayer and Doz. Dr. K. Gewald
Institut für Organische Chemie der Technischen Universität
Mommsen-Str. 6
X 8027 Dresden (Germany)

[1] Part 64 of Organic Compounds of Sulfur; Part 63: *J. Morgenstern* and *R. Mayer*, J. prakt. Chem. [4], *34*, 116 (1966).

[2] Cf. *K. Gewald*, Habilitation Thesis, Technische Universität Dresden, 1964.

[3] For a recent summary; see *Ph. S. Landis*, Chem. Reviews *65*, 237 (1965).

[4] *R. E. Davis* and *H. F. Naksbhendi*, J. Amer. chem. Soc. *84*, 2085 (1962).

[5] Cf. *W. A. Pryor*: Mechanisms of Sulfur Reactions. McGraw-Hill, New York 1962.

[6] *M. Schmidt*, Österr. Chemiker-Ztg. *64*, 236 (1963) and literature cited.

[7] *H. Schumann* and *M. Schmidt*, Angew. Chem. *77*, 1049 (1965); Angew. Chem. internat. Edit. *4*, 1007 (1965).

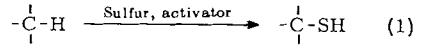
[8] *R. Wegler*, *E. Kühle*, and *W. Schäfer* in *W. Foerst*: Neuere Methoden der präparativen organischen Chemie. Vol. III, p. 1, Verlag Chemie, Weinheim 1960.

[9] *F. Asinger*, *W. Schäfer*, *K. Halcour*, *A. Saus*, and *H. Triem*, Angew. Chem. *75*, 1050 (1963); Angew. Chem. internat. Edit. *3*, 19 (1964).

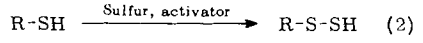
[10] *F. Asinger* and *M. Thiel*, Angew. Chem. *70*, 667 (1958).

[11] For the degradation of polysulfides and sulfanes, cf. *M. Schmidt*, *A. Fässler*, and *F. J. Rankl*, Chem. Ber. *97*, 1075, (1964); *M. Schmidt* and *R. Wägerle*, *ibid. 96*, 3293 (1963).

it should be possible to thiolate not only a CH compound [eq. (1)], but also an SH grouping [eq. (2)] at low temperatures, if necessary in the presence of an auxiliary base. This has already been achieved, in principle, in the formation of trithiolanes[9,12] tetrathianes[9,13], pentathiepanes[13], and hexathiocanes[14]. The *McMillan-King* reaction[9,15] may also be regarded as involving an intermediate thiolation.



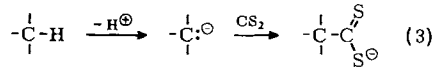
(1)



(2)

Whereas only heat-resistant products may be isolated after the reaction of sulfur on organic compounds at high temperatures, the base catalysed reaction of sulfur with suitable reactants at room temperature permits the interception of thermally labile intermediates existing in the equilibrium, in which *e.g.* S_8 may be wholly or partly incorporated.

As far as we know, the simultaneous action of carbon disulfide in thiolation reactions has not been studied. Carbon disulfide is known to add to nucleophiles at ambient temperatures. However, in the reaction of CH acids with CS_2, an auxiliary base must generally be present to act as a proton acceptor in the formation of the actual C base [eq. (3)].



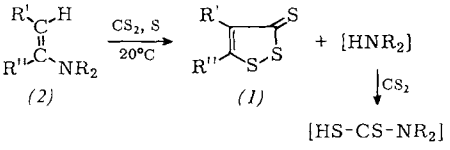
(3)

Possible reaction of the auxiliary base, *e.g.* alkoxide, with carbon disulfide presents a problem. We therefore had to use systems which contained two carbon atoms and which were already sufficiently nucleophilic to react with carbon disulfide. Such systems had to permit the cyclization step in the formation of *(1)*. Enamines, dienamines, Schiff bases, alkynes, and CH-acid nitriles were found to be particularly suitable reactants.

II. The Reaction of Enamines with Carbon Disulfide and Sulfur

The above requirements for the C_2 system are satisfied by the enamines *(2)*, which are readily available nowadays[16–18]. They are sufficiently basic and nucleophilic to activate elementary sulfur without an additional catalyst, and sufficiently reactive for the reaction with carbon disulfide; moreover, they permit the cyclization step with formation of 3*H*-1,2-dithiole-3-thiones *(1)*.

Thus the action of carbon disulfide and elementary sulfur on enamines *(2)* at room temperature, preferably in the presence of a polar solvent, leads to the formation of 3*H*-1,2-dithiole-3-thiones *(1)* with evolution of heat[19,20].



(2) *(1)*

The yields of *(1)* can sometimes be increased considerably by catalytic quantities of vulcanization accelerators such as tetramethylthiuram disulfide or 2-mercaptobenzothiazole[18]; this variation is being investigated at present. The yields in Table 1 relate to the reaction without catalysts.

It can be seen from Table 1 that the process is very flexible concerning the substituents R′ and R″.

In the preparation of cyclic enamines [*(2)*, $R'R'' = (CH_2)_n$] from ketone and amine, it should be noted that cyclohexanone tends to undergo addition to the carbonyl group, since this leads to a decrease in ring strain; this adduct is readily dehydrated to form the enamine *(2)*. On the other hand, owing to its lower ring strain, cyclopentanone is much more stable than the addition compound; moreover, dehydration of the latter to form a cyclopentene derivative is difficult. The ketone structure is also favored in the case of cycloheptanone, though the effect is not so strong as in cyclopentanone. The same order is found in the benzo series[27], the enamines of α- and β-tetralone being most readily obtainable (yield: 75–86%), followed by those of benzocycloheptanone (yield: about 60%), and finally those of α- and β-indanone (yield: 50–55%).

The yields of 1,2-dithiolethiones obtained from unsubstituted cyclic enamines with 5-, 6-, and 7-membered rings are as expected. Tetramethylene-1,2-dithiolethione [*(1)*, $R'R'' = (CH_2)_4$] is not dehydro-

[12] *J. Jentzsch*, Dissertation, Technische Universität Dresden, 1963.

[13] *B. Magnusson*, Acta chem. scand. *13*, 1031 (1959).

[14] *F. Asinger*, *W. Schäfer*, and *H. W. Becker*, Angew. Chem. *77*, 41 (1965); Angew. Chem. internat. Edit. *4*, 71 (1965).

[15] *F. H. McMillan* and *J. A. King*, J. Amer. chem. Soc. *70*, 4143 (1948).

[16] *J. Szmuszkovicz*, Advances org. Chem. *4*, 1 (1963). For the preparative importance of the enamines, see *A. Hochrainer*, Österr. Chemiker-Ztg. *66*, 355 (1965).

[17] Cf. *G. Opitz* and *A. Griesinger*, Liebigs Ann. Chem. *665*, 101 (1963) and literature cited.

[18] *J. Wehl*, Diploma Thesis, Technische Universität Dresden, 1964.

[19] *J. Fabian*, *K. Gewald*, and *R. Mayer*, Angew. Chem. *75*, 90 (1963); Angew. Chem. internat. Edit. *2*, 45 (1963).

[20] *R. Mayer*, *P. Wittig*, *J. Fabian*, and *R. Heitmüller*, Chem. Ber. *97*, 654 (1964). General procedure: The enamine (0.2 mole) is added dropwise to a vigorously stirred mixture of powdered sulfur (6.4 g, 0.2 g-atoms), CS_2 (0.6 mole), and dimethylformamide (40 ml), the temperature being maintained below 15 °C. The reaction mixture is stirred for a further 2–4 h at room temperature and is then added, with stirring, to 400 ml of water. Precipitated crude products are warmed with 50% sulfuric acid to decompose any dithiocarbamate, and diluted further with water. Liquid products are extracted into chloroform and distilled.

[21] *F. Langer*, Diploma Thesis, Technische Universität Dresden, 1965.

[22] *J. Zamocky*, Diploma Thesis, Technische Universität Dresden, 1964.

[23] *P. Bellmann*, Diploma Thesis, Technische Universität Dresden 1964.

[24] *M. Wirth*, Diploma Thesis, Technische Universität Dresden, 1965.

[24a] *R. Mayer* and *F. Wittig*, unpublished.

[24b] *L. Fabian*, Diploma Thesis, Technische Universität Dresden, 1966.

[25] *B. Neumann*, Diploma Thesis, Technische Universität Dresden 1966.

[26] *R. Mayer* and *H. Hartmann*, Chem. Ber. *97*, 1891 (1964).

[27] *G. Albrecht*, Diploma Thesis, Technische Universität Dresden, 1965.

Table 1. Preparation of 3*H*-1,2-dithiole-3-thiones *(1)* from enamines *(2)*, sulfur, and carbon disulfide.

(2)	*(1)*	Yield (%)	M.p. (°C) (b.p. (°C/mm))	Ref.
1-Diethylamino-1-butene	4-Ethyl-	50	20 (163/12)	[20]
1-Piperidino-1-heptene	4-n-Pentyl-	45	[b]	[21]
1-Piperidino-1-octene	4-n-Hexyl-	32	(150—151/0.25)	[22]
1-Piperidino-2-cyclohexylethylene	4-Cyclohexyl-	17	114	[22]
1-Piperidino-2-phenylethylene	4-Phenyl-	35	121—122	[20]
2-Morpholino-4-methyl-1-pentene	5-Isobutyl-	32	(140—145/0.5)	[18]
1-Piperidino-1-cyclohexylethylene	5-Cyclohexyl-	58	99.5—100	[23]
1-Piperidino-1-benzylethylene	5-Benzyl-	25	88	[22]
1-Morpholino-1-phenylethylene	5-Phenyl-	45	126.5	[18, 20, 24]
1-Morpholino-1-thienylethylene	5-Thienyl-	35	129	[24a]
1-Morpholino-1-*o*-tolyl-ethylene	5-*o*-Tolyl-	15	118	[24b]
1-Morpholino-1-*m*-tolyl-ethylene	5-*m*-Tolyl-	10	102—105	[24b]
1-Morpholino-1-*p*-tolyl-ethylene	5-*p*-Tolyl-	50	119—120	[18, 24]
1-Morpholino-1-(2,6-dimethyl)-phenylethylene	5-(2,6-Dimethylphenyl)-	15	88—89	[24b]
1-Morpholino-1-*p*-ethylphenyl-ethylene	5-*p*-Ethylphenyl-	10	78—79	[24b]
1-Morpholino-1-*p*-methoxyphenyl-ethylene	5-*p*-Methoxyphenyl-	62	111—112	[24]
1-Morpholino-1-*p*-chlorphenyl-ethylene	5-*p*-Chlorphenyl-	36	135	[24]
1-Morpholino-1-*p*-bromphenyl-ethylene	5-*p*-Bromphenyl-	34	130	[24]
1-Morpholino-1-*p*-nitrophenyl-ethylene	5-*p*-Nitrophenyl-	17	190—191	[24]
1-Morpholino-1-cyanophenyl-ethylene	5-*p*-Cyanophenyl-	20	188	[24]
2-Morpholino-2-butene [a]	4,5-Dimethyl-	14	96.5	[25]
2-Morpholino-2-pentene	4-Ethyl-5-methyl-	18	[c]	[25]
1-Di-n-butylamino-1-cyclopentene	4,5-Trimethylen-	58	123	[20, 26]
1-Morpholino-1-cyclohexene	4,5-Tetramethylen-	40	102	[20]
1-Morpholino-1-cycloheptene	4,5-Pentamethylen-	53	98.5	[20]
1-Morpholino-1-phenyl-1-propene	4-Methyl-5-phenyl-	27	104	[18, 27]
3-Piperidino-indene	Indeno[2,3-*d*]-	24	194	[27]
1-Cyclopentyliden-2-morpholino-2-cyclopentene	6-Cyclopentyliden-4,5-dihydro-6*H*-cyclopenta-	25	162—163	[21]
9-Morpholino-6,7-dihydro-5*H*-benzocycloheptene	7,8-Benzo-6,7-dihydro-4*H*-cyclohepta-	37	108	[27]
2-Pyrrolidino-3,4-dihydro-naphthalene	8,9-Dihydronaphtho[2,1-*c*]-	17	119	[27]
1-Morpholino-3,4-dihydro-naphthalene	4,5-Dihydronaphtho[1,2-*c*]- [d]	19	87	[27]

[a] Mixed with 2-morpholine-1-butene.

[b] Liquid; methyl iodide adduct melts at 137—138 °C.

[c] Liquid; methyl iodide adduct melts at 90 °C.

[d] 32% of 4,5-dihydro-2*H*-naphtho[2,1-*d*]-1,3-dithiole-2-thione, m.p. = 115—116 °C, is also formed.

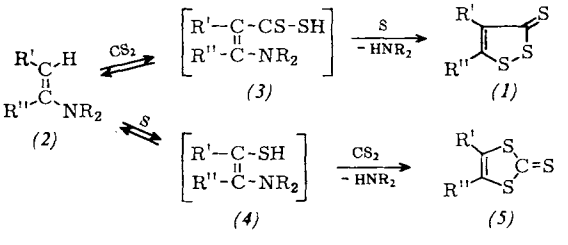
genated to the benzo derivative under the mild conditions used; similarly, the dihydronaphtho-1,2-dithiolethione obtained from enamines of α-tetralone is not converted into the naphtho compound during the reaction. However, the dehydrogenation can be subsequently carried out almost quantitatively, *e.g.* with sulfur at 220 °C, and in this way benzo- and naphtho-1,2-dithiolethiones can also be obtained from enamines [27, 28].

Alkyl aryl ketones give lower yields of enamine with increasing chain length of the aliphatic group, despite the use of longer reaction times. The yield of 1,2-dithiolethione *(1)* also decreases. This is evidently connected with electronic and steric factors, which become particularly noticeable in the branched types.

Mixtures of enamines having the double bond in different positions generally also give mixtures of 1,2-dithiolethiones. The only exception known so far is observed with a mixture of the enamines from methyl ethyl ketone, which gives only 4,5-dimethyldithiolethione [*(1)*, R′ = R″ = CH_3] [25]. (For the tautomerism of enamines, cf. [29].)

The above synthesis of 4- or 5-substituted or 4, 5-disubstituted 3*H*-1,2-dithiole-3-thiones *(1)* is adoptable and simply executed. For maximum yields, the "General Procedure" [20] should be adhered to fairly closely; changes in the conditions promote side reactions. A close study of the reaction ultimately led to other simple syntheses of organic sulfur compounds.

The combined action of carbon disulfide and sulfur on enamines should present at least two general possibilities, (i) primary reaction with carbon disulfide to form *(3)* followed by the incorporation of sulfur, and (ii) initial attack by sulfur.



It was therefore to be expected that the action of CS_2 and sulfur on enamines would lead not only to 3*H*-1,2-dithiole-3-thiones *(1)*, but also to 2*H*-1,3-dithiole-2-thiones *(5)*.

The experimental data show clearly that under the conditions used in the present work, all the alkyl-substituted enamines *(2)* studied so far gave only 1,2-dithiol-3-thiones *(1)*. Enamines of α-indanone and 1-benzocycloheptanone behave similarly [27].

With a few aryl-substituted enamines, *(5)* is formed as well as *(1)*; thus the enamines of acetophenone, propiophenone, butyrophenone, and valerophenone

[28] *P. Wittig*, Diploma Thesis, Technische Universität Dresden, 1963.

[29] *G. Bianchetti, D. Pocar, P. D. Croce*, and *A. Vigevani*, Chem. Ber. *98*, 2715 (1965); *W. D. Gurowitz* and *M. A. Joseph*, Tetrahedron Letters *1965*, 4433.

yield small amounts of *(5)* [24, 27, 30] and larger amounts (up to 50% of the mixture) are formed from enamines of α-tetralone [27], and of deoxybenzoin [31]. Enamines of isovalerophenone and of caprophenone give *(5)* only [27]. Neither *(1)* nor *(5)* has so far been isolated in the case of β-tetralone. Within the limits prescribed for the reaction conditions, the ratio of *(1)* to *(5)* cannot be appreciably altered by varying the reaction conditions and solvent, or by variation of the order of addition of the reactants. The only known exceptions are observed with enamines of ring-substituted acetophenones, where the formation of the 2*H*-1,3-dithiole-2-thione system is favored by an increase in the reaction temperature to 50 °C. (For the side reactions occuring in this case, cf. Sections III and IV).

Steric factors undoubtedly play an important part in the above reactions. Thus the 1,3 system *(5)* is evidently favored when the bulky thiocarbonyl group would not have sufficient room in a 1,2 system *(1)*. However, this is no longer the case in the enamines of α-tetralone and of acetophenone. The 1,2-dithiolethione *(1)* is also always formed in the aliphatic series, in spite of any bulky groups. Thus the question of whether *(5)* or *(1)* is formed probably also depends on electronic factors; owing to the electron-attracting action of the aryl groups, aryl-substituted enamines have a lower electron density on the enamine double bond than alkyl-substituted enamines.



Consequently, the electrophilic carbon disulfide preferentially adds to the much more reactive aliphatic compounds, which, according to experimental observations, is equivalent to the formation of the 1,2 system *(1)*. In the aromatic series, the attack of carbon disulfide is inhibited by the lower electron density on the β-C atom, so that the equilibrium reaction discussed below leads to the thiolation product *(4)* as well as to *(3)* (since the position of the equilibrium depends *inter alia* on the nucleophilic strength of the double bond in the enamine), and hence to a mixture of *(1)* and *(5)*, or occasionally even exclusively to *(5)*. It must be assumed that the enamine initially undergoes a reversible attack by the sulfur as well as by the carbon disulfide. The stabilization of the intermediates, which are formulated as *(3)* and *(4)*, undoubtedly depends on factors that cannot be determined quantitatively at present, such as the electrophilicity of the reactants and the tendency of the product to be formed, *i.e.* the rate of the irreversible stabilization reaction.

The fact that complex equilibrium reactions are involved in the reaction of enamines with CS_2 and sulfur is clear from the following observations. Though there is no longer any doubt that the reaction of an enamine of cyclohexanone with elementary sulfur leads to the thiolation product *(6)*, the subsequent introduction of carbon disulfide results in the formation of the compound *(1a)*. However, the expected 1,3-compound *(5)*, with R'R'' = $(CH_2)_4$, cannot be detected. We have shown, *e.g.* by interception with isothiocyanate, that the intermediate *(6)* is formed, *i.e.* the primary thiolation product of an enamine of cyclohexanone or cyclopentanone. The introduction of isothiocyanate leads smoothly to the adducts *(7)* (*N*-substituted 4-dialkylaminothiazolidine-2-thiones), which react readily with acid to form the stable Δ⁴-thiazoline-2-thiones *(8)*. This led to a new and efficient synthesis of these substances by the action of sulfur and isothiocyanates on enamines [32] (see Table 2). (For the formation of thiazolinethiones *(8)* from α-mercaptoketones and isothiocyanates, cf. [33].)

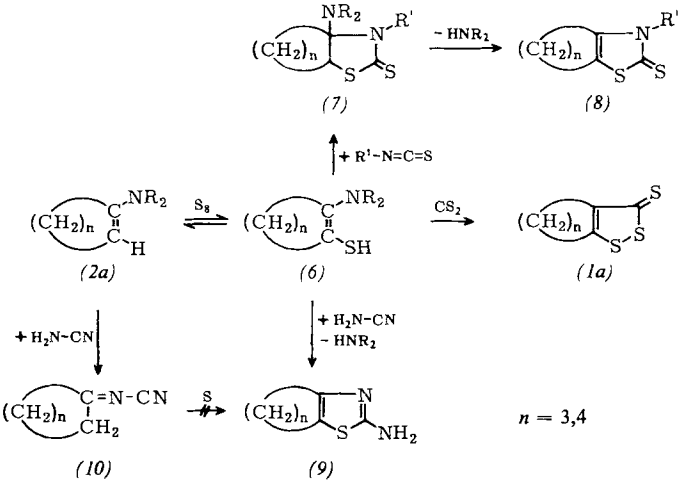
Table 2. Thiazolidine-2-thiones *(7)* and Δ⁴-thiazoline-2-thiones *(8)* from enamines, isothiocyanates, and sulfur [32].

Enamine	Isothiocyanate	*(7)* M.p. (°C)	*(7)* Yield (%)	*(8)* M.p. (°C)	*(8)* Yield (%)
1-Morpholinocyclohexene	Phenyl-	123–127	40	150–151	71
1-Dibutylaminocyclohexene	Phenyl-	70–80	38	150–151	65
1-Piperidinocyclohexene	Methyl-	[a]	60	103	60
1-Morpholinocyclopentene	Phenyl-	150–152	66	116	95
1-Morpholinocyclopentene	Methyl-	[a]	40	104–105	50

[a] Colorless oil, not distillable.

The analogous reaction with isocyanates, which leads to the formation of 2-thiazolidones *(11)*, has now also been described [34].

Finally, the thiolation product *(6)* can also be detected indirectly by the reaction of the enamine *(2a)* with sulfur and cyanamide in alcohol or in dimethylformamide, which yields 2-aminothiazoles *(9)* [35, 36]. A similar reaction takes place with other enamines. *(9)* is formed only when the enamine *(2a)* is first treated with sulfur and then with cyanamide; if the enamine is allowed to react first with cyanamide, it forms the known condensation product *(10)* [37], which does not react further with sulfur.



To summarize, therefore, we can say that the reaction of enamines *(2)* with sulfur and carbon disulfide leads, in the aliphatic series exclusively, and in the aromatic

[30] *R. Prousa*, Diploma Thesis, Technische Universität Dresden, 1965.

[31] *G. Laban*, Diploma Thesis, Technische Universität Dresden, 1965.

[32] *H. Hartmann* and *R. Mayer*, Z. Chem. *5*, 152 (1965); *H. Hartmann*, Dissertation, Technische Universität Dresden, 1965.

[33] *K. Rühlmann, A. Grosalski*, and *U. Schräpler*, J. prakt. Chem. *11*, 54 (1960).

[34] *K. Ley* and *R. Nast*, Angew. Chem. *77*, 544 (1965); Angew. Chem. internat. Edit. *4*, 519 (1965).

[35] *K. Gewald, H. Spies*, and *R. Mayer*, unpublished.

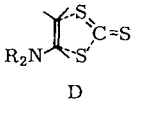
[36] Cf. *K. Gewald, H. Böttcher*, and *R. Mayer*, J. prakt. Chem. *23*, 298 (1964).

[37] *N. A. Goldberg* and *V. G. Golov*, Chim. Nauka i Prom. *4*, 138 (1959).

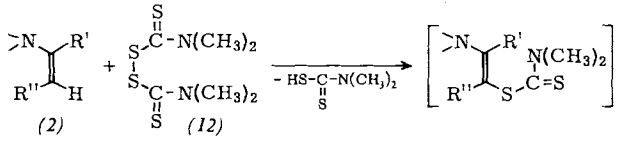
series mainly, to 3*H*-1,2-dithiole-3-thiones *(1)*, and that the formation of 2*H*-1,3-dithiole-2-thiones *(5)* is observed only with a few types of enamines. The occasional formation of *(5)* in our synthesis of *(1)* represents a new discovery. However, since the ratio of *(1)* to *(5)* is largely independent of the reaction conditions discussed here, it is not yet clear why the yield of *(1)* is so strongly dependent on the reaction conditions.

Mention should first be made of another point. 2*H*-1,3-dithiole-2-thiones *(5)* should also be formed from enamines and carbon disulfide in accordance with principle D, by primary attack of the carbon disulfide on the enamine with formation of a CS bond. However, since carbon disulfide alone reacts with the enamine to give only a C–C bond, the incorporation of the CS_2 grouping in the desired direction can be achieved only with the aid of a CS_2 derivative in which the S atom is more electrophilic than the carbon of the thiocarbonyl group. This requirement has been shown to be satisfied by thiuram disulfides *(12)*, enamines being sufficiently nucleophilic to cleave the disulfide bridge in such compounds. In the presence of hydrogen sulfide, the intermediate is stabilized by formation of the 1,3-dithiolethione *(5)* [38,39].

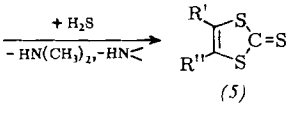
The yields are between 50 and 70%. 1,2-Dithiolethiones *(1)* are not formed in this reaction.



D



(2) *(12)*

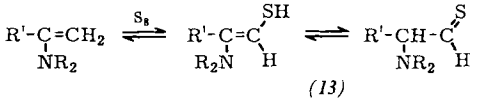


(5)

(a) R'R'' = $-(CH_2)_n-$; n = 3,4,5
(b) R' = C_6H_5, R'' = H
(c) R' = C_6H_5, R'' = CH_3

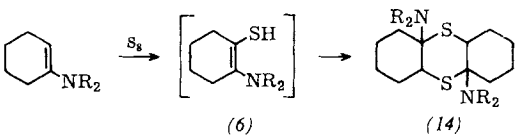
III. The Reaction of Enamines with Sulfur

Let us now return to the thiolation of enamines:



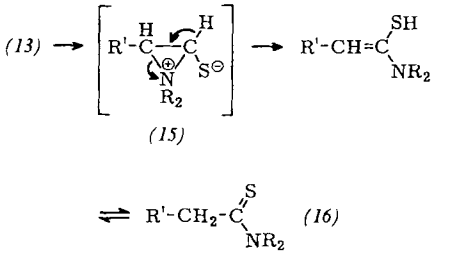
(13)

The intermediate *(13)* is undoubtedly extremely reactive, and should undergo stabilization, even when no other component (such as carbon disulfide or isothiocyanate) is available. In the case of morpholinocyclohexene, it was already known [40] that a hydrogenated thianthrene *(14)* is formed in benzene at 90 °C.



(6) *(14)*

However, thiolated enamines of the type *(13)*, unlike those of the type *(6)*, should become stable by formation of the thioamide *(16)*.

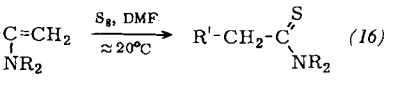


(15)

(16)

Aziridinium ions have often been postulated as intermediates in rearrangements [41], which, however, are not directly comparable with the rearrangement of aziridines into enamines, cf. [42]. The rearrangement of *(13)* into *(16)* is simply a nucleophilic attack of an amine on a thiocarbonyl group or on an enthiol. Reactions of this type always result in addition to the C atom [43]. Thioamides *(16)* therefore occur as by-products in our synthesis of 1,2-dithiolethiones, and should be the main product when the amines react in the presence of sulfur but in the absence of carbon disulfide.

Though the formulation of the rearrangement *(13)* → *(16)* is speculative, it has been fully corroborated in preparative work [18,30]. Thus elementary sulfur reacts with suitable enamines at room temperature (preferably in dimethylformamide) with direct formation of thioamides, sometimes in very high yields [44].



(16)

During the initial thirty minutes of the reaction, the temperature of the reaction mixture rises by 4–5 °C; no resinification occurs, but a brown to red color develops with simultaneous more or less rapid dissolution of the sulfur. Hydrogen sulfide is not formed under these conditions [30]. (Concerning the reaction of amines with sulfur, which is sometimes exothermic, and the resulting activation of the sulfur, cf. [4,8]). In general, the yield of thioamide can be increased by the use of longer reaction times, by stirring the reaction mixture, or by increasing the quantity of dimethylformamide. The yields of thioamide also depend on the nature of the amine component in the enamine. This dependence has been studied for enamines of acetophenone [30]. 1-Morpholino-1-phenylethylene reacts very well (yield up to 95%), whereas the pyrrolidino compound and 1-diisobutylamino-1-phenylethylene give only small quantities of thioamide *(16)*. Under the same conditions, the enamines of acetophenone with diisopropylamine and *N*-methylaniline give no thioamide. (Concerning the problems of the synthesis of thioamides, cf. [44a].)

[38] *E. Fanghänel*, Z. Chem. *4*, 41 (1964).

[39] *E. Fanghänel*, unpublished.

[40] *Y. Nomura* and *Y. Takeuchi*, Bull. chem. Soc. Japan *36*, 1044 (1963); Chem. Zbl. *1964*, 49-0874.

[41] For a review, see *P. E. Fanta* in *A. Weissberger*: The Chemistry of the Heterocyclic Compounds. Vol. 19, Part I, p. 548. Interscience Publishers, New York-London 1964.

[42] *A. B. Turner*, *H. W. Heine*, *J. Irving*, and *B. Busch jr.*, J. Amer. chem. Soc. *87*, 1050 (1965); cf. *G. H. Alt* and *A. J. Speziale*, J. org. Chemistry *31*, 1340 (1966).

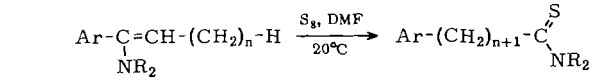
[43] *R. Mayer et al.*, unpublished.

[44] *R. Mayer* and *H. Wehl*, Angew. Chem. *76*, 861 (1964); Angew. Chem. internat. Edit. *3*, 705 (1964).

[44a] *W. Walter* and *K.-D. Bode*, Angew. Chem. *78*, 517 (1966); Angew. Chem. internat. Edit. *5*, 447 (1966).

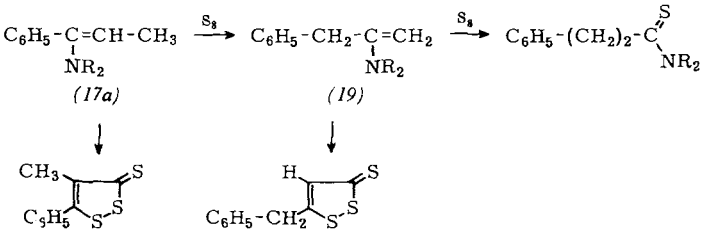
The similarity to the Willgerodt-Kindler reaction (cf. [9,44a] and the literature cited there), *i.e.* the action of sulfur on the enamine components (ketone and amine) at about 130 °C, is obvious, particularly since we have shown that catalysts that favor the enamine formation give increased yields of thioamide *(16)* in the Willgerodt-Kindler reaction. Since the enamine reacts with sulfur at room temperature to form the thioamide *(16)*, the high temperature in the Willgerodt-Kindler reaction is evidently necessary for the enamine formation [18, 30, 43].

This observation, which was also made by *F. Asinger et al.* [9, 45,46], has been confirmed by other workers [47] who found that enamines were formed in the reaction of sulfur with methyl ketones in the presence of secondary amines, and that these enamines themselves reacted with sulfur to form thioamides, though a reaction time of 4 hours at 125 °C was required. An apparently important point is the fact that enamines of the types *(17)* and *(18)* also give thioamides with sulfur at room temperature [30,44]. However, enamines with longer chains give much lower yields and enamines of isobutyrophenone and isovalerophenone do not give thioamides at room temperature [30].



(17), n = 1
(18), n = 2

The fact that enamines of propiophenone *(17a)* react with sulfur at room temperature to give thioamides has led to an interesting observation [18, 30, 48]. This reaction proceeds analogously to that of the enamines of methyl ketones, but the enamine *(17a)* first isomerizes to give *(19)* [48a].

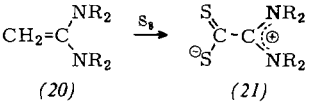


The terminal double bond in *(19)* reacts with sulfur to give the thioamide. The isomerization of the enamine *(17a)* is "catalysed" by sulfur. However, a relatively long time is required for establishment of the equilibrium, so that when one mole of sulfur is used per mole of *(17a)*, the unrearranged compound is also consumed in side reactions. This leads to a decrease in the yield of thioamide from longer-chain enamines.

We also interpret the "migration" of the carbonyl group of aryl ketones to the end of the chain in the Willgerodt-Kindler reaction as an isomerization of the initially formed enamine, at least for the types of compounds discussed here (cf. [49]). As soon as an enamine with a terminal double bond [type *(19)*] is present, the equilibrium is disturbed with irreversible formation of a thioamide. It should also be mentioned that the sulfur-"catalysed" conversion of *(17a)* into *(19)* can also be utilized for a planned synthesis of 1,2-dithiolethiones by the combined action of carbon disulfide and sulfur on enamines [48]. Whereas the normal procedure leads to 4-methyl-5-phenyl-3*H*-1,2-dithiole-3-thione, a modified procedure gives considerable quantities of the 5-benzyl-3*H*-1,2-dithiole-3-thione derived from *(19)*. 1 mole of sulfur and 1 mole of *(17a)* are first allowed to react for a relatively short time in dimethylformamide (this leads mainly to *(19)* and very little thioamide), and the carbon disulfide is then added.

In the normal operation, some thioamide is naturally always formed as a by-product in the synthesis of *(1)*. However, if the operations are carried out quickly and if the sulfur is not allowed to act on the enamine for too long, the thioamide formation is largely suppressed in favor of the 1,2-dithiolthione. Otherwise, suitable structural types lead mainly to thioamides.

In contrast to the action of sulfur on enamines, which yields thioamides, the reaction of endiamines *(20)* with sulfur under similar conditions leads, not to analogues of thioamides, but to high-melting colored salts having the structure *(21)* [50]. These salts are also obtained by the reaction of tetraaminoethylenes with carbon disulfide [51].



(20) *(21)*

The reaction of 1-morpholino, 1-diisobutylamino-, 1-di-n-butylamino, or 1-di-n-propylamino-1-phenylethylene with sulfur in dimethylformamide at room temperature (see Table 3) yields a yellow by-product having m.p. 207 °C. This compound becomes the main product at 50–80 °C, and can be isolated in a yield of approximately 50% together with the thioamide [30]. The compound, which can also be obtained from the

Table 3. *N*-substituted phenylthioacetamides and 2-benzylidene-4-phenyl-2*H*-1,3-dithiole *(22)* from enamines of acetophenone and sulfur in dimethylformamide at 20 °C [30].

Amine component	Thioamide Yield (%)	*(22)* Yield (%)
Morpholine	95	1
Piperidine	86	—
Pyrrolidine	4 [a]	— (1% Diphenylthiophene)
Di-n-propylamine	—	3.3
Di-n-butylamine	—	9.1
Diisobutylamine	3 [a]	15

[a] Yield determined indirectly by hydrolysis to phenylacetic acid.

[45] *F. Asinger* and *K. Halcour*, Mh. Chem. *94*, 1029, 1047 (1963); ibid. *95*, 24 (1964).

[46] *F. Asinger*, personal communication (Feb. 16th, 1965).

[47] *T. Bacchetti*, *A. Allemagna*, and *B. Danieli*, Tetrahedron Letters *1965*, 2001.

[48] *R. Mayer* and *H. Prousa*, Z. Chem., in preparation.

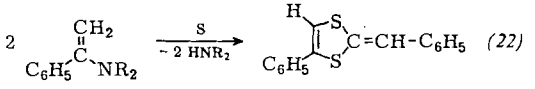
[48a] For ketone isomerization with sulfur and amines, cf. *F. Asinger*, *H. Offermanns*, and *H. D. Köhler*, Tetrahedron Letters *1967*, 631.

[49] *M. Carmack* and *M. A. Spielmann*, Org. Reactions *3*, 88 (1946).

[50] *D. H. Clemens*, *A. J. Bell*, and *J. L. O'Brian*, Tetrahedron Letters *1965*, 3257.

[51] *H. E. Winberg* and *D. D. Coffman*, J. Amer. chem. Soc. *87*, 2776 (1965).

Schiff base[54] or in 60% yield from phenylacetylene (see below), and the formation of which is evidently strongly favored, was characterized as 2-benzylidene-4-phenyl-2*H*-1,3-dithiole *(22)* by comparison with authentic material[52] and by an independent synthesis[53].

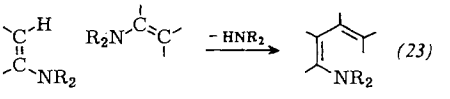


(22) was observed in 1958 as a photolysis product of 4-phenyl-1,2,3-thiadiazole[55]. The tendency of *(22)* to be formed is also observed in the normal synthesis of 1,2-dithiolethiones from 1-morpholine-1-phenylethylene, carbon disulfide, and sulfur[24] when the reaction is carried out above about 30 °C. At room temperature, *(22)* can be detected only in traces by thin-layer chromatography. Thus to synthesize definite compounds *(1)* in high yields from enamines, sulfur, and CS_2, the reaction temperature should be kept below 30 °C, and the CS_2 should be added initially to ensure that the sulfur is not allowed to act on the enamine alone.

These observations undoubtedly explain why the yields of *(1)* depend on the reaction conditions for certain enamines. However, they do not explain why this is also found with enamines that, for structural reasons, cannot form 1,3-dithiolethiones *(5)*, thioamides *(16)*, or dithioles of the type *(22)*. Other competing reactions are evidently also possible, and these will be discussed below.

IV. Reaction of Dienamines with Carbon Disulfide and Sulfur

In general, enamines are not particularly stable, and undergo polycondensation even at low temperatures. As is known, enamines obtained from aldehydes[56] give dienamines of the type *(23)*, as well as polyenamines. 1-Amino-1,3-butadienes of the type *(23)* are also formed during the thermal decomposition of enamines[56] and by the action of amines on α,β-unsaturated aldehydes followed by thermal deamination[57, 58]. (The reaction of ketals with secondary amines, on the other hand, leads to 2-amino-1,3-butadienes[59].) A pyrrolidine residue can be eliminated much more easily than *e.g.* a morpholino or a piperidino grouping; consequently, the pyrrolidinoethylenes have a particularly strong tendency to undergo self-condensation[60].



The formation of dienamines would be expected to be favored by an amine interceptor such as CS_2. Thus the action of carbon disulfide and sulfur on enamines should lead to the formation of dienamines. Like

Table 4. 2*H*-Thiopyran-2-thiones *(24)* from enamines and carbon disulfide [63a].

Enamine	*(24)*	M.p. (°C) (b.p. (°C)/mm)	Yield (%)	Ref.
1-Piperidino-1-propene	3,5-Dimethyl-	100	47	[31]
1-Piperidino-1-butene	3,5-Diethyl-	(132—134/0.1)	45—54 [a]	[31]
2-Morpholino-2-butene	3,4-Dimethyl-6-ethyl- [b]	58	3	[18, 25]
2-Morpholino-2-pentene	3-Ethyl-4-methyl-6-n-propyl-	[c]	16	[25]
1-Piperidino-2-heptene	3,5-Di-n-pentyl-	(160/0.05)	37 [a]	[31]
1-Morpholino-1-phenylethylene	4,6-Diphenyl-	123	37	[24]
1-Pyroolidino-1-phenylethylene	4,6-Diphenyl-	123	61	[18, 31]
1-Piperidino-1-phenylethylene	4,6-Diphenyl-	123	39	[31]
1-Di-n-butylamino-1-phenylethylene	4,6-Diphenyl-	123	28	[31]
1-Piperidino-2-phenylethylene	3,5-Diphenyl-	86—87	5	[31]
1-Morpholino-1-*p*-bromophenylethylene	4,6-Bis(*p*-bromophenyl)-	220—221	17	[24]
1-Morpholino-1-*p*-chlorophenylethylene	4,6-Bis(*p*-chlorophenyl)-	202—203	26	[24]
1-Morpholino-1-*p*-ethylphenylethylene	4,6-Bis(*p*-ethylphenyl)-	98—99	31	[24]
1-Morpholino-1-*p*-tolylethylene	4,6-Bis(*p*-tolyl)-	162—163	48	[24]
1-Morpholino-1-*p*-methoxyphenylethylene	4,6-Bis(*p*-methoxyphenyl)-	149—150	52	[24]

[a] Crude product. [b] Position of the alkyl group uncertain.
[c] Liquid; methyl iodide adduct melts at 117—118 °C.

[52] Supplied by Prof. *L. Horner*, Mainz, and Prof. *W. Kirmse*, Marburg, to whom we are very grateful. Thanks are also due to Dr. *G. Snatzke*, for recording and discussing the NMR spectrum.

[53] *R. Mayer, B. Hunger, R. Prousa*, and *A. K. Müller*, J. prakt. Chem., in press.

[54] *P. Schlemmer*, Diploma Thesis, Technische Universität Dresden, 1965.

[55] *W. Kirmse* and *L. Horner*, Liebigs Ann. Chem. *614*, 4(1958).

[56] *C. Mannich* and *E. Kniss*, Ber. dtsch. chem. Ges. *74*, 1629 (1941); *W. Langenbeck, O. Gödde, L. Weschky*, and *R. Schaller*, Ber. dtsch. chem. Ges. *75*, 232 (1942).

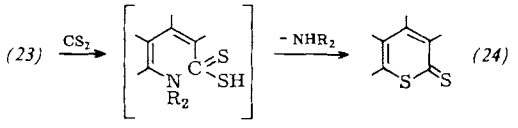
[57] *C. Mannich, K. Handke*, and *K. Roth*, Ber. dtsch. chem. Ges. *69*, 2112 (1936).

[58] *S. Hünig* and *H. Kahanek*, Chem. Ber. *90*, 238 (1957).

[59] *G. Bianchetti*, Tetrahedron Letters *1965*, 2039.

[60] Cf. *G. Opitz, H. Hellmann*, and *H. W. Schubert*, Liebigs Ann. Chem. *623*, 112 (1959).

simple enamines, these should react again with CS_2, the resulting product being stabilized by deamination to form a 2*H*-thiopyran-2-thione (α-dithiopyrone) *(24)*.



This conclusion was confirmed experimentally. α-Dithiopyrones *(24)* occur as by-products in most of our syntheses of 1,2-dithiolethiones, particularly when carbon disulfide is used in excess, when the carbon disulfide is allowed to act on the enamine *(2)* for too long in the absence of sulfur, when the reaction temperature is too high, or when relatively non-polar solvents are used instead of the required strongly polar solvents.

Only a few α-dithiopyrones *(24)* have been described so far (cf. [61,62]). It is therefore interesting to note that they can also be obtained in fairly good yield by the reaction of enamines *(2)* with carbon disulfide at room temperature in the absence of sulfur (Table 4) [63, 63a].

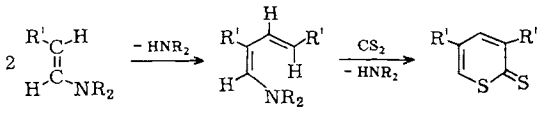
Enamines of aldehydes give 3,5-disubstituted α-dithiopyrones *(24)*, while enamines of ketones give 4,6-disubstituted derivatives. Closer investigation showed that the above considerations concerning the reaction sequence enamine → *(23)* → dithiopyrone *(24)* are also valid for the enamines of aldehydes. In this case the dienamine *(23)* can be detected as an intermediate if the addition of carbon disulfide is stopped prematurely. As expected, the separately prepared dienamines *(23)* can react with carbon disulfide at room temperature to give dithiopyrones *(24)* (see Table 5).

Table 5. 2*H*-Thiopyran-2-thiones *(24)* from dienamines and carbon disulfide [63a].

Dienamine	*(24)*	M. p. (°C) (b. p. (°C/mm)	Yield (%)	Ref.
1-Diethylamino-1,3-butadiene	*(24)*	64	16	[31]
1-Pyrrolidino-2-methyl-1,3-pentadiene	3,5-Dimethyl-	100	58	[31]
1-Piperidino-2-methyl-1,3-pentadiene	3,5-Dimethyl-	100	30	[21]
1-Piperidino-2-ethyl-1,3-hexadiene	3,5-Diethyl-	(132–134/0.1)	68 [a]	[31]
1-Piperidino-2-n-pentyl-1,3-nonadiene	3,5-Di-n-pentyl-	(160/0.5)	51 [a]	[31]

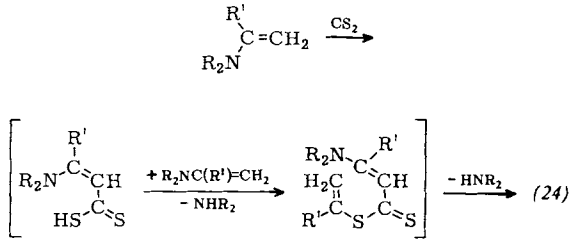
[a] Crude product.

It is also possible to prepare in this way the unsubstituted 2*H*-thiopyran-2-thione [63a], the formation of which had been previously detected in the reaction of thiacyclohexane and sulfur at high temperature [64].



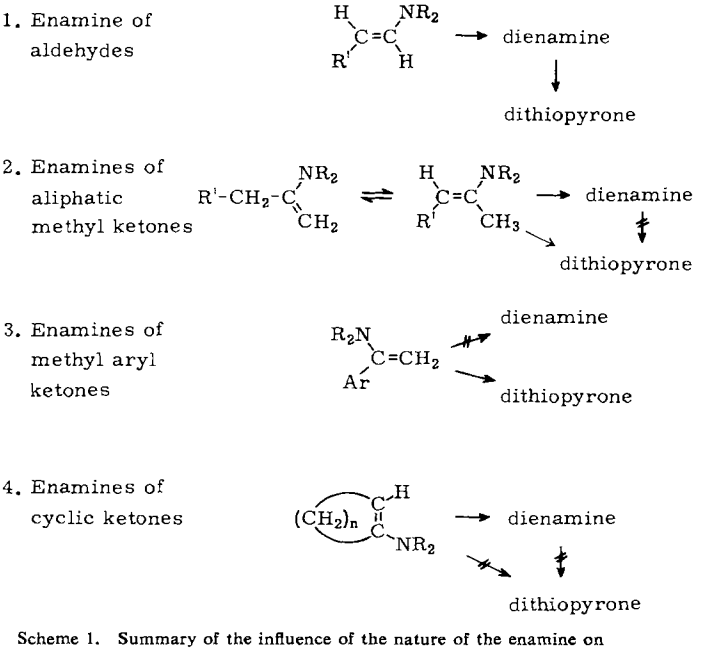
The situation is more complex in the case of enamines derived from ketones. Enamines of aliphatic methyl ketones react with carbon disulfide to form *(24)*; however, when the enamines are converted into dienamines[64a] followed by treatment with carbon disulfide, dithiopyrones *(24)* can be detected in only a few cases, and then only in traces by thin-layer chromatography. Instead of *(24)*, considerable quantities of an inner ammonium salt are obtained (for the structure of this salt, cf. [63a]).

Enamines of methyl aryl ketones cannot be converted into dienamines, but they still give dithiopyrones on treatment with carbon disulfide. Since dienamines can be ruled out as intermediates in this case, it must be assumed that dithiopyrones *(24)* can be formed from enamines of methyl ketones by some other route; for example, carbon disulfide may be added first, the intermediate dithio acid then undergoing cyclization with a second molecule of enamine.



Though enamines of cyclic ketones can be converted into dienamines, neither the enamine nor the dienamine reacts with carbon disulfide to form dithiopyrone *(24)*. Finally, neither dienamines nor dithiopyrones have so far been obtained from the enamines of higher dialkyl or aralkyl ketones.

The various types of enamine are again compared in Scheme 1. Steric factors again have an important effect



Scheme 1. Summary of the influence of the nature of the enamine on the formation of dithiopyrone.

[61] Review of thiopyran-2-thiones: *R. Mayer et al.*, Advances heterocyclic Chem., in press.

[62] *H. Behringer* and *A. Grimm*, Liebigs Ann. Chem. *682*, 188 (1965).

[63] *R. Mayer* and *J. Wehl*, Angew. Chem. *77*, 261 (1965); Angew. Chem. internat. Edit. *4*, 246 (1965).

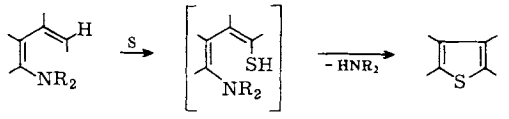
[63a] *R. Mayer, G. Laban*, and *M. Wirth*, Liebigs Ann. Chem., in press.

[64] *R. Mayer*, Chem. Ber. *90*, 2362 (1957).

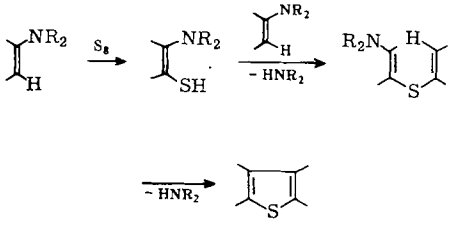
[64a] Cf. *P. Madsen* and *S. O. Lawesson*, Recueil Trav. chim. Pays-Bas *85*, 753 (1966).

on the reactions described here. Though the nature of the amine component can influence the yields (cf. Table 4), the formation of thiopyranthione depends mainly on the bulk of the substituents in the enamine.

Dienamines should also undergo thiolation with elementary sulfur, particularly since the product can be stabilized by cyclization to form the thiophene ring.



The action of sulfur on enamines should also lead occasionally to thiophenes.

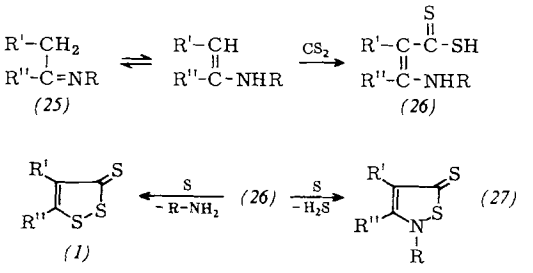


However, it has been found that much higher temperatures are required for the preparation of thiophenes from both enamines and dienamines than for the synthesis of 1,2-dithiolethiones or thioamides. Consequently, thiophenes have so far been detected only in traces (if at all) as by-products of the synthesis of 1,2-dithiolethiones at room temperature. Thiophene is also detected only in traces in the reaction of 1-diethylamino-1,3-butadiene with sulfur. Enamines that condense rapidly have a stronger tendency toward thiophene formation. Thus in the reaction of the labile 1-pyrrolidine-1-phenylethylene with sulfur in dimethylformamide at 20 °C, about 2% of 2,4-diphenylthiophene is obtained as a by-product of the thioamide synthesis described in Section III. Large quantities of diphenylthiophene (about 20%, and 30% in the presence of *p*-toluenesulfonic acid) are also formed from acetophenone and pyrrolidine at 130 °C under the conditions of the Willgerodt-Kindler reaction; this does not necessarily mean that thiophenes cannot be formed by other routes in this reaction [65]. (Concerning thiophenes as by-products of the Willgerodt reaction, cf. also [66], and concerning the thiophene derivatives observed in the reaction of enamines with sulfur at 125 °C, see [47].)

V. Reaction of Ketimines with Carbon Disulfide and Sulfur

In some cases Schiff bases exist in equilibrium with enamines [67]; it was therefore to be expected that Schiff bases react with carbon disulfide and sulfur in the same way as enamines [67a]. (Concerning the treatment of Schiff bases with sulfur, cf. also [9].)

However, it was found that ketimines first react with carbon disulfide to form isolable dithio acids *(26)* [68], which have not so far been detected in the reactions of enamines.



The further stabilization of *(26)* in the presence of sulfur can take place in two ways, both of which can be achieved in practice [12,69]. On the one hand, *(26)* may be *S*-thiolated and converted into 3*H*-1,2-dithiole-3-thiones *(1)* with elimination of amine. This is a special case of the synthesis of *(1)* from enamines as described above. Unlike the enamines, Schiff bases *(25)* in the enamine-like equilibrium form have a *N*-hydrogen atom that can be split off. Secondly, in the presence of sulfur, *(26)* can be dehydrogenated with elimination of H_2S, with formation of novel Δ^3-isothiazoline-5-thiones *(27)*. The dehydrogenation *(26)* → *(27)* can also be brought about by other oxidizing agents, such as iodine.

Table 6. Δ^3-1,2-Thiazoline-5-thiones *(27)* from ketimines, carbon disulfide, and sulfur [69, 70].

Ketimine	*(27)*	M.p. (°C)	Yield (%)
N-Cyclohexylidene-cyclohexylamine	2-Cyclohexyl-3,4-tetramethylene-	195—196	50
N-Cyclohexylidene-isopropylamine	2-Isopropyl-3,4-tetramethylene-	167—168	35
N-Cyclohexylidene-n-propylamine	2-n-Propyl-3,4-tetramethylene-	125—126	30
N-Cyclohexylidene-n-butylamine	2-n-Butyl-3,4-tetramethylene-	74	25
N-Cyclohexylidene-allylamine	2-Allyl-3,4-tetramethylene-	105—106	27
N-Cyclohexylideneaniline	2-Phenyl-3,4-tetramethylene-	134	12
N-Cyclohexylidene-benzylamine	2-Benzyl-3,4-tetramethylene-	170—172	14
N-Cyclohexylidene-α-phenylethylamine	2-(α-Phenylethyl)-3,4-tetramethylene-	100—101	25
N-Cyclohexylidene-β-phenylethylamine	2-(β-Phenylethyl)-3,4-tetramethylene-	187—188	20
N-Cyclohexylidene-β-hydroxyethylamine [a]	2-(β-Hydroxyethyl)-3,4-tetramethylene-	165—166	25
N-Cyclopentylidene-cyclohexylamine	2-Cyclohexyl-3,4-pentamethylene-	168—172	15
N-(1-Phenylethylidene)-cyclohexylamine	2-Cyclohexyl-3-phenyl-4-methyl-	143—144	32
N-(3-Pentylidene)-cyclohexylamine	2-Cyclohexyl-3-ethyl-4-methyl-	149—150	10

[a] In equilibrium with 1-oxo-4-azaspiro[4,5]decane (2,2-pentamethylene-1,3-oxazolidine).

[65] *F. Asinger* and *A. Mayer*, Angew. Chem. *77*, 812 (1965); Angew. Chem. internat. Edit. *4*, 788 (1965); *C. D. Slater* and *D. L. Heywood*, J. heterocyclic Chem. *2*, 315 (1965).

[66] *M. Carmack* and *M. A. Spielmann*, Org. Reactions *3*, 91 (1946).

[67] *R. W. Layer*, Chem. Reviews *63*, 489 (1963).

[67a] *F. Asinger*, *A. Saus*, *H. Offermanns*, and *H. D. Hahn*, Liebigs Ann. Chem. *691*, 95 (1966), and literature cited there.

[68] *R. Mayer* and *J. Jentzsch*, J. prakt. Chem. *23*, 83 (1964).

[69] *R. Mayer* and *J. Jentzsch*, J. prakt. Chem. *23*, 113 (1964).

[70] *R. Mayer*, *H.-J. Hartmann*, and *J. Jentzsch*, J. prakt. Chem. [4], *31*, 312 (1966).

The question of whether the intermediate *(26)* reacts to form *(1)* or *(27)* is determined mainly by the temperature. The reaction takes place in only a few cases below 10 °C; between 15 and 20 °C, the principal (but not the only) products are isothiazolinethiones *(27)* (see Table 6), whereas the main product at about 50 °C are 1,2-dithiolethiones *(1)* (see Table 7)[12,69]. The reaction is best carried out in dimethylformamide[70, 71].

Table 7. 3*H*-1,2-Dithiole-3-thiones *(1)* from Schiff bases, carbon disulfide, and sulfur.

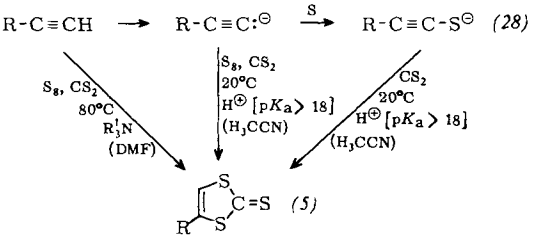
Schiff base	*(1)*	M.p. (°C) (b.p. (°C/mm))	Yield (%)	Ref.
N-Cyclohexylidene cyclohexylamine	4,5-Tetramethylene-	102	47	[69,70]
N-Cyclopentylidene-cyclohexylamine	4,5-Pentamethylene-	98	48	[70]
N-(3-Pentyliden)-β-hydroxyethylamine [a]	4-Methyl-5-ethyl-	(160–165/3)	42	[70,71]

[a] In equilibrium with 2,2-diethyl-1,3-oxazolidine.

The structure of the Schiff base *(25)* generally appears to have no appreciable effect on the direction of the reaction. However, it is interesting to note that derivatives of cyclohexanone [*(25)*, R′R″ = $(CH_2)_4$] give good yields of isothiazolinethiones *(27)*, whereas the readily obtainable, very stable dithioacid *(26)* [R′R″ = $(CH_2)_3$, R = *e.g.* cyclohexyl] derived from cyclopentanone cannot be converted into derivatives of either *(1)* or *(27)*[68,69,70]. The 5-membered ring evidently forms a compound having an exocyclic double bond rather than a cyclopentane ring, a tendency that has already been observed in another connection[72]. A preference for the formation of 1,2-dithiolethiones has so far been observed only in the Schiff bases of β-aminoethanol, which exist predominantly as oxazolidines[73].

VI. The Action of Sulfur and Carbon Disulfide on Alkynes

It is well known that acetylene and monosubstituted acetylenes react as CH acids with electrophiles in the presence of an auxiliary base. It should therefore be possible to use these compounds instead of enamines as C_2 components in the synthetic principle (A) mentioned in the Introduction. This has been confirmed by preparations using acetylene and phenylacetylene[53,74,75]. In contrast to the reactions of enamines, the formation of an intermediate dithio acid is not favored in the case of the alkynes[76], whereas the primary thiolation is favored. The products are therefore of the 1,3-dithiole-2-thione type *(5)*. If sodium acetylide is used as the starting material, no auxiliary base is required and the action of sulfur and carbon disulfide in the presence of a protonic solvent leads, even at room temperature, to good yields of 1,3-dithiol-2-thiones (*e.g.* 60% of *(5)*, R = C_6H_5, and 25% of the unsubstituted compound)[53,74,77,78].



The reaction is generally applicable. For example, if selenium is used instead of sulfur, the reaction with phenylacetylene leads smoothly (yield about 50%) to 5-phenyl-1,3-thiaselenole-2-thione[79]. This reaction evidently proceeds *via* the thiolation product *(28)*, which can be prepared from sodium phenylacetylide and sulfur[80]. Thus the thiolate *(28)* may be used directly as the starting material.

We found[53,81] that sodium phenylethynylthiolate dimerizes very rapidly in the presence of acids or other H-active compounds having a pK_a value < 18, with formation of 2-benzylidene-4-phenyl-1,3-dithiole *(22)*, which can be obtained in better yields (about 60%) in this way than from enamines and sulfur.

Similarly, the very stable selenium analogues of *(22)*[53] are obtained from sodium phenylacetylide and selenium[82] *via* sodium phenylethynylselenolate.

The synthesis of 1,3-dithiolethiones *(5)* from CS_2, sulfur, and sodium phenylacetylide requires the presence of a proton-transfer agent, which may be identical with the polar solvent. However, this solvent should have a pK_a value > 18 (*e.g.* acetonitrile), since the yield of 1,3-dithiolethione is otherwise reduced as a result of the very fast dimerization of the intermediate *(28)* to form the compound *(22)*. Even in methanol ($pK_a = 16$), the main product is *(22)*[53].

Some interesting results were obtained in attempts to catalyse the synthesis of 1,3-dithiolethiones from alkynes, CS_2, and sulfur by means of amines. Whereas phenylacetylene, CS_2, and sulfur react in the presence of tertiary amines (though a temperature of about 80 °C is required in this case) to form phenyl-1,3-dithiolethiones, the tertiary amine acting as an auxiliary base, the reaction in the presence of secondary amines leads, not to 1,3-dithiolethiones, but to phenylthioacetamides. This is interesting, since the thiolate *(28)* adds on *e.g.* morpholine or diethylamine, even in the cold, to form thioamides[53].

[71] *H.-J. Hartmann*, Diploma Thesis, Technische Universität Dresden, 1964.

[72] Cf. *G. Hornke*, *H. Krauch*, and *W. Kunz*, Chemiker-Ztg. *90*, 840 (1966).

[73] *E. D. Borgmann*, *E. Zunkin*, and *S. Pinchar*, Recueil Trav. chim. Pays-Bas *71*, 168 (1952).

[74] *R. Mayer*, *B. Gebhardt*, *J. Fabian*, and *A. K. Müller*, Angew. Chem. *76*, 143 (1964); Angew. Chem. internat. Edit. *3*, 134 (1964).

[75] *A. K. Müller*, Diploma Thesis, Technische Universität Dresden 1964.

[76] For the addition of dithiocarbamates to alkynes, cf. *J. C. Sauer*, J. org. Chemistry *24*, 1952 (1950); *J. L. Garraway*, J. chem. Soc. (London) *1962*, 4077.

[77] *B. Gebhardt*, Dissertation, Technische Universität Dresden, 1964.

[78] *R. Mayer* and *B. Gebhardt*, Chem. Ber. *97*, 1298 (1964).

[79] *R. Mayer* and *A. K. Müller*, Z. Chem. *4*, 384 (1964).

[80] *M. Schmidt* and *V. Potschka*, Naturwissenschaften *50*, 302 (1963).

[81] *B. Hunger*, Diploma Thesis, Technische Universität Dresden, 1965.

[82] Cf. *L. Brandsma*, *H. Wijers*, and *J. F. Arens*, Recueil Trav. chim. Pays-Bas *81*, 583 (1962); *L. Brandsma*, *H. Wijers*, and *C. Jonker*, *ibid. 83*, 208 (1964); *L. Brandsma*, *ibid. 83*, 307 (1964).

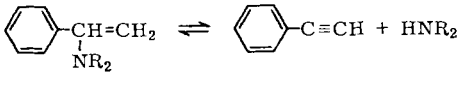
(28) $\xrightarrow{H^{\oplus}}$ [R-C≡C-SH ⇌ R-CH=C=S] *(28a)*

$$\xrightarrow{HNR'_2} R\text{-}CH_2\text{-}C(=S)\text{-}NR'_2$$

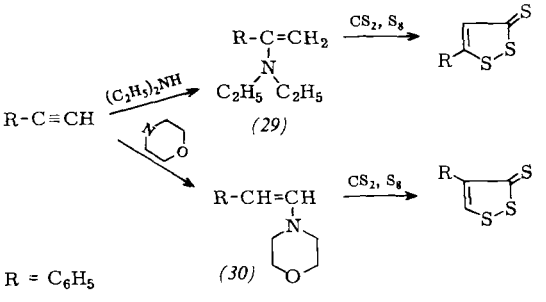
The analogous addition of mercaptans to alkynethiolates *(28)*, which leads to dithio esters, has now also been described [82a]. The thioketene *(28a)* is proposed as an intermediate (cf. [53]).

The similarity to the Willgerodt-Kindler reaction is again obvious, particularly since it is known that the reaction of phenylacetylene, sulfur, and morpholine at about 150 °C leads to phenylthioacetomorpholide [83,84].

Since the reactions of sulfur at room temperature with enamines of acetophenone (see Section III) and with sodium phenylacetylide in the presence of secondary amines lead to the same thioamide, an equilibrium could exist between the enamine and the alkyne + amine [49,84].



The conversion of the enamine into phenylacetylene has not so far been achieved under such mild conditions. However, we have been able to show indirectly [85] that phenylacetylene and a secondary amine react to form the enamine. Thus when sodium phenylacetylide in dimethylformamide at about 130 °C is treated with morpholine or diethylamine followed by the addition of sulfur and carbon disulfide in the cold, the products contain 4-phenyl-1,3-dithiolethione and the corresponding 1,2-dithiolethione, the 5-phenyl derivative of the latter being obtained in the presence of diethylamine and the 4-phenyl derivative in the presence of morpholine. The addition of the amines to phenylacetylene, evidently on steric grounds, leads to the enamines *(29)* and *(30)* respectively, which necessarily give the two isomeric 1,3-dithiolethiones.



R = C_6H_5

[82a] *P. J. W. Schuijl, L. Brandsma,* and *J. F. Arens,* Recueil Trav. chim. Pays-Bas *85*, 889 (1966).

[83] *M. Carmack* and *DeLos F. DeTar,* J. Amer. chem. Soc. *68*, 2029 (1946).

[84] Cf. *H. Kaltwasser,* Chem. Techn. *9*, 392 (1957).

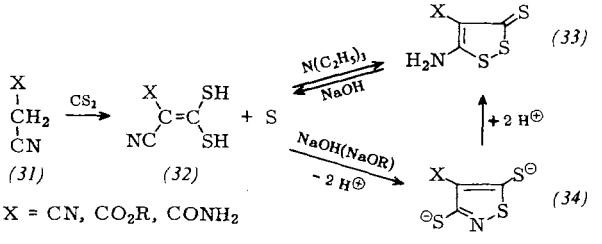
[85] *R. Mayer* and *H. Viola,* unpublished.

VII. The Reaction of Nitriles Containing Active Methylene Groups with Carbon Disulfide and Sulfur

Nitriles *(31)* having an active methylene group in the α-position (*e.g.* malonodinitrile and ethyl cyanoacetate) very readily add to carbon disulfide in the presence of auxiliary bases to form salts of the dithiocarboxylic acids *(32)*, which are unstable in the free state [86]. The action of sulfur and carbon disulfide on the nitrile at room temperature in a polar solvent and in the presence of triethylamine leads to the formation of 5-amino-3*H*-1,2-dithiole-3-thiones *(33)* [87] (see Table 8).

Table 8. 5-Amino-3*H*-1,2-dithiole-3-thiones *(33)* and isothiazoles from nitriles having active methylene groups, carbon disulfide, and sulfur [87].

Nitrile	X	*(33)* M.p.	*(33)* Yield (%)	3,5-Bis(methylmercapto)isothiazole M.p. (°C)	3,5-Bis(methylmercapto)isothiazole Yield (%)
Malonodinitrile	4-Cyano-	> 230 dec.	86	133	60
Methyl cyanoacetate	4-Methoxycarbonyl-	197–199	30	130–132	40
Cyanoacetamide	4-Carbamoyl-	260–264	26	—	—



X = CN, CO_2R, $CONH_2$

Whereas the very weakly basic 1,2-dithiolethione derivatives *(32)*, which are similar in their behavior to 3-amino-Δ^3-[1,2,4]dithiazoline-5-thione [88,89], are extremely stable to acids, the action of strong bases leads to a reversal of their formation, with decomposition into sulfur and the salt of the dithio acid *(32)*; the latter gradually takes up sulfur again to form the salt of the dimercaptoisothiazole *(34)*.

The reaction of nitriles with carbon disulfide in the presence of strong bases (*e.g.* sodium alkoxide) leads immediately to *(34)* as the only product; it can be isolated as the *S*-methyl derivative. The free thiol very rapidly rearranges to form *(33)*.

Independently of our work, *Söderbäck* [90] and *Hatchard* [91] reported the conversion of *(32)* (X = CN) into the isothiazole *(34)* [90,91] and the rearrangement *(34)* → *(33)* (X = CN); however, *(33)* is formulated as the imine [90].

[86] *R. Gompper* and *W. Töpfl,* Chem. Ber. *95*, 2861 (1962).

[87] *K. Gewald,* Z. Chem. *3*, 26 (1963); J. prakt. Chem., *31*, 214 (1966).

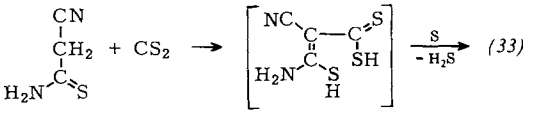
[88] *A. Hantzsch* and *M. Wolvekamp,* Liebigs Ann. Chem. *331*, 265 (1904).

[89] *E. Söderbäck,* Acta chem. scand. *1*, 529 (1947).

[90] *E. Söderbäck,* Acta chem. scand. *17*, 362 (1963).

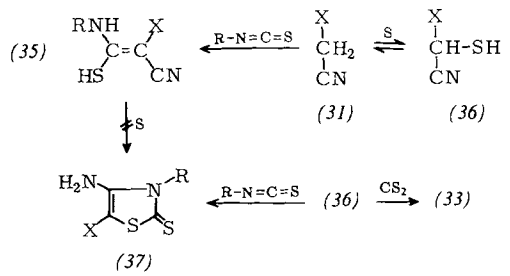
[91] *W. R. Hatchard,* J. org. Chemistry *28*, 2163 (1963); *29*, 660, 665 (1964).

The 1,2-dithiolethione *(33)* (X = CN) is also formed by the reaction of carbon disulfide with cyanothioacetamide in the presence of sulfur or iodine as oxidizing agents [87].



It should also be mentioned that *(33)* (X = CO_2R, $CONH_2$) can be obtained directly from *(32)*. Thus when acetic acid is added to the disodium salt of *(32)*, *(33)* is formed as a stabilization product *via* a desulfurization reaction that has not yet been explained [96]. The formation of *(33)* from nitriles, CS_2, and sulfur is analogous to the synthesis of 1,2-dithiolethiones from enamines (Section II). In this case the C base must be produced by the action of an auxiliary base; the cyclization step is a nucleophilic addition to the C=N group, while the enamine is stabilized by addition and elimination. This reaction again leads exclusively to the 1,2-dithiole system, irrespective of the order of addition of the reactants. Though *(31)* is evendently easily thiolated (thus elementary sulfur dissolves rapidly *e.g.* in ethyl cyanoacetate in the presence of triethylamine), the sulfur is displaced gain by the subsequent action of electrophiles such as carbon disulfide.

The interception of the α-thiolated nitrile *(36)* has so far been accomplished only with isothiocyanates. Whereas the action of CS_2 following the treatment of the nitrile with sulfur in the presence of triethylamine leads to the 1,2-dithiolethione system *(33)*, a strongly exothermic reaction takes place with isothiocyanates, and Δ^4-4-aminothiazoline-2-thiones *(37)* are formed in good yields [2,92] (see Table 9). *(37)* is also formed by the combined action of isothiocyanate and sulfur on nitriles having active methylene groups in dimethylformamide at room temperature, but not when the isothiocyanate and the nitrile are allowed to react first. The addition product *(35)*, which is already known [93], does not take up further sulfur, even on heating. *(37)* is also formed when the primary amine and CS_2 are used instead of the isothiocyanate. Triethylamine is added to the mixture of CS_2, amine (*e.g.* aniline or allylamine), sulfur, and nitrile in dimethylformamide. However, the yields obtained are lower than when the isothiocyanates are used.

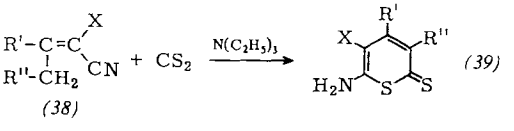


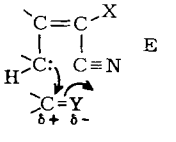
We were also interested in the behavior of the nitriles *(38)*, which are readily obtainable from nitriles having active α-methylene groups and carbonyl compounds by the Knoevenagel-Cope reaction, toward carbon disulfide and sulfur.

(38) should react with 1,2-bifunctional compounds such as CS_2 to form 6-membered heterocycles. In fact, some nitriles *(38)* add on carbon disulfide in dimethyl formamide at room temperature, with triethylamine as the auxiliary base, to form 6-amino-2*H*-thiopyran-2-thiones *(39)* [2,94] (see Table 10).

Table 10. 6-Amino-2*H*-thiopyran-2-thiones *(39)* from nitriles *(38)* and carbon disulfide [94].

Nitrile *(38)*	*(39)*	M.p. (°C)	Yield (%)
2-Cyano-3-ethyl-2-penteno-nitrile	3-Methyl-4-ethyl-5-cyano-	171—172	70
Cyclohexylidenemalono-dinitrile	3,4-Tetramethylen-5-cyano-	270—272	85
Cyclopentylidenemalono-dinitrile	3,4-Trimethylen-5-cyano-	253	57
2-Cyano-3-methylcinnamonitrile	4-Phenyl-5-cyano-	266—268	66
Ethyl-2-cyano-3-methyl-cinnamate	4-Phenyl-5-ethoxycarbonyl-	201—203	67
Ethyl-2-cyano-3-benzyl-crotonate	3-Phenyl-4-methyl-5-ethoxycarbonyl-	164—165	40





The reaction is analogous to the reaction of dienamines with carbon disulfide (Section IV). *(39)* with R′R″ = $(CH_2)_4$, X = CN can also be obtained directly in 60% yield by a single-vessel reaction from cyclohexanone,

Table 9. Δ^4-4-Aminothiazoline-2-thiones *(37)* from nitriles having active methylene groups, isothiocyanates, and sulfur [92].

Nitrile	Isothiocyanate	*(37)*	M.p. (°C)	Yield (%)
Malonodinitrile	Phenyl	3-Phenyl-5-cyano-	283—285	80
Ethyl cyanoacetate	Phenyl-	3-Phenyl-5-ethoxy-carbonyl-	221—223	70
Ethyl cyanoacetate	Methyl-	3-Methyl-5-ethoxy-carbonyl-	173	35
Cyanoacetamide	Allyl-	3-Allyl-5-carbamoyl-	172—173	88
Cyanoacetamide	Phenyl-	3-Phenyl-5-carbamoyl-	248—250	56

[92] *K. Gewald*, J. prakt. Chem. *32*, 26 (1966).

[93] Cf. *A. D. Grabenkov, P. C. Pelkiss*, and *L. N. Kulayeva*, Ž. obšč. Chim. *32*, 2248 (1962).

[94] *K. Gewald*, J. prakt. Chem. *31*, 205 (1966).

CS_2, and malonodinitrile in alcohol and in the presence of triethylamine or sodium hydroxide.

However, the generalization of the reaction is subject to limitations. It appears that only strong CH-acid alkylidene compounds can add on CS_2; derivatives of cyanoacetic ester ($X = CO_2R$) react only when R′ or R″ is an aryl group. The competing process in the reaction of alkylidenemalonodinitriles *(38)* ($X = CN$) is their base-catalysed dimerization [95], which can be largely suppressed in dimethylformamide. If the dimerization is not sterically hindered (as in *(38)*, $R' = R'' = CH_3$; $R' = CH_3$, $R'' = C_2H_5$; $R' = H$, R'' = alkyl; $X = CN$ for all compounds), this becomes the only reaction, and the addition of CS_2 does not take place. Addition of CS_2 to *(38)* and dimerization of *(38)* may be regarded as a special case of a general addition principle E, but one in which the dimerization plays the dominant role. However, according to observations made so far, isothiocyanates [2,96] also add to *(38)*.

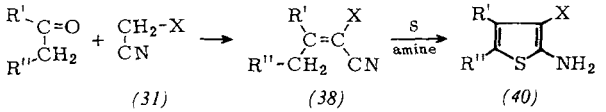
It should be possible to thiolate nitriles of the type *(38)* on the methylene group in the presence of auxiliary bases, cyclization to form the thiophene system being a possibility for the stabilization of the thiol. The reaction of sulfur with *(38)* proceeded surprisingly smoothly and uniformly. In the presence of secondary amines, and preferably in alcohol as the solvent, 2-aminothiophenes *(40)* [97] are formed even at room temperature, sometimes in very good yields (see Table 11, variant b).

Table 11. 2-Aminothiophenes *(40)* from carbonyl compounds R′—CO—CH_2—R″, nitriles having active methylene groups X—CH_2—CN *(31)*, and sulfur [97].

R′	R″	X	Yield (%) [a]	Yield (%) [b]	M.p. (°C) (b.p. (°C/mm))
H	CH_3	C_2H_5OCO	42	—	46 (159–161/19)
H	C_2H_5	C_2H_5OCO	75	—	73
H	C_6H_5	C_2H_5OCO	75	—	123–124
H	C_6H_5	NH_2CO	45	—	218–220
CH_3	CH_3	CN	42	41	141–142
CH_3	CH_3	C_2H_5OCO	39	49	91–92
CH_3	C_2H_5	CH_3OCO	40	50	(153–155/11)
$(CH_2)_4$		CN	86	90	147–148
$(CH_2)_4$		C_2H_5OCO	82	91	115
$(CH_2)_4$		C_6H_5CO	40	80	155
$(CH_2)_4$		NH_2CO	61	71	189–190
$(CH_2)_3$		C_2H_5OCO	45	42	91
C_6H_5	H	C_2H_5OCO	—	62	98
C_6H_5	CH_3	C_2H_5OCO	—	50	93
CH_3	C_6H_5	C_2H_5OCO	—	38	95
CH_3	C_6H_5	NH_2CO	—	58	184–185
CH_3	CH_3CO	CH_3OCO	31	—	161
CH_3	C_2H_5OCO	C_2H_5OCO	32	—	108–109

[a] From the components indicated.

[b] The carbonyl compound and the nitrile are first condensed; the yield is based on the alkylidene or arylalkylidene compound used.



(31) *(38)* *(40)*

Two possibilities must be considered for the incorporation of sulfur into *(38)*. *(38)* may be thiolated directly, or it may be cleaved by the secondary amine in an initial equilibrium, the sulfur then being taken up by the resulting enamine. The latter possibility is opposed by the fact that the reaction also proceeds in the presence of triethylamine, although much more slowly [98].

It is unnecessary in most cases to isolate *(38)*; the carbonyl compound and the nitrile may be allowed to react with sulfur in a single-vessel reaction in the presence of diethylamine or piperidine (see Table 11, variant a). In this way, aliphatic ketones and aldehydes having a free α-methylene group (with the exception of acetone [99] and acetaldehyde) and β-dicarbonyl compounds [98] can be converted into 2-aminothiophene derivatives *(40)*. The most important nitrile components are malonodinitrile, cyanoacetic ester, cyanoacetamide, and ω-cyanoacetophenone. The reaction of ketones and sulfur with cyanamide instead of with nitriles having active methylene groups leads to 4,5-disubstituted-2-aminothiazoles [36,100]. In this case, however, the first step cannot be a condensation (cf. Section II: for the α-thiolation of carbonyl compounds, cf. [9,10]).

Carbonyl compounds with less reactive carbonyl groups, such as alkyl aryl ketones, can be converted into thiophenes by thiolation only in the form of their alkylidene derivatives *(38)*. Finally, the enamine may be used instead of the free carbonyl compound [97,100a]. The condensation step [enamine + nitrile → *(38)*] is then facilitated; this variant is therefore particularly suitable for the reaction of inert carbonyl compounds. However, it offers few preparative advantages over the thiolation of *(38)*. Thiophenes of the type *(40)* are also formed in the reaction of α-mercaptoketones with nitriles having active methylene groups [101]. The 4,5-tetramethylenethiophenes *(40)* derived from cyclohexanone can be smoothly dehydrogenated as acyl derivatives with sulfur at high temperatures, so offering a new route to 2-aminobenzo[*b*]thiophene derivatives [99,102].

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[100a] Cf. *V. I. Shvedov* and *A. N. Grinev*, Z. org. Chim. *1*, 2228 (1965).

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[102] *K. Gewald*, *G. Neumann*, and *H. Böttcher*, Z. Chem. *6*, 261 (1966).

The Bucherer Reaction and the Preparative Use of its Intermediate Products

BY H. SEEBOTH [*]

Dedicated to Professor A. Rieche on the occasion of his 65th birthday

The study of purified intermediate products of the Bucherer reaction has shown that this reaction proceeds, not via bisulfite addition compounds of the keto form of the naphthols and the ketimine form of the naphthylamines, but via tetralonesulfonic acids and tetraloniminesulfonic acids. The intermediates lead to compounds that are otherwise difficult or impossible to obtain, and some of which are new. The mechanism of the Bucherer reaction is discussed in detail.

1. Introduction

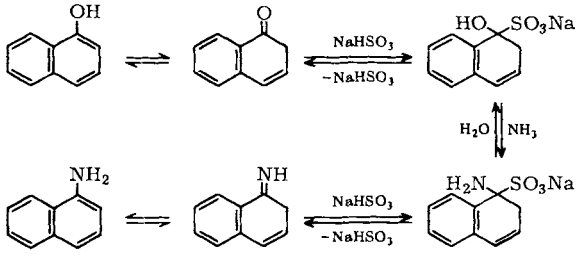
The Bucherer reaction provides a relatively simple method for the conversion of aromatic amines into hydroxy compounds or of hydroxyaromatic compounds into primary, secondary, and tertiary aromatic amines. It proceeds in the aqueous phase in the presence of sulfurous acid or its salts, and is used *e.g.* for the preparation of many naphthalene derivatives, which are particularly important as dye intermediates. Although only a few benzene derivatives react, the Bucherer reaction has been successfully used in many cases with anthracene and phenanthrene derivatives, as well as with heterocyclic compounds.

Several reports have been published on the preparative importance of the Bucherer reaction [1]; some recent examples of its application are:

The natural products cupreine and (+)-equilenin have been converted into 6-aminocinchonidine [2] and (+)-3-aminodeoxyequilenin [3], respectively, in good yield by the action of NH_4HSO_3. Many aminoquinoline and aminoisoquinoline derivatives have been obtained with the aid of the Bucherer reaction [1b]. Other successful applications of the sulfite reaction to heterocyclic compounds are the conversion of 2-aminobenzo-1,3-thiazoles into hydroxy compounds [4] and the conversion of 8-hydroxycinnoline into 8-aminocinnoline [5].

A modified process developed by *MacDonald* and *Chechak* [6], in which the organic compound is made to react in a sealed tube at 100 °C in a water/dioxane mixture (1:1 v/v) which is previously saturated with SO_2 at 0 °C, has also proved useful for the preparation of hydroxyphenanthrenes [7]; this method is recommended when the starting compound is completely insoluble in water. Taking the conversion of α-naphthol into *N,N*-dimethyl-*N'*-1-naphthylpropylenediamine as an example, *Werbel* [8] showed that the reaction is advantageously carried out in aqueous $Na_2S_2O_4$ solution instead of in aqueous $NaHSO_3$ solution.

Until recently the views of *Woroshzow* [9], *Friedländer* [10], *Raschig* [11], and *Fuchs* [12–14] were considered to apply, *i.e.* that the reaction proceeded *via* bisulfite adducts of the tautomeric keto or ketimine forms of the naphthols or naphthylamines, in accordance with Scheme 1, and that it should be regarded as a series of equilibrium reactions.



Scheme 1.

[*] Dr. habil. H. Seeboth
Institut für Organische Chemie
der Deutschen Akademie der Wissenschaften zu Berlin
An der Rudower Chaussee
X 1199 Berlin-Adlershof (Germany)

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[9] *N. N. Woroshzow*, J. russ. physik.-chem. Ges. *47*, 1669 (1915); Chem. Zbl. *1916*, II 256; Liebigs Ann. Chem. *381*, 50 (1916); Ber. dtsch. chem. Ges. *62*, 57 (1929).

[10] *P. Friedländer*, Ber. dtsch. chem. Ges. *54*, 620 (1921).

[11] *F. Raschig*, Ber. dtsch. chem. Ges. *59*, 859 (1926).

[12] *W. Fuchs* and *W. Stix*, Ber. dtsch. chem. Ges. *55*, 658 (1922).

[13] *W. Fuchs* and *H. Pirak*, Ber. dtsch. chem. Ges. *59*, 2454, 2458 (1926).

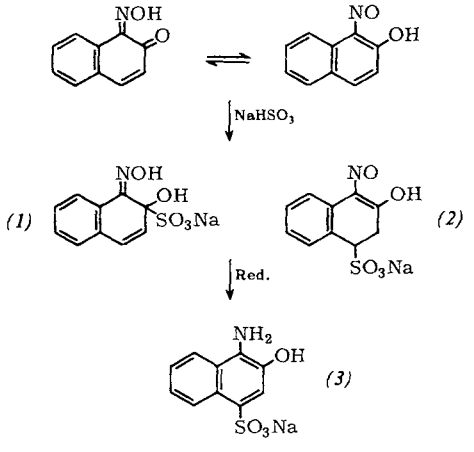
[14] *W. Fuchs* and *F. Niszel*, Ber. dtsch. chem. Ges. *60*, 209, 2058 (1927).

The pure bisulfite adducts of 2-hydroxy-, 4-hydroxy-, and 5-hydroxynaphthalene-1-sulfonic acid were first prepared by *Ufimtsev*[15,16], who confirmed the proposed course of the reaction on the basis of his experiments[17].

The kinetics of the Bucherer reaction were first studied by *Cowdrey* and *Hinshelwood*[18] for the conversion of 4- and 5-amino- and 5-dimethylaminonaphthalene-1-sulfonic acids into the corresponding hydroxynaphthalenesulfonic acids. The rate-determining step is first order with respect to the aminonaphthalenesulfonic acid and the bisulfite. The rate constants k_2 [g mole^{-1} l h^{-1}] of the bimolecular reaction *e.g.* in the case of 4-aminonaphthalene-1-sulfonic acid are 8.52×10^{-2} at 80.5 °C and 19.1×10^{-2} at 99.8 °C; the activation energy of the reaction is 11.8 kcal/mole.

The kinetics of the conversion of naphthols into naphthylamines were studied for 4-hydroxy- and 5-hydroxynaphthalene-1-sulfonic acids[19]. The activation energy of the formation of the bisulfite adduct of 4-hydroxynaphthalene-1-sulfonic acid was found to be 16.8 kcal/mole, and that of its decomposition reaction to be 24.2 kcal/mole. The rate of conversion of the naphthols into naphthylamines by heating with ammonia and ammonium sulfite is directly dependent on the concentrations of the naphthol, the ammonium ions, and the sulfite ions, and is independent of the concentration of excess free ammonia. The reaction is reversible, and the position of the equilibrium depends on the concentration of free ammonia, but not on the presence of ammonia or sulfite ions. *Cowdrey* and *Hinshelwood* regard Scheme 1 as basically correct. However, since the addition of $NaHSO_3$ to the ketimine form of 5-dimethylaminonaphthalene-1-sulfonic acid during the conversion of the latter into 5-hydroxynaphthalene-1-sulfonic acid is not feasible, these authors believe that $NaHSO_3$ may add on to the C=C double bond adjacent to the OH or NH_2 group. *Kozlov* and *Veselovskaya*[20] reached similar conclusions in a kinetic study of the formation of α- and β-naphthylamines by amination of α- and β-naphthols.

A different view is held by *Bogdanov*[21]. Since the bisulfite adduct of α-nitroso-β-naphthol can be converted into 1-amino-2-hydroxynaphthalene-4-sulfonic acid *(3)* by reduction, this author believes that the sulfo group is attached to C-4, even in the bisulfite adduct, *i.e.* that the $NaHSO_3$ adds to the C=C double bond between C-3 and C-4 to form *(2)*, contrary to the usual formulation *(1)*.



[15] *V. N. Ufimtsev*, Ž. prikl. Chim. *17*, 557 (1944).

[16] *V. N. Ufimtsev*, Ž. prikl. Chim. *18*, 214 (1945).

[17] *V. N. Ufimtsev*, Doklady Akad. Nauk. SSSR *60*, 239 (1948).

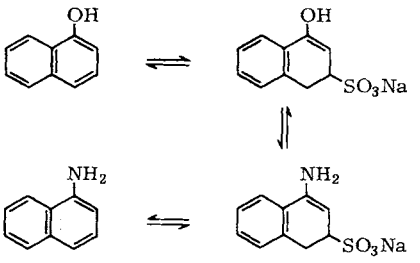
[18] *W. A. Cowdrey* and *C. N. Hinshelwood*, J. chem. Soc. (London) *1946*, 1036.

[19] *W. A. Cowdrey*, J. chem. Soc. (London) *1946*, 1041, 1044, 1046.

[20] *V. V. Kozlov* and *I. K. Veselovskaya*, Ž. obšč. Chim. *28*, 3333 (1958); *30*, 4088 (1960).

[21] *S. V. Bogdanov*, Ž. obšč. Chim. *2*, 9 (1932).

Bogdanov has also applied this assumption to the Bucherer reaction, and has proposed the (unverified) course shown in Scheme 2. This scheme has been severely criticized[22,23].



Scheme 2.

2. Preparation and Constitution of the Intermediate Products

a) Bisulfite Adducts of Naphthols

Rieche and *Seeboth* started their study of the course of the Bucherer reaction in 1955. In the preparation of a number of pure bisulfite adducts, they were able to correct a number of earlier ideas[24].

It has long been known that naphthol-bisulfite adducts are stable in aqueous and acidic solution at 20 °C, and that they decompose into $NaHSO_3$ and naphthol under the action of alkalis or when continuously heated in aqueous mineral acids. These naphthol-bisulfite adducts do not couple with diazonium salts, and, unlike the bisulfite adducts of aldehydes and ketones, they are not reduced to the corresponding sulfinic acids by zinc and hydrochloric acid[15,25]. The bisulfite adducts of β-naphthols are less stable than those of α-naphthols.

The isolated bisulfite adducts of the naphthols do not behave as $NaHSO_3$ adducts of the keto form of naphthols[24]. These ketone adducts would be expected to readily lose water with reformation of the aromatic system, so offering a convenient synthesis of sulfonic acids; however, this reaction does not take place. Moreover, no hydroxy groups capable of being esterified could be detected in the $NaHSO_3$ adduct by the action of acetic anhydride, acetyl chloride, or benzoyl chloride; in every case, the bisulfite adduct was recovered unchanged. *Ufimtsev* and *Chernyak*[26] tried unsuccessfully to make the bisulfite adducts of 5-hydroxynaphthalene-1-sulfonic acid, resorcinol, and 2-methyl-1,4-naphthoquinone react in aqueous solution with acetic anhydride. These authors assumed that their failure was due to the fact that tertiary alcohols are difficult to esterify; however, the OH groups

[22] *V. N. Ufimtsev*, Ž. prikl. Chim. *17*, 159 (1944).

[23] *E. M. Bamdas*, *D. A. Botschvar*, and *M. M. Schemyakin*, Ž. obšč. Chim. *21*, 1287 (1951).

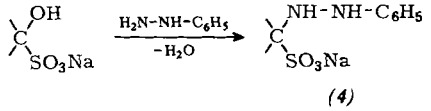
[24] *A. Rieche* and *H. Seeboth*, Liebigs Ann. Chem. *638*, 43 (1960).

[25] *K. Reinking*, *E. Dehnel*, and *H. Labhardt*, Ber. dtsch. chem. Ges. *38*, 1069 (1905).

[26] *V. N. Ufimtsev* and *M. I. Chernyak*, Ž. obšč. Chim. *21*, 1883 (1951).

of the bisulfite adducts of aldehydes and ketones can in principle be esterified [27].

The bisulfite adducts of naphthols also fail to undergo replacement of the sulfo group by a cyano group, which is another characteristic reaction of bisulfite adducts of aldehydes and ketones. "Pressureless" hydrogenation to form tetralin derivatives in the presence of high-activity catalysts (*e.g.* Rh on $BaSO_4$) was also found to be impossible. On the other hand, the $NaHSO_3$ adducts of the naphthols react smoothly with ketone reagents such as phenylhydrazine, semicarbazide, and hydroxylamine, the reaction being accompanied by the elimination of water [24]. The condensation products are resistant to alkalis, and are broken down into the starting compounds (bisulfite adduct and the nitrogen compound) when heated in mineral acids. The reaction of the bisulfite adducts with phenylhydrazine had already been observed by *Ufimtsev* [28], who assumed that water was eliminated between the phenylhydrazine and the hydroxy group, and that the condensation products were α-(2-phenylhydrazino)sulfonic acids *(4)*; however, no analogue of this reaction appears to be known.

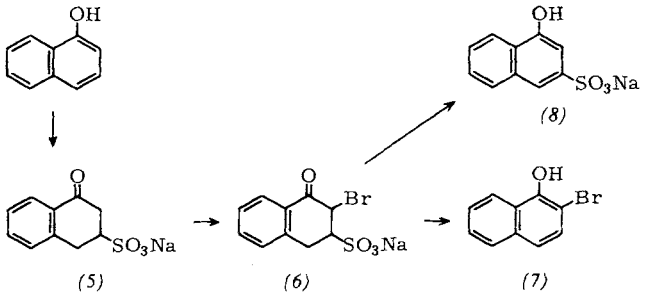


(4)

The IR spectra provided final proof that the intermediates of the Bucherer reaction are not bisulfite adducts of ketones, but are in fact ketones. Like α-tetralone, the adducts of α-naphthols give pronounced keto bands at 1695 and 1610 cm^{-1} [24]. $NaHSO_3$ adducts of β-naphthols, like β-tetralone, give a strong carbonyl band at 1720 cm^{-1} [29]. The spectra of the products of condensation with carbonyl reagents clearly show the presence of a C=N double bond, (*e.g.* a band at 1625 cm^{-1} for the 11-semicarbazone, and bands at 1610 and 1650 cm^{-1} for the 5-oxime).

Thus the intermediates of the Bucherer reaction must be formulated as α- or β-tetralonesulfonic acids, depending on whether they are formed from α- or β-hydroxynaphthalene derivatives. The reactions with carbonyl reagents yield oximes, semicarbazones, and phenylhydrazones. Several indications, and in particular the observation that, on addition of bisulfite to α,β-unsaturated carbonyl compounds, the sulfo group becomes attached to the β-C atom [30], suggest that the sulfo group is in position 3 with respect to the keto group.

The constitution of the bisulfite adduct of α-naphthol has been proved as follows [31]:



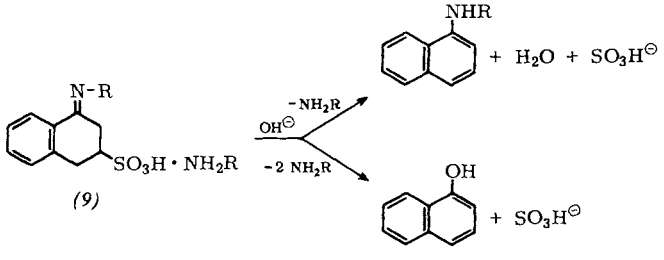
Bromination of *(5)*, analogous to that of α-tetralone [32], yields 2-bromo-1-tetralone-3-sulfonic acid *(6)*, which loses $NaHSO_3$ under the action of alkalis to form 2-bromo-1-naphthol *(7)*. *Krollpfeiffer* and *Müller* [33] have prepared *(7)* by the elimination of HBr from β,β-dibromo-α-tetralone. The structure of the 2-bromo-1-naphthol is proved by the formation of 2,4-dibromo-1-naphthol on bromination. When 2-bromo-1-tetralone-3-sulfonic acid *(6)* in acetate buffer solution is treated with small quantities of an organic base, HBr is eliminated and 1-hydroxynaphthalene-3-sulfonic acid *(8)* is formed. *(8)* was identified by paper chromatography (coupling with *p*-nitraniline to form a dye), as the *p*-toluidine and as the *S*-benzylthiouronium salt.

Conversion of the brominated bisulfite adduct of α-naphthol into 2-bromo-1-naphthol and 1-hydroxynaphthalene-3-sulfonic acid proves that the adduct is 2-bromo-1-tetralone-3-sulfonic acid *(6)*. The bisulfite adducts of the α-naphthols must therefore be 1-tetralone-3-sulfonic acids.

b) Bisulfite Adducts of Naphthylamines

Despite numerous attempts, no bisulfite adducts of naphthylamines have been obtained by reactions in aqueous $NaHSO_3$ solution. This is understandable, since the ketimines corresponding to the tetralonesulfonic acids are very readily hydrolysed.

However, reaction of the ammonium salts of the tetrasulfonic acids with an amine, which also acts as the solvent, yields the ketimines *(9)* (IR bands at 1620 to 1640 cm^{-1}) of the ammonium tetralonesulfonates [34, 35]; the water formed during the reaction is distilled off with the solvent.



[27] *R. L. Shriner* and *A. H. Land*, J. org. Chemistry *6*, 888 (1941).

[28] *V. N. Ufimtsev*, Ž. obšč. Chim. *16*, 1845 (1946).

[29] *A. Rieche* and *H. Seeboth*, Liebigs Ann. Chem. *638*, 76 (1960).

[30] See, *e.g. J. H. deBoer*, Recueil Trav. chim. Pays-Bas *71*, 814 (1952).

[31] *A. Rieche* and *H. Seeboth*, Angew. Chem. *70*, 52, 312 (1958); Liebigs Ann. Chem. *638*, 57 (1960).

[32] *A. L. Wilds*, J. Amer. chem. Soc. *64*, 1421 (1942).

[33] *F. Krollpfeifer* and *A. Müller*, Ber. dtsch. chem. Ges. *68*, 1169 (1935).

[34] *A. Rieche* and *H. Seeboth*, Liebigs Ann. Chem. *638*, 66 (1960).

[35] *H. Seeboth* and *A. Rieche*, Liebigs Ann. Chem. *671*, 77 (1964).

The ketimines are hydrolysed by dilute acids to give the tetralonesulfonic acid and the amine; treatment with hot 2N NaOH yields a mixture of *N*-alkyl-naphthylamine and naphthol.

c) General Methods for the Preparation of Tetralonesulfonic Acids

The tetralonesulfonic acids (see Table 1) are generally prepared by heating a naphthol or naphthylamine for 6 to 30 hours in $NaHSO_3$ solution with a 3- to 10-fold excess of $NaHSO_3$; the reaction is usually carried out in a 35 to 40% $NaHSO_3$ solution. The reaction temperature should initially be about 80 °C, and subsequently raised to 90 °C.

Table 1. Tetralonesulfonic acids obtained in the pure state.

Starting material	Tetralonesulfonic acid	Ref.	Remarks [a]; decomp. temp. (°C)
2,7-Dihydroxynaphthalene	6-Hydroxy-3-tetralone-1-sulfonic acid	[12, 24]	
1,5-Dihydroxynaphthalene	5-Hydroxy-1-tetralone-3-sulfonic acid	[12, 24]	Strongly colored and unstable
1,4-Dihydroxynaphthalene	1-Hydroxy-4-tetralone-2-sulfonic acid	[13, 24]	
1,8-Diaminonaphthalene	8-Benzoylamino-1-tetralone-3-sulfonic acid	[24]	T, 225–228
1,8-Diaminonaphthalene	8-Amino-1-tetralone-sulfonic acid	[24]	
α-Naphthol, α-Naphthylamine	1-Tetralone-3-sulfonic acid	[36, 24]	S–B, 142
4-Aminonaphthalene-1-sulfonic	4-Tetralone-1,2-disulfonic acid	[15, 19, 24]	Bis-S–B, 224–227
5-Aminonaphthalene-1-sulfonic	1-Tetralone-3,5-disulfonic acid	[15, 37, 38]	Bis-S–B, 182–185
1-Aminonaphthalene-6-sulfonic	1-Tetralone-3,6-disulfonic acid	[38]	Bis-T, 135
1-Aminonaphthalene-7-sulfonic	1-Tetralone-3,7-disulfonic acid	[38]	Bis-T, 222–224
3-Hydroxynaphthalene-2-carboxylic acid	3-Tetralone-1-sulfonic acid	[29]	S–B, 178–179
2-Aminonaphthalene-1-sulfonic acid	2-Tetralone-1,4-disulfonic acid	[16]	Bis-S–B, 154–155
2-Hydroxy-1-sulfonaphthalene-3-carboxylic acid	2-Tetralone-1,4-disulfonic acid	[39c]	Bis-S–B, 154–155

[a] S–B = *S*-benzylthiouronium salt, T = *p*-toluidine salt.

Where the reaction time is relatively long, SO_2 is passed in at intervals for 20 to 30 min, the reaction mixture being vigorously stirred. With naphthols or naphthylamines that are substantially insoluble in water, the reaction mixture is clear at the end of the reaction. The reaction is complete when no coupling takes place on addition of a diazonium salt to a sample of the solution.

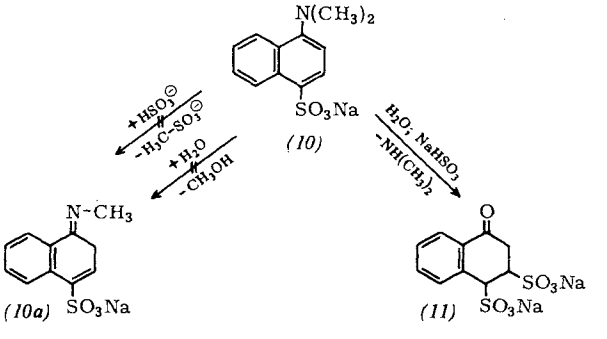
The isolation and purification of the tetralonesulfonic acids is often difficult and laborious. The excess $NaHSO_3$, which interferes with product recovery from the reaction solution, is removed by addition of HCl and passage of a current of air through the solution until no more SO_2 escapes. The solution is then evaporated down under vacuum. The inorganic salts (mainly NaCl) precipitate out first. The subsequent precipitates are tested for tetralonesulfonic acid by checking whether the action of alkalis leads to the elimination of $NaHSO_3$ and formation of a naphthol. In many cases the tetralonesulfonic acids can be separated from inorganic salts by precipitation from methanol, ethanol, or acetone; repeated recrystallization (from C_2H_5OH/H_2O) or reprecipitation (from aqueous solution by the addition of ethanol or acetone) is generally required for purification. The pure tetralonesulfonates crystallize well. They are readily soluble in water and insoluble in organic solvents. The toluidine and *S*-benzylthiouronium salts, which are sparingly soluble in water, may be used for identification. Thin layer and paper chromatography are suitable methods for testing purity and uniformity of the product [24].

3. Mechanism of the Bucherer Reaction

The conversion of α-naphthols into naphthylamines, and *vice versa*, under the catalytic action of bisulfite is seen to proceed *via* 1-tetralone- and 1-tetralonimine-3-sulfonic acids. Similarly, the reaction of β-naphthols and β-naphthylamines with $NaHSO_3$ yields the sodium 3-tetralone- or sodium 3-tetralonimine-1-sulfonates.

Addition of $NaHSO_3$ to the C=C double bond of the keto form of the naphthols or of the ketimine form of the naphthylamines is incompatible with the fact that *N,N*-dialkylated naphthylamines, which cannot normally give a ketimine form, can also be converted into naphthols by means of $NaHSO_3$. A more detailed insight was obtained by the study of the reaction of sodium 4-dimethylaminonaphthalene-1-sulfonate *(10)* with $NaHSO_3$ [34].

(10) reacts with $NaHSO_3$ in the same way as 4-amino- and 4-hydroxynaphthalene-1-sulfonic acids, with formation of disodium 4-tetralone-1,2-disulfonate *(11)*. If one adduct were formed *via* a reactive ketimine



form *(10a)*, a methyl group would have to be removed. If this occurred by hydrolysis, methanol should be formed. A second, but less likely possibility, would be methylation of the bisulfite anion to form methane-

[36] *S. V. Bogdanov* and *N. N. Karandashcheva*, Ž. obšč. Chim. *26*, 3365 (1956).

[37] *I. M. Kogan* and *A. I. Nikolayeva*, Ž. prikl. Chim. *11*, 652 (1938).

[38] *A. Rieche* and *H. Seeboth*, Liebigs Ann. Chem. *638*, 101 (1960).

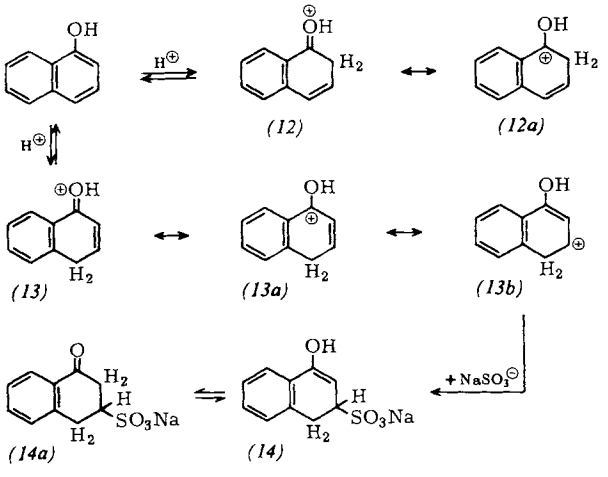
[39a] *A. Rieche* and *H. Seeboth*, Liebigs Ann. Chem. *638*, 81 (1960).

[39b] *H. Seeboth*, *D. Bärwolff*, and *B. Becker*, *ibid. 683*, 85 (1965).

[39c] *H. Seeboth*, *H. Neumann*, and *H. Görsch*, Liebigs Ann. Chem. *683*, 93 (1965).

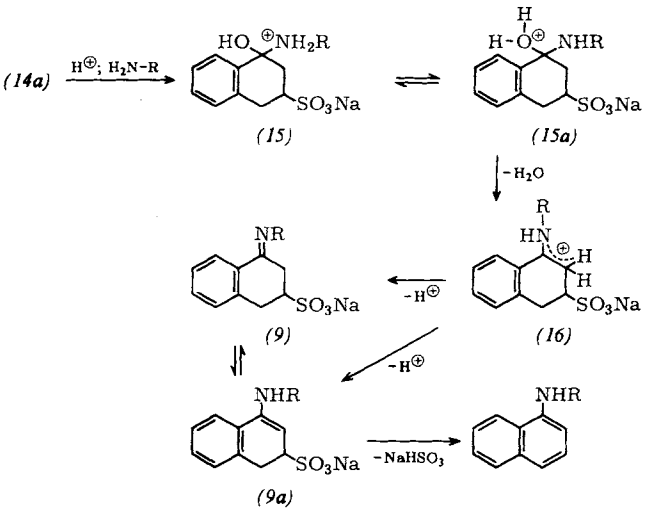
sulfonic acid. However, in the reaction *(10)* → *(11)*, neither methanol nor methanesulfonic acid was found, nor was the methylamine that would be expected as a hydrolysis product of any ketimine form that might occur. On the other hand, 80% of the theoretically expected amount of dimethylamine was isolated. The starting compound *(10)* shows no tendency to lose the dimethylamino group by hydrolysis, even on prolonged heating in 0.1 N to 1 N sulfuric acid. It must therefore be concluded that bisulfite can add directly to naphthol or naphthylamine in the Bucherer reaction.

The first step may be assumed to be the electrophilic addition of a proton to a C atom having a high electron density, *i.e.* C-2 or C-4 in α-naphthols or α-naphthylamines. (An energy of about 25 kcal/mole is required for the dearomatization of the first ring in the naphthalene system). α-Naphthol, for example, gives the resonance-stabilized proton adducts *(12)* and *(13)*. A bisulfite anion can then add to C-3 *via (13b)* to form the compound *(14)*, which tautomerizes to give the lower-energy form *(14a)*.



Whereas the first step in additions of nucleophiles to olefines, *i.e.* the addition of a proton, is accelerated by an increase in the $H^{\oplus}$ concentration, this is not the case in the Bucherer reaction, since protonation eliminates the +M effect of the amino or hydroxy group. It is possible that naphthalene derivatives having substituents with a +M effect can add $NaHSO_3$. Attempts to add $NaHSO_3$ *e.g.* to 4-chloronaphthalene-1-sulfonic acid were unsuccessful. It may be concluded, therefore, that the rate of formation of 4-chloro-1,2-dihydronaphthalene-1,2-disulfonic acid is lower than its rate of decomposition; stabilization as in the case *(14)* → *(14a)* is not possible in this instance. The formation of 4-hydroxynaphthalene-1-sulfonic acid or its bisulfite adduct, which might have been expected in the reaction of chloronaphthalenesulfonic acid, was not observed.

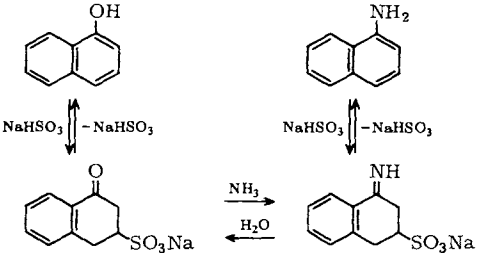
The amination of the tetralonesulfonic acids, *e.g. (14a)*, starts with a nucleophilic attack by the amine. The protonated species *(15)* loses water from its tautomeric form *(15a)* to give the resonance-stabilized cation *(16)*, which can lose $H^{\oplus}$ in two ways to give stable molecules. Ketimines[34,35] which can be converted into naphthylamines[34] have been isolated from tetralonesulfonic acids and amines. Under the conditions of the Bucherer reaction, the intermediate formation of *(9)* is unnecessary. It is possible that owing to the strong inductive effect of the sulfo group, a proton is lost from C-2 of the compound *(16)* to give the sulfonic acid *(9a)*, which contains an enamine grouping; *(9a)* is unstable and rapidly loses sulfite to form a naphthylamine.



Thus in the conversion of naphthols into naphthylamines, the primary products from naphthols and $NaHSO_3$, *i.e.* tetralonesulfonic acids, form tetraloniminesulfonic acids in the presence of an excess of amine. The tetraloniminesulfonic acid (or rather its enamine form) is stabilized by loss of $NaHSO_3$ and formation of the naphthylamine. The "enaminesulfonic acids", which in the case of primary and secondary amines exist in equilibrium with the more stable ketimine form, are unstable.

In the conversion of naphthylamines into naphthols, the "enamine-" or tetraloniminesulfonic acid formed from the naphthylamine and $NaHSO_3$ is hydrolysed to the tetralonesulfonic acid, which is stable in acidic media and decomposes into naphthol and sulfite only under the action of alkalis.

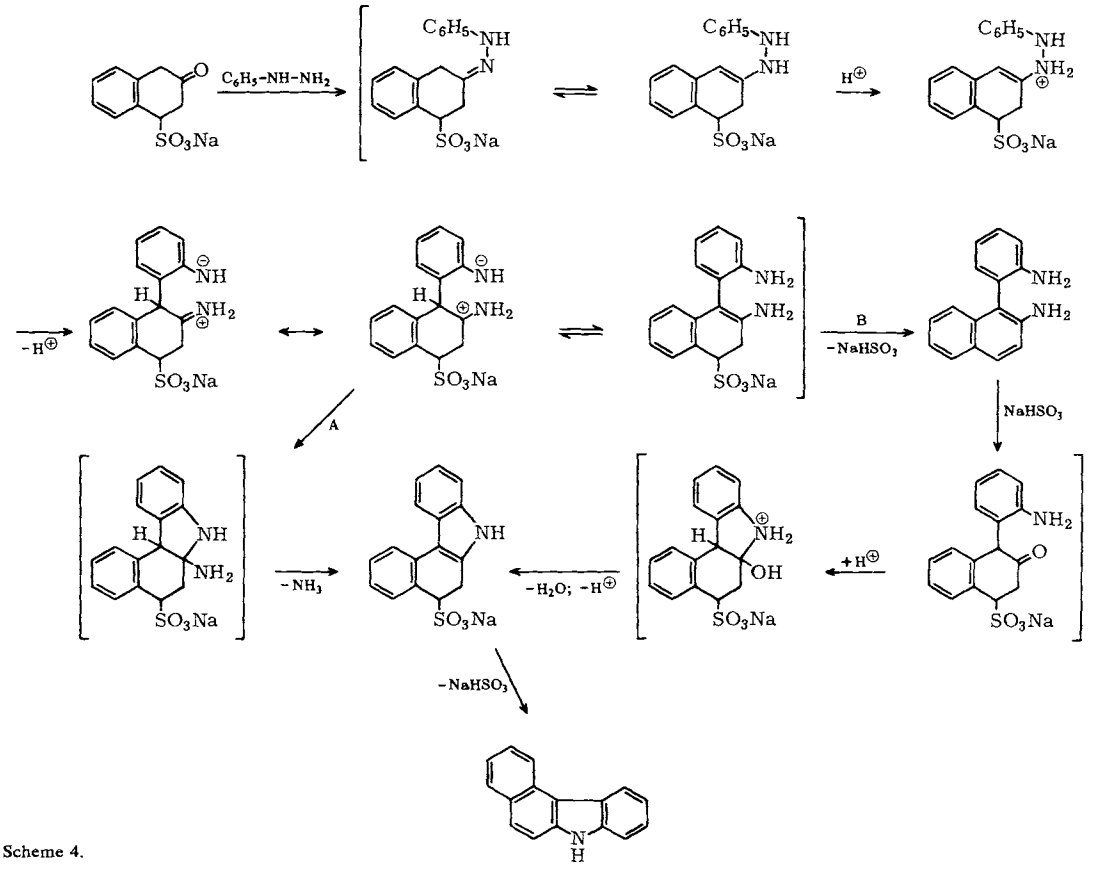
Thus the course of the Bucherer reaction may be summarized as in Scheme 3; all the reaction steps are equilibria.



Scheme 3.

4. Mechanism of the Bucherer Carbazole Synthesis

Knowledge of the intermediates of the Bucherer reaction made it possible to elucidate fully the reactions involved in the Bucherer synthesis of carbazoles from naphthols or naphthylamines and phenylhydrazine in the presence of $NaHSO_3$[39]. The reaction of α-naphthols or α-naphthylamines with phenylhydrazine and



Scheme 4.

$NaHSO_3$ leads to stable 1-tetralonephenylhydrazone-3-sulfonic acids, which form 1,2-benzocarbazoles, among other products, on treatment with acids. In the β-naphthalene series, the reaction does not generally stop at the 2-tetralonephenylhydrazonesulfonic acid stage, but gives 1,2-dihydro-3,4-benzocarbazole-2-sulfonic acid (which readily loses $NaHSO_3$ under the action of acids or bases) or 3,4-benzocarbazole, depending on the conditions (see Scheme 4).

Scheme 4 shows the formation of 3,4-benzocarbazoles. The reaction of sodium 3-tetralone-1-sulfonate with phenylhydrazine in 40% acetic acid at room temperature leads smoothly to phenylhydrazinium 1,2-dihydro-3,4-benzocarbazole-2-sulfonate [39a]. No 2-amino-1-(2-aminophenyl)naphthalene is formed. It may be concluded, therefore, that the reaction proceeds exclusively by route A.

The formation of 3,4-benzocarbazole from β-naphthol [14] or 2-hydroxynaphthalene-3-carboxylic acid [40a] and phenylhydrazine in aqueous $NaHSO_3$ solution in a single-vessel process (30 and 18 hours respectively; 100 °C) yields considerable quantities of 2-amino-1-(2-aminophenyl)naphthalene as a by-product. The observation that this diamine gives 3,4-benzocarbazole in 15% yield when heated for $2^1/_2$ hours in 2 N HCl, but in 89% yield when heated for $2^1/_2$ hours in aqueous SO_2 solution [14, 39a] suggests that the formation of carbazoles from naphthols and phenylhydrazine in the presence of $NaHSO_3$ also proceeds by route B. The conversion of the diamine into benzocarbazole by treatment with $NaHSO_3$ is a normal Bucherer reaction.

In principle, the Bucherer carbazole synthesis, the Fischer indole synthesis [40b], and the Borsche-Drechsel carbazole synthesis from phenylhydrazones and cyclanones [40c] all proceed in a similar manner. The analogy between the formation of carbazoles from naphthols, phenylhydrazine, and $NaHSO_3$ and the Fischer indole synthesis has already been pointed out by *Bucherer* and *Seyde* [40a].

5. Selectivity and Limited Scope of the Bucherer Reaction

The course proposed by *Rieche* and *Seeboth* for the Bucherer reaction provides an explanation for the fact that the reactions proceed readily in some cases, and with difficulty or not at all in others. This is illustrated by the following examples.

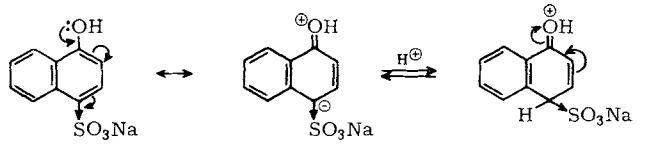
4-Hydroxy- and 4-aminonaphthalene-1-sulfonic acids react more readily than α-naphthol or α-naphthylamine with $NaHSO_3$. This is due to the −I effect of the sulfo group, which strongly favors the addition of a proton to C-4 and the nucleophilic attack of $NaSO_3^{\ominus}$ on C-3.

In 1-hydroxynaphthalene-2-sulfonic acid *(18)*, the −I effect of the sulfo group and the weakening of the +M effect of the hydroxy group by hydrogen bonding with the sulfo group

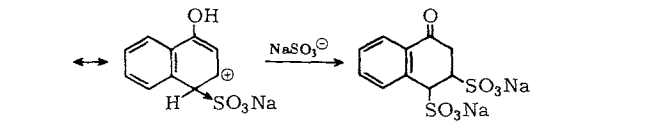
[40a] *H. Th. Bucherer* and *F. Seyde*, J. prakt. Chem. [2] *77*, 403 (1908).

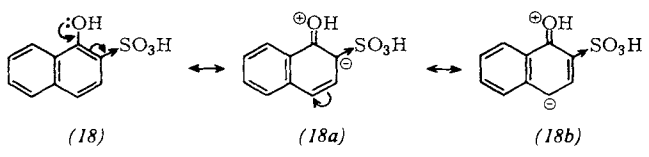
[40b] *G. M. Robinson* and *R. Robinson*, J. chem. Soc. (London) *125*, 827 (1924); *R. B. Carlin*, J. Amer. chem. Soc. *74*, 1077 (1952); *A. E. Arbusov* and *Y. P. Kitayev*, Ž. obšč. Chim. *27*, 2328 (1957); *K. Clusius* and *H. R. Weisser*, Helv. chim. Acta *35*, 400 (1952); *B. Robinson*, Chem. Reviews *63*, 373 (1963).

[40c] *N. Campbell* and *B. M. Barclay*, Chem. Reviews *40*, 359 (1947); *Ng. Ph. Buu-Hoi*, *Ng. Hoan*, and *Ng. H. Khoi*, Recueil Trav. chim. Pays-Bas *69*, 1053 (1953).

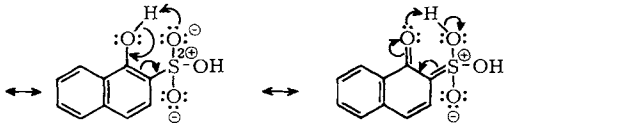


(17)





(18) (18a) (18b)



(18c) (18d)

lead to a lower electron density on C-4. The importance of the limiting form *(18b)* is less than that of *(18a)*, and the strong −I effect of the SO_3H group, which favors the nucleophilic addition of $NaSO_3^\ominus$ in 4-hydroxynaphthalene-1-sulfonic acid *(17)*, is considerably reduced by interaction [cf. *(18c)*] with the OH group. Consequently, protonation at C-4 and nucleophilic attack of $NaSO_3^\ominus$ on C-3 are hindered. In 1-hydroxynaphthalene-3-sulfonic acid, the addition of a proton to C-4 and the addition of $NaSO_3^\ominus$ to C-3 are again inhibited by the negative charge on C-3. The last two acids do not undergo the Bucherer reaction. It is thus clear why OH and NH_2 groups in *m*-hydroxy- and *m*-aminonaphthalenesulfonic acids cannot be interchanged by the sulfite reaction.

The selectivity frequently exhibited by the reaction is now also understandable. In 4,5-diaminonaphthalene-1-sulfonic acid, for example, only the amino group in the *p*-position with respect to the sulfo group reacts, and the product is 5-amino-4-hydroxynaphthalene-1-sulfonic acid[41], the reasons being the same as those given for the formation of *(17)*.

The preparation of 7-amino-1-hydroxynaphthalene-3-sulfonic acid ("γ-acid") from 1,7-dihydroxynaphthalene-3-sulfonic acid[42] is selective because a *m*-tetralonesulfonic acid intermediate can be formed only by the ring containing the β-hydroxy group, so that only the β-hydroxy group can be replaced by the amino group.

It is now also possible to explain why only one substituent can be exchanged in diamino- and dihydroxynaphthalenes and in aminonaphthols. Thus if the two functional groups are attached to different rings, the replacement of the second would require the dearomatization of the benzene ring in the tetralonesulfonic acid. If both substituents are attached to the same ring, a second addition of $NaHSO_3$ is no longer opssible.

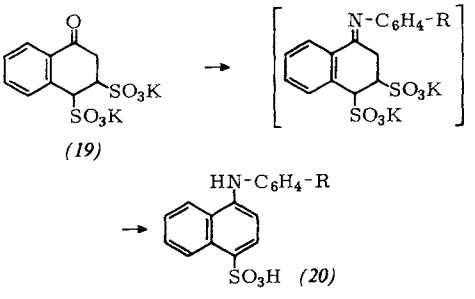
6. The Preparative Use of Tetralonesulfonic Acids

The intermediates of the Bucherer reaction have provided access to many compounds that are difficult or impossible to prepare by other methods. The use of salts of tetralonesulfonic acids is limited mainly by their instability in alkaline media and by their insolubility in organic solvents; however, it is often possible to use salts of organic bases, which are soluble in methanol, ethanol, and other water-miscible solvents.

a) Preparation of *N*-Arylated α-Naphthylamines and Naphthyl Sulfides

β-Naphthalene derivatives are generally smoothly aminated by alkyl- and arylamines under the conditions of the Bucherer reaction. Arylaminations of α-naphthalene derivatives, on the other hand, take place only in exceptional cases[1,43]. This is due to the lower nucleophilic strength of the arylamines as compared with the alkylamines, and to the lower electron density on the carbonyl carbon atom of 3-tetralone-1-sulfonic acids as compared with 1-tetralone-3-sulfonic acids.

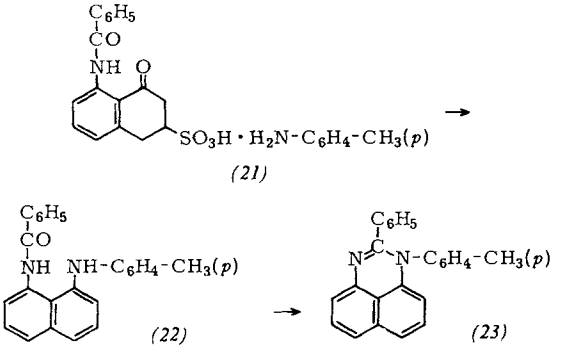
The reaction of 1-tetralone-3-sulfonic acids in anhydrous media with aromatic amines in the presence of strong acids yields 1-arylaminonaphthalenes, owing to the increase in the polarity of the carbonyl group[44]. *N*-Substituted naphthionic acids *(20)* are obtained in good yield from dipotassium 4-tetralone-1,2-disulfonate *(19)* *e.g.* in acetic acid or diglycol in the presence of small quantities of concentrated H_2SO_4.



(19) (20)

R = $CH_3(p)$; $OCH_3(p)$; $NO_2(p)$; $Cl(o, m, p)$

N-Arylated α-naphthylamines are formed when sodium 1-tetralone-3-sulfonate is heated for about 7 min at 180–200 °C with amine hydrochlorides. However, the action of one equivalent of $(NH_4)_2SO_4$ or NH_4Cl on sodium 1-tetralone-3-sulfonate at 210–230 °C yields α,α'-dinaphthylamine (probably *via* α-naphthylamine). In the pyrolysis of the *p*-toluidine salt of 8-benzoylamino-1-tetralone-3-sulfonic acid *(21)*, reaction again



(21) (22) (23)

[41] *H. Th. Bucherer*, J. prakt. Chem. [2] *70*, 349 (1904).

[42] *H. Th. Bucherer*, J. prakt. Chem. [2] *69*, 89 (1904).

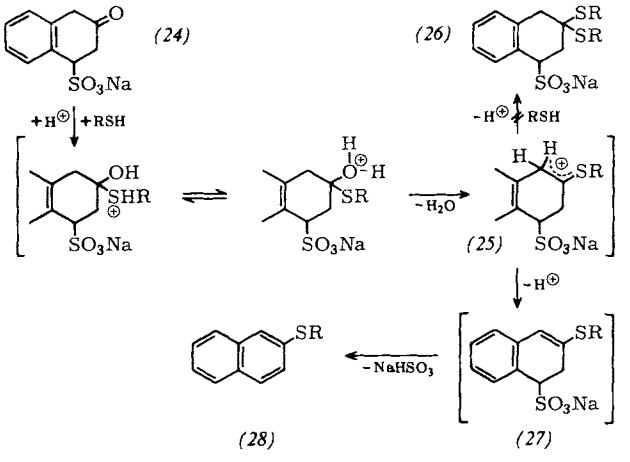
[43] *O. Limpach* and *K. Hager*, US-Pat. 2059466 and Brit. Pat. 451348 (Dec. 28th, 1934); Chem. Zbl. *1937*, I 1017.

[44] *A. Rieche* and *H. Seeboth*, Liebigs Ann. Chem. *638*, 92 (1960).

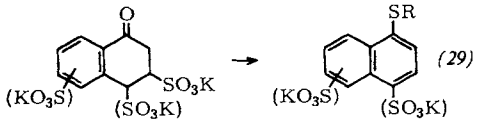
does not stop at the 8-benzoylamino-1-(*p*-tolylamino)-naphthalene stage *(22)*, but proceeds further to give 2-phenyl-1-(*p*-tolyl)perimidine *(23)* with elimination of water.

The ammonium salts of 4-tetralone-1,2-disulfonic acid do not form an *N*-substituted naphthionic acid when heated to 205–215 °C, but give *N*-substituted α-naphthylamines, with hydrolysis of the sulfo group on C-4.

In the study of the reaction of tetralonesulfonic acids with other nucleophiles that undergo acid-catalysed reactions with carbonyl compounds, it was found that thiols react smoothly with formation of naphthyl sulfides [45]. Sodium 3-tetralone-1-sulfonate *(24)* reacts in glacial acetic acid in the presence of small quantities of hydrochloric acid to give excellent yields of β-naphthyl sulfides *(28)*. Dithioacetals *(26)* are not formed; the assumed intermediate *(25)* appears to be very rapidly stabilized by loss of a proton and $NaHSO_3$, since the sodium 3-alkylthio-1,2-dihydronaphthalene-1-sulfonate *(27)* was not detected. 1-Tetralone-3-sulfonates



also react with thiols in glacial acetic acid at 20 °C when dry HCl gas is passed through the solution. This process is particularly suitable for the synthesis of 1-alkylthio- and 1-arylthionaphthalenesulfonic acids such as *(29)*, which are practically impossible to prepare in the usual manner (*via* naphthalenesulfonyl chlorides) [46].

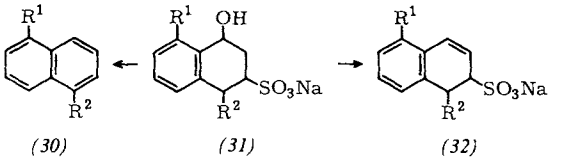


R = C_2H_5, C_6H_5, CH_2-C_6H_5, H_2C-$(CH_2)_n$-CH_3, H_2C-CO_2H

b) Reduction of Intermediates of the Bucherer Reaction

Reduction of tetralonesulfonic acids can be used for the preparation of ac-hydroxytetralinsulfonic acids, which had not previously been described in the literature [47].

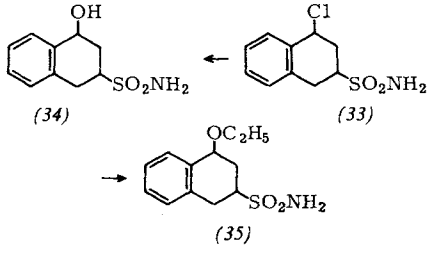
Sodium 1-tetralone-3-sulfonate can be converted into 1-hydroxytetralin-3-sulfonic acid *(31)*, $R^1 = R^2 = H$, by three methods: with sodium amalgam at pH = 6–7, with amalgamated aluminum [48], and by hydrogenation under pressure (40 atm, 80 °C, Raney nickel). The sodium salt of 8-amino-1-hydroxytetralin-3-sulfonic acid *(31)*, $R^1 = NH_2$; $R^2 = H$, and the dipotassium



salt of 4-hydroxytetralin-1,2-disulfonic acid *(31)*, $R^1 = H$; $R^2 = SO_3H$, were prepared in the pure state only by reduction of the corresponding tetralonesulfonic acid with activated aluminum.

The salts of the ac-hydroxytetralinsulfonic acids are stable toward dilute acid and alkali in aqueous solution at room temperature. They are decomposed by hot concentrated alkalis or hot 40% H_2SO_4 into water, SO_2, and naphthalene [or naphthalene derivatives *(30)*]. This reaction could be used for the elimination of hydroxy groups from naphthols *via* their bisulfite adducts. Attempts to dehydrogenate ac-hydroxytetralinsulfonic acids with sulfur or selenium lead to naphthalenes, but not to naphthols. The action of hot dilute mineral acids leads to elimination of water and formation of 1,2-dihydronaphthalenesulfonic acids *(32)*.

The sodium or *p*-toluidine salt of 1-hydroxytetralin-3-sulfonic acid reacts with thionyl chloride in dimethylformamide [49] to form 1-chlorotetralin-3-sulfonyl chloride, which gives 1-chlorotetralin-3-sulfonamide *(33)* on treatment with NH_3 gas in benzene. *(33)* is hydrolysed to 1-hydroxytetralin-3-sulfonamide *(34)* when heated in 2N Na_2CO_3 solution, and is alcoholysed to 1-ethoxytetralin-3-sulfonamide *(35)* in hot absolute alcohol.



The tetraloniminesulfonic acids *(36)*, which can be obtained from 1-tetralone-3-sulfonic acids and amines [34, 35], give *N*-substituted 1-aminotetralin-3-sulfonic acids *(37)* in yields of between 50 and 70% on reduction with $NaBH_4$ [50]. The compounds are very stable toward hot acids and bases.

[45] *H. Seeboth*, Mber. dtsch. Akad. Wiss. Berlin, in press.

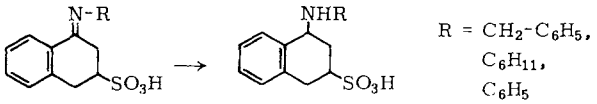
[46] *D. Klamann* and *Ch. Weiske*, Mh. Chem. *96*, 2025 (1965).

[47] *H. Seeboth* and *A. Rieche*, Liebigs Ann. Chem. *671*, 70 (1964).

[48] Cf. *H. Wislicenus* and *L. Kaufmann*, Ber. dtsch. chem. Ges. *28*, 1323 (1895).

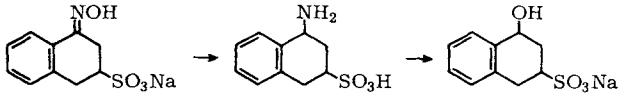
[49] Cf. *H. H. Bosshard*, *R. Mory*, *M. Schmid*, and *H. Zollinger*, Helv. chim. Acta *42*, 1653 (1959).

[50] Cf. *E. Schenker*, Angew. Chem. *73*, 99 (1961).



(36) *(37)*

1-Aminotetralin-3-sulfonic acid *(39)* can be obtained in good yield by reduction of the Na salt of 1-hydroxyiminotetralin-3-sulfonic acid *(38)* with sodium amalgam at pH = 7–8 or with activated aluminum [35]. A process reported by *Bogdanov* [51], namely, reduction of *(38)* with zinc in the presence of copper acetate, yields only unchanged starting material and a little 1-tetralone-3-sulfonic acid [35].



(38) *(39)* *(40)*

(39) is very stable toward acids and bases, and cannot be dehydrogenated to 1-aminonaphthalene-3-sulfonic acid with sulfur. Treatment with HNO_2 yields 1-hydroxytetralin-3-sulfonic acid *(40)* (the amino and sulfo groups are *cis* and equatorial).

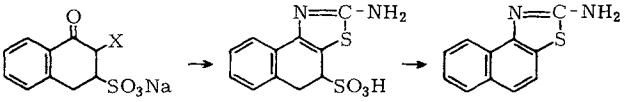
c) Preparation and Use of Halogenated Tetralonesulfonic Acids

1-Tetralone-3-sulfonic acids can be halogenated in position 2 [31, 38]. Bromination or chlorination takes place *e.g.* in aqueous solution in the presence of carbon tetrachloride as a solubilizing agent for the halogen. 2-Halogeno-1-tetralone-3-sulfonic acids *(41)* lose sulfite under the action of alkalis, with formation of bromonaphthols. It is possible in this way to prepare 2-bromo-1-hydroxynaphthalene-5-, -6-, and -7-sulfonic acids and 2-bromo- and 2-chloro-1-naphthol, which are otherwise obtainable only with difficulty, if at all [38].

The dehydrohalogenation of *(41)*, *i.e.* conversion into 1-hydroxynaphthalene-3-sulfonic acid, can be accomplished with catalytic quantities of carbonyl reagents (phenylhydrazine, hydrazine, or hydroxylamine) in alcohol in the presence of sodium acetate [52] or in acetate buffer solution with small quantities of organic bases or hydrazine. This method has been used for the preparation of 1-hydroxynaphthalene-3-sulfonic acid, and also of the 1-hydroxynaphthalene-3,5--3,6-, and -3,7-disulfonic acids. There is no need to isolate the halogenotetralonesulfonic acids; the acidic aqueous solution obtained on halogenation is simply neutralized with sodium acetate, a little hydrazine hydrate is added, and the solution is heated for about 10 min.

3-Bromo-4-tetralone-1,2-disulfonic acid could be only incompletely dehydrobrominated. On heating in benzylamine, 4-hydroxynaphthalene-1,2-disulfonic acid is isolated only in small yields as the bis-(*S*-benzylthiouronium) salt, together with 2-bromo-1-hydroxynaphthalene-4-sulfonic acid.

Hantzsch's classic thiazole synthesis [53], in this case the reaction of sodium 2-bromo-1-tetralone-3-sulfonate *(41)*, X = Br, and thiourea, leads to the formation of 2-amino-4,5-dihydrothiazolo[4,5-*a*]naphthalene-4-sulfonic acid *(42)* [54]. In acetate-buffered aqueous solution, the yield of *(42)* is 50%, whereas the



(41), X = Cl, Br *(42)* *(43)*

yield obtained in methanol is only 25% [55]; 1-hydroxynaphthalene-3-sulfonic acid is also formed. When *(42)* is heated in 2N NaOH, it loses bisulfite to form 2-aminothiazolo[4,5-*a*]naphthalene *(43)*, which can also be obtained from 1-(α-naphthyl)thiosemicarbazide [56] and from α-naphthylthiourea [57]. The synthesis *via (41)* is simpler, since *(42)* can be conveniently obtained in a single-vessel process from 1-tetralone-3-sulfonic acid [58].

d) Aminomethylation of 1-Tetralone-3-sulfonic Acid

Sodium 1-tetralone-3-sulfonate, like α-tetralone [59], reacts with formaldehyde and amines (*e.g.* morpholine, diethylamine, piperidine, and benzylamine) at 20 °C to form derivatives of 2-aminomethyl-1-tetralone-3-sulfonic acid *(44)* [60]. Although the keto group of *(44)* does not react with carbonyl reagents, its presence is demonstrated by bands at 1605 and 1680 cm^{-1} in the IR spectrum.

When heated in dilute alkalis, the compounds *(44)* lose sulfite and form Mannich bases *(45)* of α-naphthol [61]. Attempted reduction of 2-morpholinomethyl-1-tetralone-3-sulfonic acid led to 1-hydroxy-2-morpholinomethyltetralin-3-sulfonic acid *(46)*, $R^1 + R^2 = CH_2-CH_2-O-CH_2-CH_2$, which loses H_2SO_3 and H_2O in hot 65% sulfuric acid to form 2-morpholinomethylnaphthalene *(47)*, $R^1 + R^2 =$ $CH_2-CH_2-O-CH_2-CH_2$.

[51] *S. V. Bogdanov*, Ž. obšč. Chim. *28*, 1324 (1958).

[52] Cf. *V. R. Mattox* and *E. C. Kendall*, J. Amer. chem. Soc. *70*, 882 (1948); *C. Djerassi*, *ibid. 71*, 1003 (1949); *W. W. Rinne*, *H. R. Deutsch*, *M. I. Bowman*, and *I. B. Joffe*, *ibid. 72*, 5759 (1950).

[53] *A. Hantzsch*, Ber. dtsch. chem. Ges. *21*, 942 (1888).

[54] *H. Seeboth*, Mber. dtsch. Akad. Wiss. Berlin *6*, 268 (1964).

[55] Cf. *H. Bredereck*, *R. Gompper*, and *F. Reich*, Chem. Ber. *93*, 723 (1960).

[56] *M. Preund*, Ber. dtsch. chem. Ges. *24*, 4178 (1891).

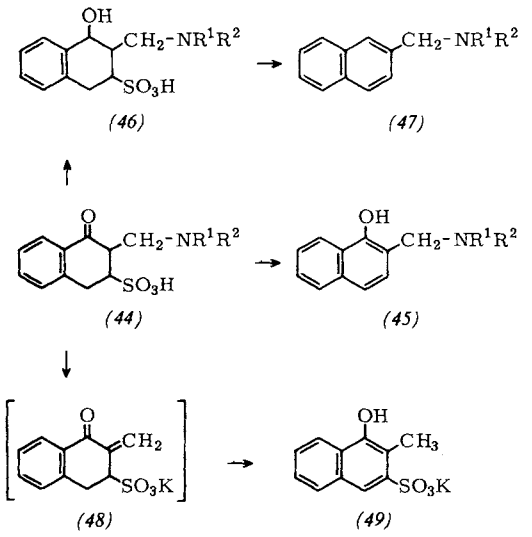
[57] *R. D. Desai*, *R. F. Hunter*, and *M. A. Kureishy*, J. chem. Soc. (London) *1936*, 1668.

[58] *K. Riethdorf*, Diploma Thesis, Humboldt-Universität Berlin, 1964.

[59] *C. Mannich* and *O. Hieronimus*, Ber. dtsch. chem. Ges. *75*, 49 (1942); *A. H. Sommers*, US-Pat. 2848449 (Aug. 31st, 1955); Chem. Zbl. *1960*, 3676.

[60] *H. Seeboth* and *B. Bornowski*, Liebigs Ann. Chem., *700*, 50 (1966).

[61] Cf. *K. Auwers* and *A. Dombrowski*, Liebigs Ann. Chem. *344*, 280 (1906); *W. T. Caldwell* and *Th. R. Thompson*, J. Amer. chem. Soc. *61*, 2354 (1939); *J. R. Feldman* and *E. C. Wagner*, J. org. Chemistry *7*, 31 (1942); *J. W. Cornforth*, *R. H. Cornforth*, and *R. Robinson*, J. chem. Soc. (London) *1943*, 168.



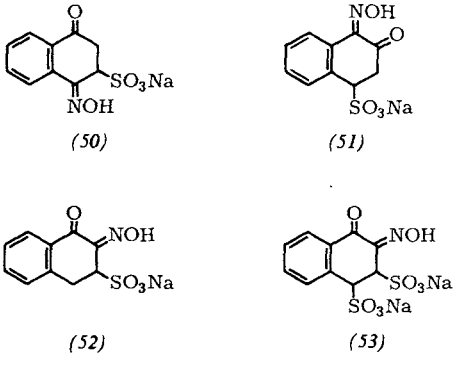
(46) (47) (44) (45) (48) (49)

$R^1 + R^2 = -CH_2-CH_2-O-CH_2-CH_2-$; $-(CH_2)_5-$;
$R^1, R^2 = C_2H_5$; $R^1 = H$, $R^2 = CH_2C_6H_5$

When the compounds *(44)* are heated in alcohol in the presence of an equivalent amount of $KHCO_3$, amine is eliminated and the potassium salt of 1-hydroxy-2-methylnaphthalene-3-sulfonic acid *(49)* is formed *via* the unstable methylene ketone *(48)* [62].

e) Bisulfite Adducts of Nitrosonaphthols

The hydroxyiminotetralonesulfonic acids *(50)* to *(53)* may be regarded as adducts of $NaHSO_3$ with 4-nitroso-1-, 1-nitroso-2-, and 2-nitroso-1-naphthol and with 1-hydroxy-2-nitrosonaphthalene-4-sulfonic acid. These substances are more stable than the bisulfite adducts discussed so far; for example, they do not decompose



(50) (51) (52) (53)

in alkaline solution at 20 °C. The adducts *(50)* and *(51)* are formed from $NaHSO_3$ and the corresponding nitrosonaphthol [21,63,64], whereas the compounds *(52)* and *(53)* cannot be obtained in this way. A well-known method for the separation of 2- and 4-nitroso-1-naphthols is based on the fact that 4-nitroso-1-naphthol forms a bisulfite adduct, while 2-nitroso-1-naphthol does not [63]. 2-Nitroso-1-naphthols, like 1-hydroxynaphthalene-2-sulfonic acids, evidently do not add $NaHSO_3$.

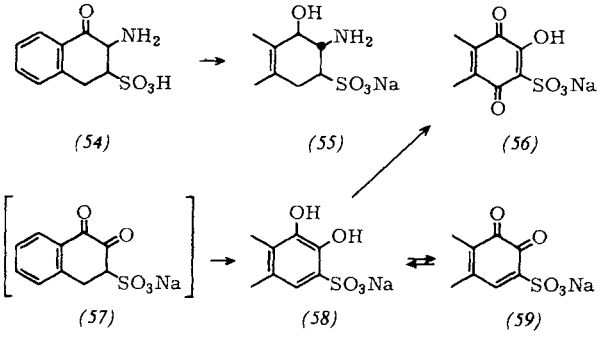
[62] Cf. *M. Mühlstädt* and *O. Scholz*, Chem. Ber. *97*, 1 (1964).

[63] *N. N. Woroshzow* and *S. W. Bogdanow*, Ber. dtsch. chem. Ges. *62*, 68 (1929).

[64] *S. V. Bogdanov*, Ž. obšč. Chim. *2*, (64) 770 (1932).

Seeboth and *Becker* [65] found that 1-tetralone-3-sulfonic acids react with HNO_2 to form 2-hydroxyimino-1-tetralone-3-sulfonic acids. Thus *(53)* was prepared from dipotassium 4-tetralone-1,2-disulfonate [31] and *(52)* from sodium 1-tetralone-3-sulfonate and isoamyl nitrite [65]. The IR spectrum of *(52)*, like that of α-tetralone, contains strong carbonyl bands at 1680 and 1600 cm^{-1}; there is no evidence of the existence of the tautomeric nitrosonaphthol form [66].

2-Hydroxyimino-1-tetralone-3-sulfonic acids undergo a number of interesting reactions. Hydrogenation (Raney nickel in water/methanol) of *(52)* yields the inner salt of 2-amino-1-tetralone-3-sulfonic acid *(54)*, which can be converted into *trans*-2-amino-1-hydroxytetralin-3-sulfonic acid *(55)* by the action of $NaBH_4$ as a suspension in methanol. When *(54)* is heated for a short time in 20% hydrochloric acid, it forms 2-amino-1-naphthol hydrochloride and 1-hydroxynaphthalene-3-sulfonic acid.



(54) (55) (56) (57) (58) (59)

When the sodium salt *(52)* is heated in 30% hydrochloric acid, it is hydrolysed to 1,2-dioxotetralin-3-sulfonic acid *(57)*, which rearranges to give the more stable tautomer, sodium 1,2-dihydroxynaphthalene-3-sulfonate *(58)*. *(58)* is stable in acidic media, but in alkaline solution it is oxidized by air to 3-hydroxy-1,4-naphthoquinone-2-sulfonic acid *(56)*. The action of nitrous acid on *(58)* in acidic solution leads to oxidation, with formation of the orange Na salt of 1,2-naphthoquinone-3-sulfonic acid *(59)*, which has a relatively low solubility. However, *(59)* is more easily obtained by the action of HNO_2 or isoamyl nitrite on *(52)* in acidic aqueous solution, or directly from the Na salt of 1-tetralone-3-sulfonic acid with an excess of isoamyl nitrite at 20 °C [67]. *(59)* can be reduced to 1,2-dihydroxynaphthalene-3-sulfonic acid *(58)* with phenylhydrazine [68], $NaBH_4$, or sulfurous acid.

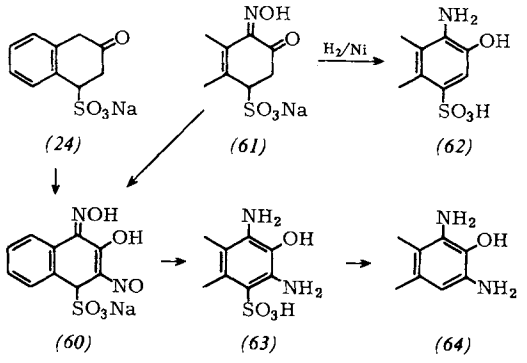
The sodium salt of 3-tetralone-1-sulfonic acid *(24)* reacts with 2 moles of nitrous acid to form 4-hydroxyimino-3-hydroxy-2-nitroso-1,4-dihydronaphthalene-1-sulfonic acid *(60)*. The same product is obtained from 1-hydroxyimino-2-tetralone-4-sulfonic acid *(61)* and isoamyl nitrite in concentrated hydrochloric acid [65].

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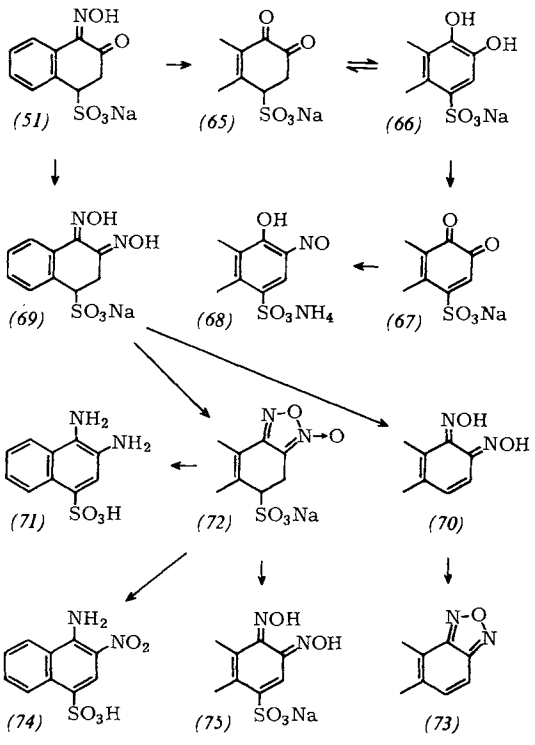
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Hydrogenation of *(60)* in methanol/water in the presence of Raney nickel yields 2,4-diamino-3-hydroxynaphthalene-1-sulfonic acid *(63)*; this reaction is similar to the conversion of *(61)* into 1-amino-2-hydroxynaphthalene-4-sulfonic acid *(62)* by reducing agents [21,69]. A remarkable feature in both cases is the aromatization under hydrogenating conditions. The sulfo group in *(63)* is removed hydrolytically when the compound is heated in 40% sulfuric acid. 1,3-Diamino-2-naphthol *(64)* is stable as the hydrochloride [70] or sulfate; the free base is extremely readily oxidized.

Bogdanov [71] observed a number of interesting reactions of 1-hydroxyimino-2-tetralone-4-sulfonic acid *(51)*. In hydrochloric acid solution, the action of hydroxylamine hydrochloride leads to the formation of the ammonium salt of 1-hydroxy-2-nitrosonaphthalene-4-sulfonic acid *(68)*. Contrary to *Bogdanov*'s assumption [71], the reaction probably proceeds analogously to the formation of 1,2-naphthoquinone-3-sulfonic acid from 2-hydroxyimino-1-tetralone-3-sulfonic acid, as follows: *(51)* is hydrolysed to the unstable 1,2-dioxotetralin-4-sulfonic acid *(65)*, which tautomerizes to form 1,2-dihydronaphthalene-4-sulfonic acid *(66)*; *(66)* is then oxidized to 1,2-naphtho-quinone-4-sulfonic acid, which condenses with hydroxylamine.

The reaction of *(51)* with hydroxylamine hydrochloride in the presence of sodium acetate yields 1,2-bis-(hydroxyimino)tetralin-4-sulfonic acid *(69)*, which loses sulfite at low temperatures to form 1,2-naphthoquinone dioxime *(70)*, and at high temperatures forms [2,1,3]oxadiazolo[4,5-*a*]naphthalene *(73)* *via* *(70)*. Oxidation of *(69)* with HNO_3, HNO_2, or H_2O_2 leads to the bisulfite adduct of [2,1,3]oxadiazolo[5,4-*a*]naphthalene 3-oxide *(72)* [72]. This can be reduced to 1,2-diaminonaphthalene-4-sulfonic acid *(71)* with zinc in alkaline media. When *(72)* is heated for 10 min in soda solution, 1-amino-2-nitronaphthalene-4-sulfonic acid *(74)* is obtained together with products such as naphtho[1,2-*d*]furazan 3-oxide; *(74)* is hydrolysed to 1-hydroxy-2-nitronaphthalene-4-sulfonic acid on prolonged heating [73]. Treatment of *(72)* with sodium



hydroxide solution leads to isomerization to the dioxime of 1,2-naphthoquinone-4-sulfonic acid *(75)*.

Similar reactions have been carried out *e.g.* with the bisulfite adducts of 2-hydroxy-1-nitrosonaphthalene-6- and -7-sulfonic acids [71,74] and of 1-nitroso-2-anthrol [75].

6. Conclusion

This review provides an example of the many revelations and the many preparative and industrial applications that lie hidden in "classical" chemistry. Owing to lack of space, no mention has been made of the application of the Schmidt reaction [76] to tetralonesulfonic acids [54], the formation of substituted naphthylhydrazines in the "single-vessel process" from 2-hydroxynaphthalene-3-carboxylic acid, acid hydrazide, and bisulfite [39b], or the synthesis of new carbazole derivatives [39b,39c]. The bisulfite adducts of azo compounds of naphthols and naphthylamines [39a,77] have also been omitted from the discussion.

The results described should provide an incentive for further experiments, *e.g.* on the stereochemistry of actetralinsulfonic acid derivatives. The principal outcome of this report is the elucidation of the mechanism of the Bucherer reaction, which has been used in industry for almost 70 years.

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The Solvent Dimethyl Sulfoxide

BY D. MARTIN, A. WEISE, AND H.-J. NICLAS [*]

Dedicated to Professor Alfred Rieche on the occasion of his 65th birthday.

The dipolar aprotic solvent dimethyl sulfoxide is liquid over a wide range of temperatures, is a strong electron donor, and has a high polarity. It is therefore an excellent and selective solvent for many organic and even polymeric compounds, and can enter into H-bonding and dipole-dipole association. The structure of dimethyl sulfoxide, with a "hard" oxygen atom and a "soft" sulfur atom, leads to good solvation of cations and poor solvation of anions. Mixtures of alkoxides with dimethyl sulfoxide are therefore among the most strongly basic systems in organic chemistry, and are excellently suited for the deprotonation of weakly acidic OH, NH, and CH bonds, for eliminations, and for the initiation of polymerizations.

I. Introduction

The classic principle "like dissolves like" is valid only as a rule of thumb. A deeper understanding of solvent properties has been gained by classification into protonic and dipolar aprotic solvents. According to *Parker* [1], protonic solvents are proton donors such as water, alcohols, carboxylic acids, and formamide. Dipolar aprotic solvents such as dimethylformamide, dimethylacetamide, tetramethylurea, dimethyl sulfoxide, acetonitrile, and nitrobenzene are characterized by dielectric constants $\varepsilon > 15$ and dipole moments $\mu > 3$ D. Since the hydrogen in these compounds is firmly bound, they cannot act as proton donors. The solvating powers of the two groups of solvents can be estimated from these properties:

1. Protonic solvents solvate anions by ion-dipole interactions and by strong hydrogen bonding, the ease of solvation increasing with decreasing size and increasing electronegativity of the anion: $SCN^- < I^- < N_3^- < Br^- < Cl^- \ll F^- \approx OH^-$ [2,3].

2. Anions are much less strongly solvated by dipolar aprotic solvents, owing to the absence of hydrogen bonding; in this case the large polarizable anions are more easily solvated than the small, more electronegative anions, so that the solvation series given under 1 is reversed [2,3].

3. Cations are generally less strongly solvated in protonic solvents than anions [3,4]. The reverse is true for dipolar aprotic solvents [1].

Thus the ability of a solvent to act as a proton or electron donor characterizes the solvent better than its polarity.

Among the dipolar aprotic solvents, dimethyl sulfoxide (DMSO) has become increasingly important in recent years. This importance is due not only to its high solvent power for many inorganic and organic compounds and its compatibility with many container materials [5], but also to its ease of production [5] and its pharmacological harmlessness [6–10,15]. *Schläfer* and *Schaffernicht* [14] have described the physical properties of DMSO and its use as a solvent in inorganic chemistry. (Other reviews: [5,11–13].)

The present article deals mainly with the use of DMSO in organic reactions and as a solvent for organic compounds. Special emphasis is placed on examples that show DMSO to possess special properties within the series of dipolar aprotic solvents. Apart from the formation of the methylsulfinyl carbanion in reactions with bases, we shall not discuss the cases in which DMSO enters into reaction and does not act merely as a solvent.

[*] Dr. habil. D. Martin, Dipl.-Chem. A. Weise, and Dipl.-Chem. H.-J. Niclas
Institut für Organische Chemie
der Deutschen Akademie der Wissenschaften zu Berlin
An der Rudower Chaussee
X 1199 Berlin-Adlershof

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II. Physical Properties

Dimethyl sulfoxide is a colorless, odorless, and hygroscopic liquid with a slightly bitter taste. At 20 °C it has an equilibrium moisture content of 10% water [16]. Some of its physical properties [17] are listed in Table 1, and the bond lengths and valence angles [18–21] are shown in Figure 1.

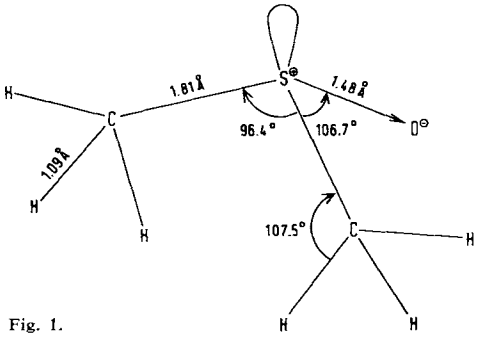
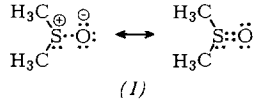


Fig. 1.

DMSO is best formulated as a resonance hybrid *(1)* [14, 39] of the canonical structure having a polarized S–O bond and that having a (p → d)$_\pi$ SO double bond [31, 40]. This representation agrees best with the physical properties and the reactivity of the compound.



(1)

The high boiling point (189 °C), the entropy of vaporization of 29.6 cal deg^{-1}mole^{-1} (which is even higher than that of water), and the results of cryoscopic in-

Table 1. Physical constants of dimethyl sulfoxide.

		Ref.
M.p.	18.55± 0.02 °C	[14]
Solidification point	18 °C, 18.5 °C	[22,23]
B.p.	189.0± 0.2 °C/760 mm	[14]
	79.8 °C/16 mm	[24]
	72.5 °C/12 mm	[24]
Coefficient of cubic expansion	0.00088	[25]
Specific heat at 25 °C	0.4698 cal/g	[5]
Heat of fusion at 18.4 °C	20 cal/g	[5,25]
Entropy of fusion	10.4 cal deg^{-1}mole^{-1}	[26]
	11.4± 0.2 cal deg^{-1}mole^{-1}	[27]
Heat of vaporization at 189 °C	175 cal/g	[5]
Entropy of vaporization	29.6 cal deg^{-1}mole^{-1}	[14]
Heat of combustion	6050 cal/g	[5,25]
Vapor pressure at 20 °C	0.37; 0.417 mm	[14]
Flash point (open dish)	95 °C	[5,25]
Heat of formation (from S_{rhomb} and $C_{graphite}$)	—47.7 kcal/mole	[25]
Density at 20 °C	1.1000 g/cm^3	[14]
Molar volume at 20 °C	71.03 cm^3/mole	[14]
Refractive index n_D^{20}	1.4783	[14]
Molar refraction	20.12 cm^3	[14]
Surface tension at 20 °C	46.2 dyne/cm	[14]
Parachor	184.4	[14]
Viscosity at 20 °C	2.47$_3$ cP	[14]
Dielectric constant at 20 °C	48.9	[14]
	45	[5,25]
	47.6 at 23 °C	[28]
Dipole moment	4.3± 0.1 D	[14]
Specific conductivity at 20 °C	3×10^{-8} Ω^{-1}cm^{-1}	[14]
Cryoscopic constant	4.4; 4.36	[24,26]
pK_a $H^{\oplus}\ominus CH_2$–SO–CH_3	31.3	[29,30]
pK_a CH_3–$^{\oplus}$SOH–CH_3	0.911	[31]
Mass spectrum	m/e = 63 (≈ 100%) $CH_3SO^{\oplus}$	[14,32]
	m/e = 45 (≈ 60%) $CH{\equiv}S^{\oplus}$	
	m/e = 61 (≈ 20%) CH_3–S=$CH_2^{\oplus}$	
NMR spectrum	τ = 7.38 (in $CDCl_3$) based τ = 7.50 (in CCl_4) onTMS	[33]
	^{13}C–H coupling constant 138 sec^{-1}	[34]
UV spectrum	250 μ; 0% transmission	[14,35]
	400 μ; 100% transmission	
IR and Raman Spectra	SO stretching vibration:	
	DMSO (gas) 1102 cm^{-1}	[36]
	[D_6]-DMSO (gas) 1096 cm^{-1}	[36]
	Solvent-dependence	[37]
	Complete band analysis	[36,38]

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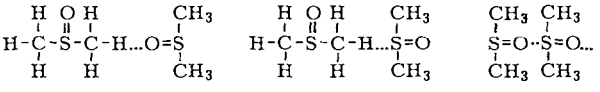
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vestigations in benzene [26] show that liquid DMSO is strongly associated. The associates, which could be formed by O–H *(2)* [14] as well as by S–H *(3)* [14] and S–O *(4)* [1] bridges, are broken down between 40 and 60 °C, as can be seen from the temperature-dependence of several physical properties (density, refractive index, increase in the limiting conductivity, and decrease in the Walden product, $\lambda_0 \cdot \eta_0 = \text{const.}$) [1,14]. The associates can rearrange in the presence of proton donors (cf. Section III).



(2) *(3)* *(4)*

The partial decomposition observed during boiling at normal pressure is strongly dependent on the impurities present, and decreases with increasing purity. The thermal decomposition is catalysed by acids [5,41] and inhibited by sodium formate, oxalate, and chloride, by borax, and by barium hydroxide [42]. When DMSO is refluxed for three days, 3.7% of volatile products are formed: dimethyl sulfide, dimethyl sulfone, dimethyl disulfide, bis(methylthio)methane, water, and paraformaldehyde [43].

As a solvent for spectroscopic studies, DMSO frequently offers decisive advantages in addition to its excellent solvent properties (cf. Section IV). Owing to the strong association of the OH and NH protons with DMSO (Section III) their rates of exchange are reduced. Thus the spin-spin splitting of the OH protons can be observed in the NMR spectrum, and also sharp NH resonance lines are recorded (example: sugar osazones [44]). Hydrogen bonding shifts the OH resonance lines to lower fields ($\tau \leqslant 6.0$); below 25 mole-%, the position of the OH lines is independent of concentration [45]. The methanol OH proton gives a quartet, and primary, secondary, and tertiary alcohols give clearly resolved triplets, doublets, and singlets [45] (examples: study of the conformation of epimeric cyclohexanols [46] and anomeric sugars [47,48]). [D_6]-DMSO (cf. Section VI) can be used for the study of tautomerism in pyrimidines and nucleosides [49], and unlike deuterochloroform it can be used, because of its greater solvent power, for the NMR spectroscopy of steroids [50].

DMSO is highly transparent between 350 and 2200 μ (see Table 1), whereas water absorbs at 1300 μ. DMSO can therefore be advantageously used instead of water for spectroscopic studies in the near IR region [51].

Owing to its good solvent properties and its favorable melting point, DMSO can also be used as a solvent in cryoscopic molecular-weight determinations by the *Beckmann* method [24,52].

III. Association and Solvation in Dimethyl Sulfoxide

Electron donor(D)–acceptor(A) molecular complexes exist in equilibrium with ion pairs, which are partly dissociated into free, solvated ions. The position of the equilibrium [eq. (a)] is determined by the nature of the solvent and of the donor-acceptor system. In most of the cases studied so far, $k_1 \gg k_2$, k_3 [53].

$$D + A \underset{}{\overset{k_1}{\rightleftharpoons}} (D \ldots A \longleftrightarrow D^{\delta\oplus} \ldots A^{\delta\ominus}) \overset{k_2}{\rightleftharpoons} (D^{\oplus}A^{\ominus})\ \text{solv.}$$

$$\overset{k_3}{\rightleftharpoons} D^{\oplus}_{\text{solv.}} + A^{\ominus}_{\text{solv.}} \qquad \text{(a)}$$

The equilibrium constants and the enthalpy change (ΔH) for equation (a) can be easily determined, and can be used for the comparison of the strengths of electron donors [54]. For example, the donor strength toward $SbCl_5$ was found to decrease in the order pyridine > DMSO > dimethylacetamide > dimethylformamide > diethyl ether > acetone > acetonitrile [54]. A study of dimethyl sulfoxide with various acceptors gave the order $SbCl_5$ > phenol > I_2, the ΔH values being −29.8, −6.5±0.2, and −4.4±0.3 kcal/mole respectively [54,55].

Similar considerations apply to proton donor and acceptor equilibria [eq. (b)] [56].

$$\underset{}{AH} + B \rightleftharpoons \underset{\text{(5)}}{AH \ldots B} \rightleftharpoons \underset{\text{(6)}}{A^{\ominus} \ldots HB^{\oplus}} \rightleftharpoons \underset{\text{(7)}}{A^{\ominus}_{\text{solv.}} + HB^{\oplus}_{\text{solv.}}} \qquad \text{(b)}$$

H-bridge; H-bridged ion-pair

DMSO contains two acceptor sites: the oxygen atom, which is the position of highest electron density, and the sulfur atom, which, in spite of its partially positive character, still possesses nucleophilic properties because of the lone pair of electrons [see formula *(1)*] [57].

This view is supported by the complexes with palladium and platinum, in which the S atom forms a coordinate

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bond [58], and by the methylation with methyl iodide to form $[(CH_3)_3S^{\oplus}O]I^{\ominus}$ [59]. All other electron acceptors (Lewis acids), which have been studied so far, attack at the oxygen atom.

The only possible point of association for the proton is the O atom of dimethyl sulfoxide. An explanation for this is offered by the theory of "hard" and "soft" bases and acids [60,61], according to which the "hard" proton can coordinate strongly only with the "hard" oxygen atom, whereas the "soft" atoms Pd and Pt and the "soft" methyl cation can attack the "soft" S atom. For these reasons the postulated dimethyl sulfoxide-S...H association *(3)* cannot be significant. Owing to the low CH acidity of DMSO (see Table 1), however, O...H association *(2)* is also unlikely.

1. Proton Donors

Thermodynamic, dielectric, and viscometric data show the existence of a strong interaction between DMSO and water [1,62–64]. One molecule of DMSO preferentially associates with two molecules of water [1,63,65]; *Tommila* [66] has suggested the structure *(8)*.

$$(CH_3)_2\overset{\displaystyle OH_2}{\overset{|}{S}}{=}O...H\text{-}O\text{-}H \quad (8)$$

However, definite complex formation could not be detected by cryoscopic investigations [67]. It was deduced from IR- [38] and Raman-spectroscopic findings [68] that the water molecules in DMSO are subject to strong dipole-dipole interactions, and may cause a partial ionic character in *(6)*. These interpretations are supported by kinetic data [69], which also show that the DMSO–H_2O interactions are stronger than the intermolecular association of H_2O [66,70,71].

Alcohols are weaker proton donors toward DMSO, and form only H-bonded complexes *(5)*. Calorimetric determination of the partial molar enthalpy of mixing ΔH_S gave an exothermic value only for methanol (−0.34±0.03 kcal/mole, H_2O: −1.28±0.03 kcal/mole), in contrast to the higher alcohols (ethanol 0.28±0.02 kcal/mole, n-propanol 0.61±0.04 kcal/mole, and n-butanol 0.99±0.03 kcal/mole) [3].

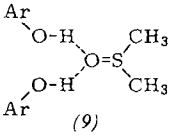
The proton association on the oxygen atom is clearly evidenced by the displacement of the SO stretching vibration to lower wave numbers as a result of the decrease in the (p → d)π-bond component [72,73]. Complexing on the S atom should lead to an increase in the frequency of the SO stretching vibration [73]. The association of DMSO with compounds containing OH groups is summarized in Table 2.

Table 2. Association of compounds containing hydroxy groups with dimethyl sulfoxide $[(CH_3)_2SO\cdots HOR]$.

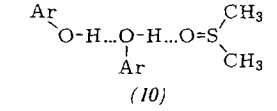
ROH	Proof of association	Ref.
AlkOH	[b]	[74]
CH_3OD	[c]	[3]
Diols, triols	[d]	[75]
Carbohydrates	[a,e]	[76]
ArOH	[b,c,f,g,h]	[37,55,56,77–79]
Alk–COOH	[b,c,h]	[74,79,80]
Ar–CH_2COOH	[h]	[79]

[a] NMR spectra, [b] heats of mixing, [c] IR and Raman spectra, [d] density anomalies and viscosity measurements at several temperatures, [e] optical rotatory dispersion, [f] dielectric measurements, [g] determination of the equilibrium constants [eq. (b)], [h] thermal analysis of binary systems.

Carboxylic acids and phenols give 1:2 as well as 1:1 associates. In the case of phenols, the structure *(9)* probably predominates over *(10)* [37].



(9)



(10)

The acidity of phenols and carboxylic acids changes significantly with the transition from protonic to dipolar aprotic solvents (see Table 3) [1,29,81]. This is

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[80] *J. J. Lindberg* and *C. Majani*, Suomen Kemistilehti *B 37*, 21 (1964); Chem. Abstr. *61*, 3745h (1964); cf. also [68].

[81] *B. W. Clare*, *D. Cook*, *E. C. F. Ko*, *Y. C. Mac*, and *A. J. Parker*, J. Amer. chem. Soc. *88*, 1911 (1966) and literature cited there.

due to the difference in the solvation of the anions and cations formed in accordance with equation (b), which displaces the equilibrium more or less towards *(7)*. If the anions are small, they are strongly solvated *via* H-bonds by protonic solvents, and HA is a relatively strong acid in water. On the other hand, DMSO solvates anions only weakly, and so decreases the acidity. Large anions (*e.g.* the picrate anion, see Table 3) are more strongly solvated by DMSO, so that the system is more strongly acidic than the aqueous system. At the same time, the strong electron-donating action of DMSO leads to strong solvation of protons, which are thus withdrawn from the reverse reaction (formation of HA).

Sulfuric and hydrochloric acids are strong acids in DMSO[29]. The *i* factor [*] for the protonation with concentrated sulfuric acid is about 2[57,82]. Nitric acid forms a 1:1 adduct with DMSO[14]. The acidity of very weak acids in DMSO mixtures has also been studied[83–85].

Table 3. pK_a values of some phenols and carboxylic acids in dimethyl sulfoxide and in water.

Acid (Ion)	pK_a (DMSO)	pK_a (H_2O)	Ref.
Picric acid	−1.9	0.71	[81]
2,4-Dinitrophenol	5.2	4.10	[81]
Salicylic acid	6.9	2.98	[29]
4-Nitrophenol	9.9	7.15	[81]
Benzoic acid	10.0	4.20	[29]
(Di-n-butylammonium)	10.3	11.31	[29]
Acetic acid	11.4	4.76	[29]

The association of OH-proton donors in DMSO shows a gradation: alcohols form H-bonds *(5)*, water and phenols form H-bonded ion pairs *(6)*, and strong acids are present as free (solvated) ions *(7)*.

In contrast to OH association, very few investigations have been carried out on NH complex formation in DMSO (see Table 4). The shifts of the NH signal to lower fields in the ^{1}H–NMR spectrum show the following sequence of electron donor strengths[86]:

DMSO > pyridine > acetone > RNO_2 > $CHCl_3$.

Table 4. Association of compounds containing NH groups with dimethyl sulfoxide.

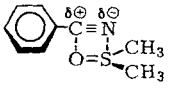
Amine	Amine:DMSO	Proof of association	Ref.
$C_6H_5NH_2$	1:1	[a, b, c]	[87]
$C_6H_5NH-CH_3$	1:1, 2:1, 3:1	[a, b, c]	[87]
$C_6H_5NH-C_6H_5$	1:1, 2:1	[a, b]	[87]
$4\text{-}H_3CC_6H_4-NH_2$	1:1	[b]	[87]
$4\text{-}BrC_6H_4-NH_2$	1:2	[d]	[88]
$(C_2H_5)_3Si-NH_2$	1:1	[d]	[89]
Sugar osazones	1:1	[e]	[44]

[a] Cryoscopic measurements, [b] refractometric measurements, [c] UV spectra, [d] IR spectra, [e] NMR spectra.

The proton donor strength of CH bonds depends on the hybridization of the C atom and on the substitution. The formation of H bonds is favored by increasing s-character $C_{(sp^3)}-H < C_{(sp^2)}-H < C_{(sp)}-H$ and by electron-attracting substituents. $C_{(sp^3)}-H$ bonds have a detectable donor action only in combination with two electron-attracting substituents[90,91], the influence of which can be expressed by "spectral displacement increments"[91]. For example, chloroform forms 1:1[71,92] ($\Delta H_S = -1.32 \pm 0.09$ kcal/mole[31]) and 2:1 complexes[92] with dimethyl sulfoxide. In compounds of the type RR'C=CHX, clearly detectable H-bonding occurs only when X and at least R or R' are electronegative; benzene requires three electron-attracting substituents, whereas alkynes having terminal triple bonds act as proton donors, even in the absence of electronegative substituents[90].

2. Dipole Associates

Nitriles and ketones form dipole-dipole complexes with DMSO, as is shown by the changes in the position and intensity of the carbonyl and nitrile absorption in the IR spectrum[93–95]. It can be seen from the arrangement *(11)* that the dipole-dipole complexes are much more sensitive to steric effects than the H-bonded complexes. The association affects the reactivity of the nitrile group, so that electrophilic attack on the N atom is facilitated[96].


(11)

As is shown by the dissociation constant, the dipole-dipole complexes are much weaker than the H-bond complexes: $K_{\text{acetone·DMSO}} = 2.7$ mole l^{-1}[95], $K_{C_6H_5CN\cdot DMSO} = 1.1$ mole l^{-1} (also $p\text{-}ClC_6H_4CN$, $p\text{-}O_2NC_6H_4CN$, and $m\text{-}O_2NC_6H_4CN$)[95], $K_{C_6H_5OH\cdot DMSO} = 5.5 \times 10^{-3}$ mole l^{-1}[55].

3. Charge-Transfer Complexes

Iodine chloride, iodine, and iodine cyanide form 1:1 complexes with DMSO (the bond strengths decreasing in the above order)[55,73,97], as can be seen from the

[*] The *i* factor is the number of particles formed on dissolution of one "molecule" of the substance.

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[96] *D. Martin* and *A. Weise*, Liebigs Ann. Chem. *702*, 86 (1967).

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lower intensities and lower frequencies (1011–1036 cm^{-1}) of the SO stretching vibrations. The reason is the same as in the H-bonded complexes, *i.e.* lowering of the (p → d)π-bond order [73]. The charge-transfer band for the iodine cyanide-DMSO complex in heptane occurs at 223 μ, and that for the iodine-DMSO complex [97] in carbon tetrachloride is at 272 μ.

IV. Solvent Power

The high and selective solvent power of DMSO is due to three important properties, *i.e.* its relatively high polarity, its ability to form hydrogen bonds, and the fact that it is liquid over a wide range of temperatures.

1. Solvent Power for Gases and Water

The gases HCl, SO_2, SO_3, and NO_2 dissolve very readily in DMSO at room temperature. At NO_2 contents higher than 25%, as with HNO_3, addition compounds having explosive properties are formed. CO_2 and NH_3 are moderately soluble, NO, CO, N_2, H_2, and O_2 are insoluble, and H_2S is oxidized to sulfur.

Ethylene oxide and unsaturated hydrocarbons such as acetylene [98,99], ethylene, and propylene are very readily soluble in DMSO, whereas the solubility of saturated hydrocarbons is low.

About 30% more acetylene dissolves in DMSO than in acetone at normal pressure; however, DMSO cannot be used as a storage liquid for acetylene, since the solubility of acetylene decreases with increasing pressure – this is in contrast with the solubility of acetylene in acetone [100]. The solubilities of some gases in dimethyl sulfoxide are given in Table 5.

Table 5. Solubilities of gases in dimethyl sulfoxide at 20.3 °C and atmospheric pressure [25].

Gas	Wt.-%	Vol. gas per vol. DMSO
SO_2		500
NH_3	2.6	40
CO	0.0	—
CO_2	0.6	4
Methane	0.0	—
Propane	—	1.8
Ethylene	0.1	1.1
Propylene	—	3.2
Isobutylene	2.5	—
Butadiene	—	30
Acetylene	2.8	30
Dimethylether	3.9	—
Ethylene oxide	—	48.2
Methanethiol	35	—

DMSO is perfectly miscible with water. Owing to the high specific heat of DMSO (see Table 1), these solutions have lower freezing points and lower viscosities than mixtures of water with glycol, glycerol, methanol, *etc.* Aqueous solutions of DMSO are therefore very suitable for use as cooling brines [25,101].

2. Solvent Power for Organic Compounds

Apart from the saturated paraffins, nearly all the common organic solvents (alcohols, glycols, ethers, aldehydes, ketones, carboxylic acids, nitriles, amines, thioethers, chloroform, and aromatic solvents) are completely soluble in DMSO. DMSO is a good solvent for fats, carbohydrates, camphor, heterocycles, dyes, and drugs. The solubilities of some organic compounds in DMSO are given in Table 6.

Table 6. Solubilities of some organic compounds in dimethyl sulfoxide [25] at 20.3 °C.

Compound	Wt.-%	Compound	Wt.-%
n-Hexane	2.6	Glycine	0
n-Decane	0.6	Methionine	0.1
n-Dodecane	0.3	Saccharose	30–50 (warm) [a]
Napthalene	27	Urea	25–55
Triethylamine	8.3	Thiourea	25–40
Di-n-butylamine	10.0	Phenol	completely miscible
Methyl laurate	6.0	Picric acid	completely miscible
Oxalic acid	26	Terephthalic acid	15–25 (warm) [a]
Citric acid	40	CS_2	45

[a] No details in original paper.

DMSO is well suited for use as a solubilizing agent in the dyeing and printing of textiles. It can be used for the preparation of pastes of naphthol-AS components, which are not obtainable by the cold dissolution method with alcohol, furthermore, it may be used for the preparation of solutions of certain naphthols, from which the naphthol is not precipitated in the aqueous-alkaline dye bath [5]. Thus cellulose fibers can be uniformly dyed in aqueous media by dispersion of the water-insoluble dye in DMSO [102]. Synthetic polymers such as Dacron, Nylon, polyvinyl chloride, and polystyrene can also be dyed with a soluble dye or with a pigment in admixture with DMSO [103]. DMSO can be used as a carrier for dyes, pigments and chemicals for rubber processing, or in pesticides. These solutions are characterized by a long storage life and a remarkable compatibility with a large number of substrates [104].

In recent years, the outstanding power of DMSO to penetrate the skin has attracted special interest as a result of the discovery that it greatly improves the percutaneous resorption of a large number of drugs [105].

Quaternary oximes such as 1-methyl-2-hydroxyiminomethylpyridinium methanesulfonate are continuously carried

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[104] Brit. Pat. 945427 (Dec. 23rd, 1963), Crown Zellerbach Corp.; Chem. Abstr. *60*, 11640f (1964).

[105] *S. W. Jacob*, *R. J. Herschler*, and *M. G. Bischel*, Belg. Pat. 644613 (Dec. 9th, 1963), Crown Zellerbach Corp.; Chem. Abstr. *63*, 9759b (1965).

through the skin of guineapigs and rats [106]. This penetration takes place only to a small extent or not at all by water. The penetration of glucocorticosteroids and hydrocortisone through human skin *in vitro* is 5 to 20 times as fast in DMSO as in 95% ethanolic solution [107]. Similar improvements in penetration have been observed in *in-vivo* studies *e.g.* with dyes, vitamins, insulin, glucocorticosteroids, and griseofulvin [107a, 108]. The stratum corneum reservoir [*] was saturated 5 min after application. This retention persists for up to 16 days, and is not affected by washing of the skin with soap, water, and ethanol [109].

3. Solvent Power for Macromolecular Compounds

DMSO has found wide use as a solvent for natural and synthetic polymers (cf. Table 7). It is an excellent solvent for polymeric carbohydrates and their derivatives, polyamides, polyvinyl compounds, resins, and paints.

Table 7. Examples of polymers soluble in dimethyl sulfoxide.

Soluble polymers	Polymers that dissolve on heating and precipitate out on cooling:
Cellit T 900 and T 1000	Polyurethanes
Cellulose acetates	Polymethacrylates
Collodion cottons	Coumarone resin
Cellulose ethers	Copal
Urea resins	Phenolic resin (Super Beck. 2000)
Epoxy resins	
Polyvinyl alcohol	Swellable polymers
Polyacrylonitrile	Plexigum M 265
Mowital B 60H	Vinoflex MP 400
Mowilith 50	
Plastopal EBS	
Shellac	
Rosin	
Chlorinated rubber	

Granulated starch [110, 111] dissolves in anhydrous DMSO without swelling. The solubility is decreased by chemical cross-links. Nonionic cellulose ethers such as methyl cellulose and methyl hydroxyethyl cellulose dissolve readily in DMSO. It is the only known organic solvent for the water-soluble ethyl hydroxyethyl cellulose [112], and is also good solvent for acetylcelluloses and nitrocelluloses. DMSO can be used in the manufacture of uniformly drying noninflammable paints with improved frost resistance and high adhesion [5]. However, since DMSO is hygroscopic, concentrations of more than 10% should not be used in air-drying paints [113]. In combination with 3 parts by volume of methylene chloride, DMSO provides an excellent, incombustible paint remover [113].

DMSO is particularly useful for the removal of polyisocyanate paints (DD paints and epoxide stoving paints), which are resistant to all the usual paint removers because of their strong internal crosslinking [5]. DMSO is a suitable solvent for polyurethanes [114] and polycaprolactam [115] at 160 °C. These solutions can be used for the production of films, sheets, and coating compositions having high strength and flexibility. The solubility of polyamides, polyureas, and polyurethanes in DMSO can in some cases be increased by a factor of four by the addition of 10% of alkali metal or alkaline-earth metal chlorides or bromides [116].

DMSO is very important as a solvent for polyvinyl compounds for the production of spinnable solutions. The disadvantages of the solvents used previously (lack of stability, large losses during processing, high toxicity, poor quality of the fibers) can in many cases be eliminated by the use of DMSO. Thus polyacrylonitrile fibers having excellent textile properties are obtained by the use of polyacrylonitrile-DMSO spinning solutions [117–119]. Acrylonitrile-methacrylate copolymers (having an average methacrylate content of 5 mole-%), which have a higher viscosity in concentrated solutions than in dimethylformamide [120] can also be converted into fibers by the wet [121] and dry spinning processes [122]. A comparison of the solubilities of several vinyl polymers showed that DMSO is a better solvent than dimethylformamide for polymers having high cohesive energies, such as polyacrylonitrile and polyvinyl alcohol [123, 124].

However, polyvinyl cyanoethyl ether, which is also readily soluble, is cleaved above 50 °C [125]. A solvent mixture of DMSO and aromatic compounds in a ratio of 25:75 to 40:60 has proved suitable for vinyl chloride-vinyl acetate copolymers [126]. DMSO is also a

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[*] The stratum corneum is the outermost layer of the epidermis.

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good solvent for polyvinyl fluoride[127,128] and polyacrolein[129].

One of the most surprising results in connection with the plastics industry was the excellent solubility of polyethylene terephthalate, which permits spinning from DMSO/water[5].

4. Utilization of the Selective Solvent Power for Separations

The selective solvent power of DMSO presents excellent possibilities for separations. *A. Waksmundzki et al.* have determined the phase equilibria and partition coefficients of liquid ternary systems of DMSO, aromatic hydrocarbons, and hexane[130], heptane[131], and octane[132]: DMSO was found to be a good selective solvent for aromatic compounds over a wide range of concentrations.

The extraction is favored by increasing molecular weight of the aliphatic and aromatic hydrocarbons *e.g.* in petroleum fractions. A mixture of DMSO with 10% of water is a particularly selective solvent[133,134]; thus, benzene (having m.p. 5.5–5.6 °C), toluene, and xylene containing less than 1% of aliphatic hydrocarbons can be extracted at 25 °C. Further, up to 96.2% of the aromatic components can be removed from a reformate (b.p. 65–180 °C) containing 40–64% of aromatics, the content of aliphatic components in the extract being less than 3%[135]. This selectivity is not affected by the presence of dienes[136].

Naphthalene hydrocarbons are also smoothly removed from non-naphthalene hydrocarbons (tetralin, alkylbenzenes)[137] and sulfur compounds from petroleum fractions[138]. In anthracene oil, the readily soluble phenanthrene and carbazole can be separated from the sparingly soluble anthracene (95% purity after two extraction stages) with DMSO[5]. Pure terephthalic acid is precipitated by water from solutions of terephthalic and isophthalic acids in DMSO[5]. The dimethyl esters of these acids can also be readily separated[139].

Other industrially important separations include: (i) the extraction of high molecular weight alkaline-earth metal sulfonates, such as are formed in the sulfonation of lubricating oils with fuming sulfuric acid followed by treatment with $Ba(OH)_2$ or $Ca(OH)_2$[140], (ii) the quantitative separation of mono- and dicarboxylic acids from montan waxes with DMSO/heptane at 90 °C[141], (iii) the extraction of water-insoluble alcohols from the hydrocarbon mixture of the Fischer-Tropsch synthesis[142], and (iv) the separation of acetylene from the pyrolysis products of hydrocarbons[143]. The ability of DMSO to absorb acetylene can be increased by the addition of dioxane, benzene, or nitrobenzene[144].

Monomeric formaldehyde having a water content of 3–5% can be dried by treatment with DMSO at 70–100 °C[145]. 1 g of DMSO can take up 0.05 g of water, and the water content of the formaldehyde can be reduced to 0.1–0.01%.

A very important application of DMSO is the extraction of plant components. At an average DMSO: wood ratio of 10:1, DMSO extracts lignin (90%) at 25 °C, and extracts lignin (93%) and pentosans (87%) at 140 °C[146–148]; 0.2% of hydrochloric or sulfuric acid must be added in order to obtain the maximum possible removal of the lignin[149]. Sodium sulfide is also claimed to have catalytic properties[150]. The lignin can be precipitated in a coarse and easily filterable form by the addition of water, and the DMSO can be recovered by fractional distillation. The hemicellulose extract contains a high percentage of the acetyl and formyl groups originally present in the wood[16].

DMSO can also be used as a selective precipitant for the partial separation of hemicelluloses. DMSO in neutral solution precipitates mainly the polysaccharides containing mannose from an extract of delignified fir wood with 18% sodium hydroxide solution[16]. Extraction experiments with wood flour have also yielded information on the structure of the carbohydrate-lignin complex bonding state[151].

The mild extracting action of DMSO permits the isolation of glycogen from rat liver in a form closer to that of native glycogen than in any other extraction known so far[152].

DMSO has also occasionally been used as the stationary phase in paper-chromatographic separations. Tropolones can be satisfactorily and reproducibly separated on paper impregnated with ethylenediaminetetraacetic acid/DMSO, with petroleum ether, cyclohexane, or isopropanol as the mobile phase[153]. Paper impregnated with DMSO can be

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used for the separation of sugar acetates, alcohols, cyclitols, and glycosides, with petroleum ether, diethyl ether, or diisopropyl ether as the mobile phase [154]. This method offers special advantages over conventional paper chromatography:

The rate of migration is strongly dependent on the structure, while the molecular weight has little influence; in the D series, the α anomers migrate more rapidly than the β-anomers, and the 2,3,6-tri-*O*-methyl derivatives of D-glucose and D-mannose, which could formerly be distinguished only with difficulty by paper chromatography, can be separated as the acetates. Investigations by *Soczewinski* have shown that DMSO can be used as the polar phase for the paper-chromatographic separation of naphthols [155] and dihydroxydibenzofurans [156]. DMSO is a highly selective solvent for gas-liquid chromatography. C_1–C_6 hydrocarbons, including olefins, show significant differences in retention volume on a firebrick-powder column with 30% of DMSO. Thus a mixture of 13 hydrocarbons from CH_4 to n-hexane could be completely separated in 35 min [157].

V. Reactions in Dimethyl Sulfoxide

The distinction between protonic and aprotic dipolar solvents has proved particularly noticeable in the kinetic study of solvent effects in S_N2 reactions [1,2]. Thus the reactivity of small anions with high charge densities increases by a factor of 10^4 to 10^{10} on changing from protonic to dipolar aprotic solvents [1]. The small anions are less reactive in protonic solvents, because of solvation (*via* H-bonds), whereas in dipolar aprotic solvents they are "bare", and are therefore very reactive. The situation is reversed for large anions having low charge densities.

The poor solvation of the attacking anions and the strong solvation of the transition states with wide charge distributions lead to a marked decrease in the activation energy of bimolecular reactions, which fall from $\geq$ 20 kcal/mole in protonic solvents to between 15 and 17 kcal/mole (and in some cases to 13 kcal/mole) in dipolar aprotic solvents [158]. The differences in the entropy of activation are smaller, but $\Delta S^{\neq}$ is always slightly lower in dipolar aprotic solvents.

The two groups of solvents do not differ so greatly in the solvation of cations, since the solvation of a given cation is determined mainly by the electron-donor strength of the solvent. However, small metal cations are more strongly solvated in dipolar aprotic solvents than in protonic solvents [3], since the solvation is promoted by prior association [1,3].

The postulate by *Hughes* and *Ingold* (cf. [159]) that bimolecular reactions with strongly polarized transition states are accelerated in proportion to the polarity of the solvent is valid only within each of the two groups of solvents [66,160]. In general the effect of changing from a protonic to a dipolar aprotic solvent is greater (*e.g.* higher reaction rates in DMSO (D.C. = 48.9) than in methanol (D.C. = 33.6)) or even reversed (higher reaction rates in DMSO than in water (D.C. = 80.4)).

The solvation effects also influence the character of the reaction. S_N1 reactions are suppressed or displaced into the S_N2 range by dipolar aprotic solvents [1].

DMSO occupies a special place among the dipolar aprotic solvents. Consideration of the polarized bonds *e.g.* of dimethylformamide, acetone, or acetonitrile shows that the partially negative *and* positive atom is "hard" in the sense of the theory of "hard" (unpolarizable) and "soft" (polarizable) acids and bases [60,61], whereas DMSO contains a partially positive "soft" sulfur atom. *R. G. Pearson* [60] has shown that, as a general rule, "hard" (*i.e.* difficulty polarizable) acids combine particularly firmly with "hard" bases, and "soft" (*i.e.* readily polarizable) acids form particularly firm bonds with "soft" bases (see also Section III). Thus the "soft" character of the electrophilic S atom and the weak CH acidity permit little interaction between DMSO and "hard" nucleophiles. The "hard" oxygen atom of DMSO limits its use as a solvent, since it reacts with "hard" electrophiles (reactive alkyl halides and alkyl sulfonates, as well as acylating agents and mineral acids). Thus the range of application of DMSO as a solvent extends from weakly electrophilic reagents to strong bases and nucleophiles.

1. The Activation of OH, NH, and CH Bonds

The usual pK_a values for alcohols (16–18) are valid only in solvents containing hydroxyl groups. With increasing DMSO content, the pK_a values of n- and t-butanol increase to a limiting value of about 30 [83, 161]. This means that alkoxides are 10^{12} to 10^{14} times as basic in pure DMSO as in alcohols. (However, this is true only of potassium and cesium alkoxides; sodium and lithium alkoxides are less basic, owing to ion-pair formation.) The quantity of methylsulfinyl carbanion existing in equilibrium with potassium t-butoxide [eq. (c)] is sufficient for quantitative interception as the benzophenone adduct *(12)* [161].

$$\begin{array}{l} CH_3\text{-}SO\text{-}CH_3 \rightleftharpoons K^{\oplus}\overset{\ominus}{C}H_2\text{-}SO\text{-}CH_3 + t\text{-}BuOH \\ \quad + \\ t\text{-}BuO^{\ominus}K^{\oplus} \end{array} \qquad (c)$$

$$\xrightarrow[2.\ H_3O^{\oplus}]{1.\ (C_6H_5)_2CO} (C_6H_5)_2C(OH)\text{-}CH_2\text{-}SO\text{-}CH_3 \quad (12)$$

Solutions of potassium t-butoxide in DMSO are among the most strongly basic systems of organic chemistry. Their basicity is equivalent to that of the sodium salt of the methylsulfinyl carbanion ($Na^{\oplus\ominus}CH_2$–SO–CH_3) [162], and is surpassed only by that of $K^{\oplus\ominus}CH_2$–$SOCH_3$. An important use of these base systems in DMSO is therefore in the deprotonation of weakly CH-acidic compounds such as triphenylmethane [83], phosphonium salts (Wittig reaction) [163], sulfoxonium and sulfonium salts [164], and sulfones [162].

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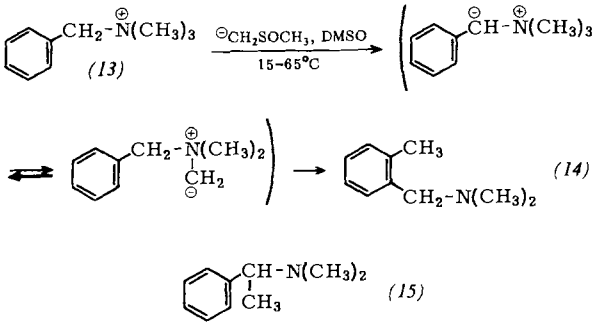
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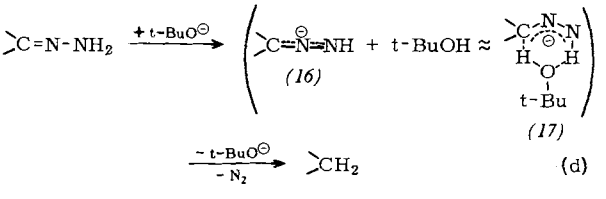
The methylsulfinyl carbanion acts as a specific deprotonating agent in the Sommelet rearrangement of benzyltrimethylammonium salts *(13)* to (2-methylbenzyl)dimethylamine *(14)* (85%, without isomers). Other bases, with the exception of alkali metal amides in liquid ammonia, are less selective. Thus butyllithium gives 35–45% of *(14)* together with 21–30% of *(15)* (Stevens shift), phenyl-lithium leads mainly to *(15)*, and sodium hydride has no effect [164a].



(13) *(14)* *(15)*

In the presence of $Na^{\oplus}$, the basicity of the alkoxide ion is weakened by ion-pair formation with the sodium ion. It thus becomes possible to titrate alcohols against $Na^{\oplus\ominus}CH_2-SO-CH_3$, using triphenylmethane as the indicator [165]. The titration of amine salts with potassium methoxide or tetrabutylammonium hydroxide gives particularly sharp end-points in DMSO [166].

The Wolff-Kishner reaction of hydrazones of aldehydes and ketones with the potassium t-butoxide/DMSO system proceeds much more rapidly (0.5–1 h at room temperature) than under the usual conditions (heating for several hours at about 200 °C) [167]. To suppress the formation of azine, which competes up to the extent of about 25%, it is recommended that the reaction time should be increased to about 8 h. The yields of hydrocarbon are then 60–90%. It can be seen from the kinetics of the reaction [168] that a hydrazone anion *(16)* is first formed from alkoxide



(16) *(17)*

(d)

and hydrazone, and that the isomerization of *(16)* to form a dense complex [probably *(17)*] solvated by DMSO is the rate-determining step [eq. (d)].

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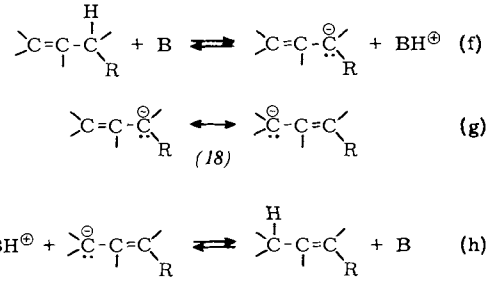
2. t-Butoxide-Catalysed Isomerization of Olefins, Stereoisomerizations, and H-D-T Exchange Reactions

A solution of potassium t-butoxide in DMSO is an excellent medium for the anionic activation of α-CH bonds in ethers [169], thioethers [170], olefins [171], and alkylaromatic compounds [172]. In these cases, the high basicity and the high solvent power act in the same direction. The mixtures are always homogeneous and easy to handle and to reproduce, and in this respect they are superior to sodium alkyls or alkali metal amides in liquid ammonia [173].

The catalytic rearrangement of allyl ethers into enol ethers in the presence of potassium t-butoxide [eq. (e)] is 10^5 times as fast in DMSO as in 1,2-dimethoxyethane/t-BuOH [169].

$$CH_2{=}CH{-}CH_2{-}O{-}R \xrightarrow[DMSO]{t\text{-}BuOK} \underset{99\%\ cis}{CH_3{-}CH{=}CH{-}O{-}R} \qquad (e)$$

According to *Schriesheim et al.* [171,173,174], simple olefins (butenes, pentenes, hexenes) can also be isomerized at a measurable rate with potassium t-butoxide in DMSO [eq. (f)–(h)] [171,173–176].



(18)

The rates and activation parameters of the isomerizations are very strongly dependent on the nature of the group R: phenyl ≈ vinyl ⋙ methyl > isopropyl > t-butyl [175]. Methylenecyclobutane isomerizes faster than methylenecyclohexane [176]. It can be seen from this and from the distinct isotope effect (k_H/k_D = 4.4 at 55 °C) in the isomerization of 1-pentene and perdeutero-1-pentene [174] that the rate-determining step is the deproponation and formation of a planar mesomeric allyl anion *(18)* in the transition state. The high

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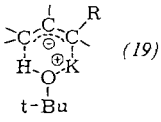
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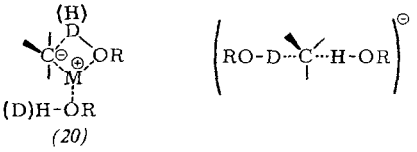
negative entropy of activation ($\Delta S^{\neq} < -20$ cal deg^{-1} mole^{-1}) and the observation that the isomerization is 16 times as fast as the H–D exchange [174] indicate an intramolecular cyclic transition state *(19)*.



(19)

The catalytic effect of lithium, sodium, and potassium alkoxides on the H–D exchange in optically active CH bonds activated by nitrile, amide, and ester groups was measured for several solvents by *Cram et al.* [177]. The rates of exchange and racemization in DMSO are higher by factors of 10^4 to 10^9 than in methanol, t-butanol, and ethylene glycol. Li, Na, and K methoxides (90% DMSO, 10% CH_3OH) are equally active at lower concentrations ($< 0.01-0.02$ M). The decrease in catalytic activity at higher concentrations owing to ion-pair formation first becomes noticeable with lithium methoxide.

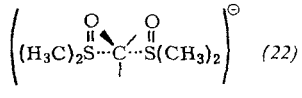
The catalytic H–D exchange in optically active compounds containing substituted benzyl groups (2-phenylbutane and 1-phenyl-1-methoxyethane) in the presence of t-butoxide [172] is approximately 10^5 times as fast in DMSO as in t-butanol or ethylene glycol. Potassium t-butoxide is 100 times as reactive as sodium t-butoxide. In the absence of substituents (CN, CO_2R) that stabilize carbanions, the steric course of the reaction is strongly dependent on the solvent (retention in t-butanol, predominantly inversion in ethylene glycol, complete racemization in DMSO). The stereospecificity in cases of retention *(20)* and inversion *(21)* is attributed to "asymmetric solvation" of the substituted benzyl carbanion. In DMSO, symmetrical solvation *(22)* of the benzyl carbanion leads to racemization. The relatively low isotope effect ($k_H/k_D = 1.7-3.0$) indicates that the exchange reaction is preceded by an equilibrium stage.



(20)



(21)



(22)

According to *Schriesheim* [178], the absence of a significant primary D–T and H–D isotope effect for the exchange between [D_3]-(and [T_3]-)toluene and DMSO in the presence of equimolar quantities of potassium t-butoxide can be explained by assuming that the ionization of the CH bond is not the rate-determining step, and that the complete ionization is instead preceded by a compact complex of the resulting anion and the resulting alcohol [eq. (i)], which must decompose before interaction with other molecules of alcohol or with the solvent can take place, and whose concentration and stability determine the rate of the reaction.

$$R\text{–}H + KOR' \rightleftharpoons (R^{\ominus}K^{\oplus}/HOR')_{solv.} \qquad \text{(i)}$$

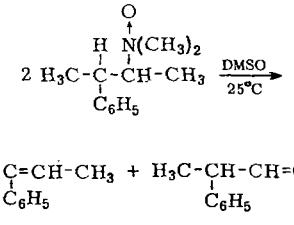
The catalytic H–D exchange on thiophene in the presence of potassium t-butoxide, in which the α-H atom is exchanged much more rapidly than the β-H atom, also proceeds at a measurable rate [179]. The α-H atoms in diethyl sulfide can be replaced with D by the deuterated sodium methylsulfinyl carbanion [170].

3. Eliminations and Dehydrations

a) In the Absence of Bases

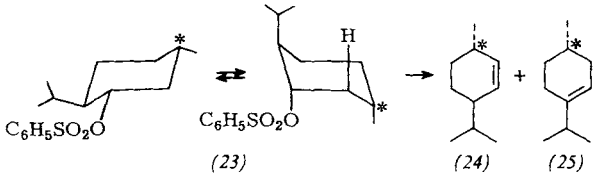
Owing to its high polarity, low nucleophilic strength, and relatively high basicity, DMSO is particularly suitable for use as a solvent in elimination reactions. t-Alkyl halides, which tend to form intermediate carbonium ions, decompose very readily in DMSO to form olefins [180]. Nucleophilic substitutions on the t-butyl residue cannot take place in DMSO [1].

Cope eliminations [eq. (j)] of tertiary amine oxides proceed 10^4 times as rapidly at 25 °C as in water [167], which deactivates the oxygen of the amine oxide by solvation.



(j)

Arylsulfonates of secondary alcohols give olefins in yields of up to 80% when heated for six hours at 100 °C in a 4- to 8-molar excess of DMSO [181]. The fact that (–)-menthyl benzenesulfonate *(23)* gives a mixture of alkenes containing 60 to 70% of (+)-Δ^3-menthene *(25)* rules out the possibility of an E_2 elimination, which would lead exclusively to (+)-Δ^2-menthene *(24)*.



(23) *(24)* *(25)*

Even pure alcohols (benzyl alcohols, secondary and tertiary alcohols, aldols, 1,2- and 1,3-diols) can be dehydrated by heating for 8 to 16 hours in DMSO at 160–185 °C [182, 183]. The yield of alkene can be

[177] *D. J. Cram, B. Rickborn, C. A. Kingsbury,* and *P. Haberfield,* J. Amer. chem. Soc. *83,* 3678 (1961).

[178] *J. E. Hofmann, A. Schriesheim,* and *R. E. Nickols,* Tetrahedron Letters *1965,* 1745.

[179] *I. O. Shapiro, A. G. Kamrad, Y. I. Ranneva,* and *A. I. Shatenshtein,* Latvijas PSR Zinatun Akad. Vestis, Kim. Ser. *1964* (5) 535; Chem. Abstr. *62,* 8955d (1965).

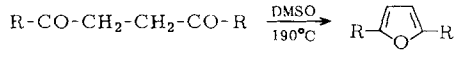
[180] *K. Heinonen* and *E. Tommila,* Suomen Kemistilehti *B 38,* 9 (1965); Chem. Abstr. *62,* 16003e (1965).

[181] *H. R. Nace,* J. Amer. chem. Soc. *81,* 5428 (1959).

[182] *V. J. Traynelis, W. L. Hergenrother, J. R. Livingston,* and *J. A. Valicenti,* J. org. Chemistry *27,* 2377 (1962).

[183] *V. J. Traynelis, W. L. Hergenrother, H. T. Hanson,* and *J. A. Valicenti,* J. org. Chemistry *29,* 123 (1964).

increased to 90% by the addition of small quantities of sulfuric acid. Under these conditions, 1,2-diols undergo partial pinacolic rearrangement while 1,4-diketones are dehydrated to form furan derivatives *(26)*.



R = CH_3, C_6H_5 *(26)*, 60-70%

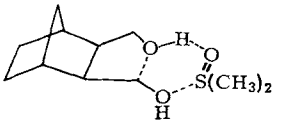
The structure of the alcohols, the catalytic effect of sulfuric acid, the pinacolic rearrangement, and the non-stereospecific course of the dehydration of *erythro*- and *threo*-1,2-diphenyl-1-propanol (50% of *cis*- and 50% of *trans*-methylstilbene in each case) [182] point to a mechanism in which carbonium ions play an important part.

If the ratio of DMSO to alcohol is reduced from 4 to 8:1 to 1:3, the yield of alkenes falls to 30%, while ether is formed to an extent of more than 50% [183]. However, ether formation can be observed even with a 12-fold excess of DMSO (8–16 h, 160 °C, 75–98%) in the case of 1,4-diols, which are converted into stable tetrahydrofuran derivatives. Equation (k) shows an example in which even primary hydroxyl groups react [184].

(k)

98%

This method is superior to all others for the preparation of tetrahydrofuran derivatives. The transition state *(27)* is postulated to explain the smooth course of the reaction.



(27)

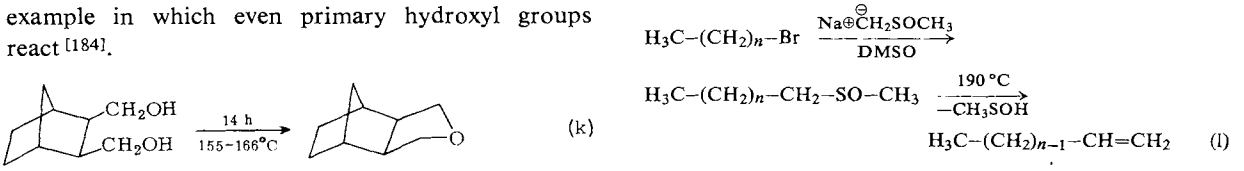
b) Eliminations and Dehydrations in the Presence of Bases

When DMSO is used as the solvent instead of alcohols, the increase in the ease of elimination of sulfonate and halide is of approximately the same magnitude as the acceleration of S_N2 reactions with nucleophiles. Alkoxide-catalysed eliminations from benzenesulfonates of primary and secondary alcohols, which require several days at 80–140 °C in alcohol or diglyme [1,2-bis(methoxy)ethane], proceed to completion within 30 min at room temperature in DMSO [185, 186], though ether formation then competes with the elimination. In the presence of potassium t-butoxide, the sulfonates of secondary alcohols give up to 80% of alkene and a little ether, while the sulfonates of primary alcohols give 20–25% of alkene and 60–70% of t-butyl ether [186]. The nature of the sulfonate residue has practically no influence on the yields or on the product distribution; however, chlorides exhibit a stronger tendency toward elimination [185]. Fluoride is such a strong base in DMSO that primary alkyl halides form olefins in the presence of fluoride [1].

It is interesting to note that even compounds containing groups which are eliminated usually only with difficulty undergo eliminations with the system potassium t-butoxide/DMSO [187, 188]. The ease of elimination from isopropyl derivatives decreases in the following order, the yields from the nitro compound onward being less than 10%: $Br^{\ominus} \approx RSO_2^{\ominus} \approx RSO^{\ominus} > NO_3^{\ominus} > SCN^{\ominus} > RS^{\ominus} > NO_2^{\ominus} > S^{2\ominus} > CN^{\ominus}$.

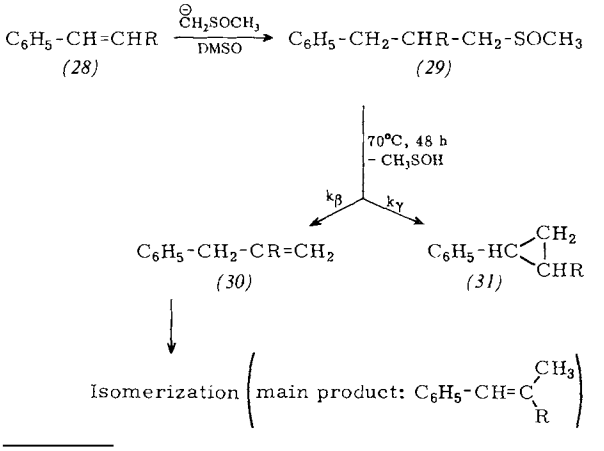
The reactivity of the t-butoxide ion decreases with increasing tendency of the cation to form ion pairs, *i.e.* in the order Cs > Rb > K ≫ Na ≫ Li.

The elimination of $RSO^{\ominus}$ from sulfoxides offers the possibility of preparing olefins with terminal double bonds from primary alkyl bromides in accordance with [eq. (l)] [189].



(l)

3-Phenyl-2-alkylpropyl sulfoxides *(29)*, which are formed by the addition of the methylsulfinyl carbanion to β-alkylstyrenes *(28)*, undergo γ-eliminations to form cyclopropane derivatives *(31)* as well as β-eliminations to form olefins *(30)* [189a]. The β-elimination proceeds mainly by the E2 mechanism [188] and the γ-elimination by the E1cB mechanism. The yield of cyclopropane derivatives increases with the size of R [R = H: 0% of *(31)*, R = t-C_4H_9: 97% of *(31)*], since it becomes increasingly difficult for the molecule to assume the conformation that favors β-elimination. The potassium salt of the methylsulfinyl carbanion is



[184] *B. T. Gillis* and *P. E. Beck*, J. org. Chemistry *28*, 1388 (1963).

[185] *N. F. Wood* and *F. C. Chang*, J. org. Chemistry *30*, 2054 (1965).

[186] *C. H. Snyder* and *A. R. Soto*, J. org. Chemistry *30*, 673 (1965).

[187] *T. J. Wallace*, *J. E. Hofmann*, and *A. Schriesheim*, J. Amer. chem. Soc. *85*, 2739 (1963).

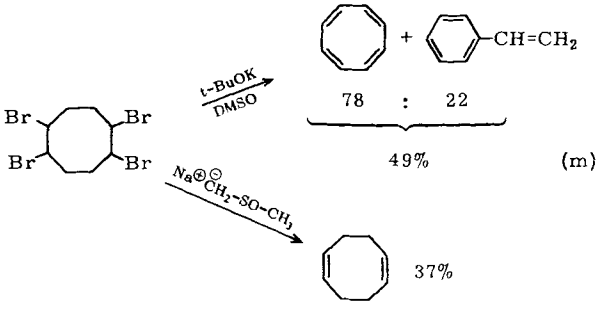
[188] *J. E. Hofmann*, *T. J. Wallace*, and *A. Schriesheim*, J. Amer. chem. Soc. *86*, 1561 (1964).

[189] *J. D. Entwistle* and *R. A. W. Jonstone*, Chem. Commun. *1965*, 29.

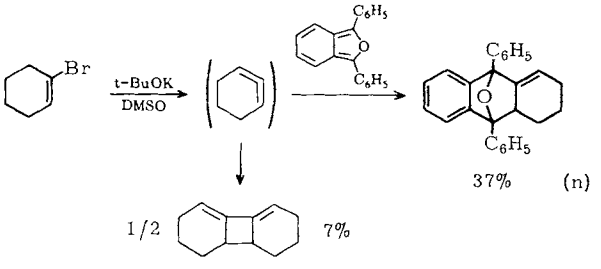
[189a] *R. Baker* and *M. J. Spille*, Chem. Commun. *1966*, 757.

less selective in the formation of *(30)* and *(31)* than the less strongly basic sodium compound.

The system potassium t-butoxide/DMSO is more suitable for dehydrohalogenations than the sodium salt of the methylsulfinyl carbanion [190], which only dehalogenates vicinal dibromides [see *e.g.* eq. (m)].



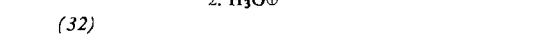
An example showing the high basicity of the system potassium t-butoxide/DMSO is the formation of 1,2-cyclohexadiene from 1-bromocyclohexene [eq. (n)] [191, 192], the diene being detected by interception with 1,3-diphenylbenzofuran and by dimerization.



The direction of elimination from 2-butyl and 2-pentyl *p*-toluenesulfonates is increasingly displaced from the Saytzeff to the Hofmann orientation in the order $C_2H_5OH/C_2H_5OK <$ $DMSO/C_2H_5OK <$ DMSO/t-BuOK [193]. Such a change in the product ratio (2-alkene:1-alkene) simply as a result of variation of the solvent and of the base strength had not been observed previously. In the opinion of *Froemsdorf* and *McCain* [193], this points to a transition state that tends toward the carbanion elimination mechanism E1cB [194], *i.e.* in which the CH bond exhibits a higher degree of heterolysis than the CX bond. However, the facts that no H–T exchange takes place in the β position with respect to the departing group and that deprotonation of a secondary CH bond takes place in preference to that of a primary CH bond suggest that elimination of $R-SO^{\ominus}$ from sulfoxides by the potassium t-butoxide/DMSO system [188] proceeds by a synchronous E 2 mechanism.

4. Nucleophilic Substitutions, Condensations, and Additions

All reactions between electrophiles, which do not react with DMSO, and nucleophiles, which are more strongly solvated in protonic solvents than in DMSO, are accelerated when DMSO is used as the solvent. It is not uncommon for the rate of reaction to be faster by a factor of 10^6 than in protonic solvents. The reactions are strictly bimolecular. Lithium or sodium ions again reduce the rate of reaction by ion-pair formation. The nucleophilic strengths of the hydroxide ion and of the alkoxides increases with the increase in their basicity (see also Section V 1), so that *e.g.* esters with strong steric hindrance [195] and epoxides [196] can be readily hydrolysed with alkali metal hydroxide/DMSO. Even non-enolizable ketones [*e.g. (32)*] can be cleaved [197].

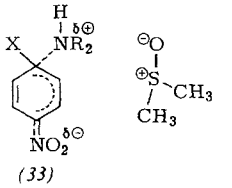


(32)

The ambidentate phenoxide ions are alkylated only on the oxygen atom in DMSO, whereas the "selective solvation" of the O atom of the phenoxide in polar solvents allows partial *C*-alkylation, the extent of which increases with proton-donor strength in the order $C_2H_5OH < CH_3OH < H_2O < F_3C-CH_2OH$ [198, 199].

Alkylcyanates ($R-O-C\equiv N$) which may act as ambidentate electrophiles, can be attacked either at the alkyl carbon atom or at the nitrile carbon atom. The point of attack is dependent on the type of nucleophile and, furthermore, is strongly influenced by the type of solvent [198a]. In DMSO, alkylation reactions are favored (see Table 8). The reason might be that attack at the nitrile carbon atom according to *(11)* is hindered by association with DMSO.

Nucleophilic substitutions in aromatic compounds are also accelerated in DMSO. The reaction of 4-nitrofluorobenzene with piperidine is 5×10^3 times as fast in DMSO as in benzene. Even the addition of 11% of DMSO increases the reaction rate by a factor of 400 [213]. The acceleration is again due to specific solvation of the transition state *(33)* by DMSO [199a]; however, polarization of the substrate as suggested by *Kingsbury* [160] may also play a role.



(33)

Table 8 shows the types of nucleophilic substitutions and condensations studied so far.

[190] *C. G. Cardenas, A. N. Khafaji, C. L. Osborn,* and *P. D. Gardner,* Chem. and Ind. *1965,* 345.

[191] *G. Wittig* and *P. Fritze,* Angew. Chem. *78,* 905 (1966); Angew. Chem. internat. Edit. *5,* 846 (1966).

[192] Cf. also *A. T. Bottini* and *W. Schear,* J. Amer. chem. Soc. *87,* 5802 (1965).

[193] *D. H. Froemsdorf* and *M. E. McCain,* J. Amer. chem. Soc. *87,* 3983; 3984 (1965).

[194] *J. F. Bunnett,* Angew. Chem. *74,* 731 (1962); Angew. Chem. internat. Edit. *1,* 225 (1962).

[195] *W. Roberts* and *M. C. Whiting,* J. chem. Soc. (London) *1965,* 1290; *F. C. Chang* and *N. F. Wood,* Tetrahedron Letters *1964,* 2969.

[196] *G. Berti, B. Macchia,* and *F. Macchia,* Tetrahedron Letters *1965,* 3421.

[197] *P. G. Gassmann* and *F. V. Zalar,* Tetrahedron Letters *1964,* 3031.

[198] *N. Kornblum, R. Seltzer,* and *P. Haberfields,* J. Amer. chem. Soc. *85,* 1148 (1963).

[198a] *D. Martin, A. Weise, H.-J. Niclas,* and *S. Rackow,* Chem. Ber., in preparation.

[199] *N. Kornblum, P. J. Berrigan,* and *W. J. le Noble,* J. Amer. chem. Soc. *85,* 1141 (1963).

[199a] *C. F. Bernasconi, M. Kaufmann,* and *H. Zollinger,* Helv. chim. Acta *49,* 2563 (1966).

Table 8. Nucleophilic substitutions, condensations, and additions in dimethyl sulfoxide.

Nucleophilic substitutions		Ref.	Condensations and additions	Ref.
Cyclo–R–Cl	+ $^{36}Cl^{\ominus}$	[200]	R–N=O + $R'NH_2$ [c]	[216a]
R–X [a]	+ $ArO^{\ominus}$	[198, 198a]	Ar–CHO + $CH_2R'_2$ [c]	[216a, b]
R–X	+ $RO^{\ominus}$	[1, 198a]	H–CHO + $CH_2R'_2$ [d]	[217]
R–X	+ $NO_2^{\ominus}$	[201]	Claisen condensation [c]	[218]
R–X	+ $OCN^{\ominus}$	[202]	Dieckmann [c] and Thorpe condensations [c]	[219]
R–X	+ $SCN^{\ominus}$	[198a, 203]	Wittig olefination of carbonyl compounds (single-step from phosphonium salts, aldehydes, and DBN [e])	[219a]
R–X	+ $CN^{\ominus}$	[198a, 204]	Polypeptide condensations	[220]
R–X	+ $N_3^{\ominus}$	[198a]	Addition of sulfonamides to CS_2	[221]
R–X	+ $I^{\ominus}$	[198a]	Addition of mercaptans to isocyanates	[222]
R–X	+ $NO_3^{\ominus}$	[198a]	Trimerization of aryl isocyanates [f]	[223]
R–X	+ $RCOO^{\ominus}$	[198a]	Bromohydrin synthesis (by reaction of olefins with NBS [g]/water)	[223a]
R–X	+ $S_2O_3^{2\ominus}$	[205]		
R–X	+ NR_3	[206]		
R–X	+ H_2N–Ar	[207]		
R–X	+ Pyrrole	[208]		
R–X	+ $^{\ominus}CR'(CO_2R'')_2$	[209]		
R–X	+ $^{\ominus}CH(CN)_2$, $^{\ominus}CH(COR')_2$	[210]		
Ar–Br	+ t-$BuO^{\ominus}$	[211]		
O_2N–Ar–X	+ $F^{\ominus}$	[212]		
O_2N–Ar–X	+ Piperidine	[213]		
$(O_2N)_2$–Ar–X	+ Piperidine	[199a]		
O_2N–Ar–X	+ $N_3^{\ominus}$	[2]		
R–Br	+ $Na^{\oplus}{}^{\ominus}CH_2$–SO–$CH_3$	[189]		
HCl [b]	+ R_2Hg	[214]		
R–CO_2R'	+ $OH^{\ominus}$(t-$BuO^{\ominus}$)	[195]		
R–SO_2R'	+ t-$BuO^{\ominus}$, $CH_3O^{\ominus}$	[215]		
Epoxide	+ $OH^{\ominus}$ ($H_3O^{\oplus}$)	[196]		

[a] R = primary or secondary alkyl residue, X = F, Cl, Br, I, sulfonate, cyanate; [b] attack of HB not rate-determining; a cyclic four-membered ring transition state is postulated; [c] in the presence of t-BuOK; [d] in the presence of C_2H_5ONa; [e] 1,5-diazabicyclo[4.3.0]non-5-ene; [f] catalysed by benzyltrimethylammonium hydroxide; [g] *N*-bromosuccinimide.

The use of DMSO as the solvent offers the following advantages: homogeneous reaction medium, high yields ($\geqslant 80\%$), relatively low temperatures (generally room temperature), and shorter reaction times (1/2 to 6 h).

5. Base-Catalysed Oxidations

DMSO is oxidized by oxygen in the presence of alkoxides to form dimethyl sulfone and methanesulfonic acid. A mixture of 80 vol-% of DMSO and 20 vol-% of t-butanol is stable towards oxygen in the presence of potassium t-butoxide (or tetramethylammonium t-butoxide) at room temperature, and in comparison with other solvent combinations, this mixture is excellently suited for base-catalysed oxidations with oxygen and for electron-transfer reactions in general [224].

Under these conditions, the rate of oxidation of triphenylmethane is the same as the rate of the H–D exchange α-deuterotriphenylmethane [216a]. It follows that the ionization of the CH bond [eq. (o)] is the rate-determining step. The carbanion intermediate reacts preferentially with the oxygen atom to form a free

[200] *H. Elias* and *S. Krutzik*, Chem. Ber. *99*, 1026 (1966).

[201] *N. Kornblum* and *J. W. Powers*, J. org. Chemistry *22*, 455 (1957).

[202] *B. L. Phillips* and *P. A. Argabright*, J. heterocyclic Chem. *3*, 84 (1966).

[203] *S. Yoneda*, *I. Morishima*, *K. Fukui*, and *Z. Yoshida*, J. chem. Soc. Japan, ind. Chem. Sect. (Kogyo Kagaku Zasshi) *68*, 1074 (1965); Chem. Abstr. *63*, 17873b (1965); *D. Martin* and *W. Mucke*, Mber. dtsch. Akad. Wiss. Berlin *6*, 362 (1964).

[204] a) *L. Friedman* and *H. Schechter*, J. org. Chemistry *25*, 877 (1960); b) *R. A. Smiley* and *C. Arnold*, *ibid. 25*, 257 (1960).

[205] *R. Fuchs* and *A. Nisbet*, J. Amer. chem. Soc. *81*, 2371 (1959).

[206] *E. Tommila* and *L. Hämäläinen*, Acta chem. scand. *17*, 1985 (1963).

[207] *T. L. Fletcher* and *Hsi-Lung Pan*, J. org. Chemistry *24*, 141 (1959).

[208] *C. F. Hobbs*, *C. MacMillin*, *E. P. Papadopoulos*, and *C. A. Van der Werf*, J. Amer. chem. Soc. *84*, 43 (1962).

[209] *H. E. Zaugg*, *B. W. Horrom*, and *S. Borgwardt*, J. Amer. chem. Soc. *82*, 2895 (1960).

[210] *J. J. Bloomfield*, J. org. Chemistry *26*, 4112 (1961).

[211] *D. J. Cram*, *B. Rickborn*, and *G. R. Knox*, J. Amer. chem. Soc. *82*, 6412 (1960).

[212] *G. C. Finger* and *C. W. Kruse*, J. Amer. chem. Soc. *78*, 6034 (1956).

[213] *H. Suhr*, Ber. Bunsenges. *67*, 893 (1963); Chem. Ber. *97*, 3277 (1964).

[214] *R. E. Dessy*, *G. F. Reynolds*, and *Jin-Young Kim*, J. Amer. chem. Soc. *81*, 2683 (1959).

[215] *F. C. Chang*, Tetrahedron Letters *1964*, 305; *E. D. M. Eades*, *D. H. Ball*, and *L. Long jr.*, J. org. Chemistry *31*, 1159 (1966).

[216] a) *G. A. Russell*, *E. G. Janzen*, *H.-D. Becker*, and *F. J. Smentowski*, J. Amer. chem. Soc. *84*, 2652 (1962); b) *G. A. Russell* and *H.-D. Becker*, *ibid. 85*, 3406 (1963).

[217] *G. Schwenker*, *W. Prenntzell*, *U. Gassner*, and *R. Gerber*, Chem. Ber. *99*, 2407 (1966).

[218] *J. J. Bloomfield*, J. org. Chemistry *27*, 2742 (1962).

[219] *J. J. Bloomfield* and *P. V. Fennessey*, Tetrahedron Letters *1964*, 2273.

[219a] *H. Oediger*, *H.-J. Kabbe*, *F. Möller*, and *K. Eiter*, Chem. Ber. *99*, 2012 (1966).

[220] *S. M. Bloom*, *S. K. Dasgupta*, *R. P. Patel*, and *E. R. Blout*, J. Amer. chem. Soc. *88*, 2035 (1966).

[221] *R. Gompper* and *W. Hägele*, Chem. Ber. *99*, 2885 (1966).

[222] *E. Dyer*, *J. F. Glenn*, and *E. G. Lendrat*, J. org. Chemistry *26*, 2919 (1961).

[223] *L. Nicholas* and *G. T. Gmitter*, J. cellular Plastics *1*, 85 (1965); Chem. Abstr. *62*, 5395a (1965).

[223a] *D. R. Dalton*, *J. B. Hendrickson*, and *D. Jones*, Chem. Commun. *1966*, 591.

[224] For a review see *G. A. Russell*, *E. G. Janzen*, *A. G. Bemis*, *E. J. Geels*, *A. J. Moye*, *S. Make*, and *E. T. Strom*: Oxidation of Hydrocarbons in Basic Solution in: Advances in Chemistry Series *51*, 112 (1965).

radical [eq. (p)], which then undergoes various free-radical steps, depending on the substrate, to form the final oxidation product [224]

$$R{-}H + B^{\ominus} \rightleftarrows R^{\ominus} + BH \qquad (o)$$

$$R^{\ominus} + O_2 \rightarrow R\cdot + O\cdot_2^{\ominus} \qquad (p)$$

The method is very effective, can be carried out at room temperature, and is characterized by relatively high reaction rates. Many compounds, except alkanes, simple alkenes (cyclohexene), and simple alkylaromatic compounds (toluene), undergo this oxidation. For example diarylmethanes can be converted into ketones, triarylmethanes into alcohols, ketones into carboxylic acids, nitroalkanes into ketones, and anilines into azobenzenes.

6. Polymerizations

The significance of DMSO in the production of polyacrylonitrile fibers [225] was increased by the observations that polyacrylonitrile can be spun not only from a solution in DMSO but furthermore that DMSO can also be used as the solvent for the polymerization of acrylonitrile. Solution polymerization in DMSO is technically easier to control than emulsion polymerization; furthermore, the chain termination observed in dimethylformamide does not occur.

Thus acrylonitrile can also be polymerized in admixture with copolymerizable monomers in DMSO and in the presence of suitable catalysts and regulators; even below 80 °C the polymerization time is short. The yield of polymer is higher than 70%, and can be adjusted in such a way as to give solutions having a polymer content of about 20% (molecular weight 42000–64000), which can be used directly for spinning.

The polymerization of acrylonitrile is industrially important, and its kinetics and mechnism have been thoroughly investigated [226, 227]. In the free-radical polymerization initiated by ammonium peroxidisulfate, the chain initiation proceeds in accordance with equation (q).

$$S_2O_8^{2\ominus} + 2\ CH_3{-}\overset{\overset{O}{\|}}{S}{-}CH_3 \rightarrow 2\ SO_4^{2\ominus} + 2\ (CH_3{-}\overset{\overset{O}{\|}}{S}{-}CH_3)^{\oplus} \qquad (q)$$

The constants for chain transfer to the solvent and to the monomer at 30 °C are 4.7×10^{-5} and 1.5×10^{-4} respectively [228]. These values are lower than those for other solvents. The activation energy was found to be approximately 18.5 (16.5 [229]) kcal/mole [228]. The reactivity of the radicals formed in the azodiisobutyronitrile-initiated polymerization is again relatively low, so that the chain transfer constant is of the same order of magnitude (2.9×10^{-5}) [4].

The polymerization of acrylonitrile and methacrylonitrile in DMSO with anionic initiation by methylsulfinyl carbanions ($CH_3{-}SO{-}CH_2^{\ominus}Na^{\oplus}$ or $Li^{\oplus}$) leads quantitatively to a high molecular weight polymer, in contrast to the reaction in dimethylformamide [230]. The methylsulfinyl carbanion catalysts are of medium activity, and allow the polymerization to proceed rapidly and exothermally. The electrolytically initiated polymerization of methacrylate in DMSO also yields polymers having a higher molecular weight than in other solvents [231].

DMSO is also a very suitable solvent for the free-radical polymerization of vinyl acetate [232, 233]. Polyvinyl acetate having a degree of polymerization of 2960 is obtained in 95% yield, and the hydrolysis by bases proceeds more completely and more uniformly in DMSO than in methanol to give a polyvinyl alcohol (degree of polymerization 1700) that is stable in aqueous solution.

DMSO has proved to be better than any other solvent examined for the γ radiation-induced graft polymerization of styrene on amylose. The grafting process is accelerated by water in quantities of less than 1% [234].

The polymerization of β-propiolactams in DMSO with butyl-lithium, sodium methoxide, KOH [235], or pyrrolidone [236] as catalysts proceeds more rapidly, even at room temperature, than in the solid state, and gives polyamides in yields of up to 97%. Polyethers have been obtained from carbohydrates and epoxides in DMSO with alkaline catalysts [237]. Dioximes can also be copolymerized with diisocyanates in DMSO in the presence of triethylamine [238].

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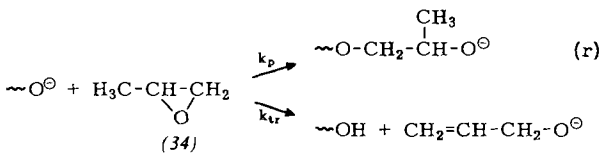
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Price and *Carmelite* have studied the kinetics of the t-butoxide-catalysed polymerization of epoxides in DMSO [239]. Epoxyethane polymerizes readily and in high yields to give a high molecular weight polymer (molecular weight up to 43000). Under the same conditions, epoxypropane *(34)* gives a polymer having a maximum molecular weight of 1200; in comparison with the polymerization without chain transfer, this corresponds to a ratio $k_p:k_{tr} = 20$ [eq. (r)]. In less reactive solvents such as ethers and alcohols, $k_p:k_{tr} \approx 50$. This means that in DMSO, the deprotonation of *(34)* by bases is favored by a factor of about 2.5, and so causes more frequent chain transfer.



(r)

(34)

Since its deprotonation is slower than that of epoxyethane by a factor of 10^4 and slower than that of epoxypropane by a factor of 10^3, DMSO itself does not hinder the chain growth. Consequently, no sulfoxide end groups can ever be detected in the polymers. 2-Methyl- and 2,3-dimethyl-2,3-epoxybutane are not polymerized by t-butoxide, but are converted into the corresponding allyl alcohols.

7. Reactivities in Dimethyl Sulfoxide Mixtures

The reactivities of nucleophiles in bimolecular reactions in protonic and nonpolar solvents can be increased by the addition of DMSO even in relatively small quantities. In general, the effect of DMSO is greater than that of any other additive with the exception of hexamethylphosphorotriamide. However, log k_2 does not vary linearly with the composition or dielectric constant of the mixture. Between a concentration of about 10% and a DMSO/HOH(R) ratio of approximately 1:2, k_2 shows a moderate increase, which is often approximately inversely proportional to the dielectric constant [66]. At concentrations above a molar ratio of 1:2, which is characterized by a special "structure" *(8)*, the accelerating effect increases more rapidly and is greatest at concentrations above 80 mole-%.

As in pure DMSO, the accelerating effect on anions in mixtures is greater than that on neutral nucleophiles [160, 206]. Thus the participation of the neighboring carboxyl group in the solvolysis of α-bromoacetic acid in 80% aqueous DMSO is five times as strong for the anion as for the free acid [240]. On the other hand, acid-catalysed hydrolyses (hydrolysis of acetals [241] and esters [71]) are mainly inhibited by the addition of DMSO.

Though several investigations on the mechanism of the accelerating effect of DMSO in dilute solution have been reported [66, 70, 160, 240, 242–245], no uniform picture has been established so far. The formation of a highly reactive sulfonium intermediate $RO-S^{\oplus}(CH_3)_2X^{\ominus}$ can be ruled out, since a doubly bimolecular reaction cannot be detected either stereochemically or kinetically [70].

The increase in the ρ value of the alkaline hydrolysis of *p*- and *m*-substituted ethyl benzoates [242, 243] and the decrease in the value of $\Delta H^{\neq}$ with increasing DMSO concentration indicate that DMSO has a marked influence on the solvation of the transition state. However, since no equilibrium relationships can be detected between ROH, $RO^{\ominus}$, DMSO, the dimethylsulfoxonium ion $(CH_3)_2S^{\oplus}OH$, and the course of the reaction [160], and since the catalytic effect of DMSO in mixtures with alcohols is practically the same for all anions and electrophiles within a given reaction type (independence of substrate) [160], the interaction between DMSO and the transition states must be regarded as nonspecific. In agreement with this, the view [1, 245] that the DMSO "liberates", and so activates the solvated anions simply by association with the protonic solvents, must be limited:

a) Dilute solutions (< 30 mole-% of DMSO) exhibit considerable acceleration of the reaction, though a sufficiently large number of proton-donor molecules are still present.

b) In concentrated solutions, DMSO strengthens the association between the anion (when it is "hard") and the proton donor.

c) Up to high concentrations, DMSO has no influence on the ρ values of the reaction between phenoxides and 2,4-dinitrochlorobenzene in $DMSO/CH_3OH$, as must be the case if there is effective breakdown of the H-bonds to the phenoxide ion.

Thus the effect of DMSO in dilute solutions is due only to breakdown of the outermost parts of the protonic solvation shell surrounding the anion (or to destruction of the "hard, pseudopolymeric structure" of the protonic solvent) [160].

However, reactions have also been reported in which even very small quantities of DMSO have a catalytic or inhibiting effect. *Cooper* and *Elliott* [246] found that the KOH-catalysed conversion of octamethylcyclotetrasiloxane *(35)* into the high molecular weight polymer *(36)* at 95 °C is accelerated by factors of 100 to 1000 by small quantities of DMSO (0.5%).

$$\frac{x}{4}[(CH_3)_2SiO]_4 \xrightarrow[0{,}01\text{–}0{,}1\%\ DMSO]{12\text{–}100\ ppm\ KOH} [(CH_3)_2SiO]_x$$

(35) *(36)*

Rapid equilibration also occurs in a mixture of *(35)* with hexamethyldisiloxane at 80 °C with 0.01% of KOH and 1% of DMSO. The first step in these base-catalysed reactions is the formation of metal siloxides and their dissociation to form free siloxide ions [eq. (s)]. The catalytic effect of DMSO is due to specific solvation of the cation, leading to promotion of the solvation of the metal siloxide which can then react preferentially with the Si–O dipoles that are present in high concentration.

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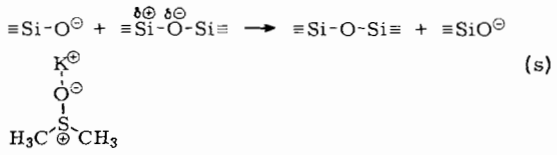
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(s)

A high dipole moment ($\mu \geqslant 3.7$ D) and solubility in water are essential properties of an organic solvent if it is to catalyse the formation of polyurethane foams [247]. Among the sulfoxides, the catalytic action increases with decreasing size of the groups attached to the sulfur atom: $Ar_2SO < (i\text{-}C_4H_9)_2SO < (n\text{-}C_4H_9)_2SO < (CH_3)_2SO$. Sulfoxides inhibit the autoxidation of squalene by suppression of the homolytic decomposition of the primary hydroperoxides, the effect increasing with increasing α-branching (di-t-butyl sulfoxide is 144 times as effective as DMSO) [248]. The sulfoxides are not effective in the presence of alkyl, alkoxy, alkylperoxy, or acyloxy radicals. Their specific inhibiting action on the primary hydroperoxides consists in the formation of strong H-bonds, which are destroyed by the addition of carboxylic acids.

The polymerization of vinyl compounds can also be suppressed by DMSO (in concentrations of from 0.05 to 5%) [249]. However, the polymerization can then be started by the addition of suitable initiators.

An interesting observation is the inhibiting action of DMSO on free-radical biological redox depolymerizations. Thus DMSO inhibits the decomposition of hyaluronic acid, the principal polysaccharide of the ventricular fluid, by reducing agents such as ascorbic acid, hydroquinone, or tetracycline in the presence of oxygen, the inhibiting effect increasing with the DMSO concentration [250].

The stabilization of trichloroethylene and perchloroethylene by the addition of 0.5 to 5% of DMSO is of practical interest [251].

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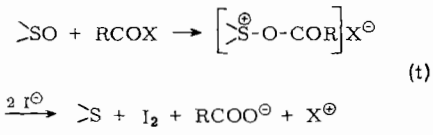
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VI. Purification of Dimethyl Sulfoxide

Commercial DMSO generally contains about 0.5% of water, small quantities of dimethyl sulfide, and dimethyl sulfone. Purification presents no difficulties, and can be achieved by fractional vacuum distillation, fractional extraction [252], treatment with activated charcoal [253] or molecular sieves [31, 176, 246], or column chromatography [254]. Very pure DMSO is obtained by fractional vacuum distillation under carefully dried nitrogen [14, 24]. The process is preferably carried out in such a way that subsequent slight recontamination in the vapor phase is impossible. To obtain anhydrous DMSO, vacuum distillation at 18 mm Hg over calcium hydride has proved suitable for most purposes [218, 239].

The purity can be established by conductivity measurements [14], and titration with Karl Fischer solution is used for the determination of water [14]. Traces of water can escape detection in gas-chromatographic purity checks; IR and mass spectrometry are more suiable methods [176]. Dimethyl sulfoxide (and sulfoxides in general) can be quantitatively determined by iodometric titration of acyloxysulfonium salts in accordance with equation (t) [255]:



(t)

[D_6]-Dimethyl sulfoxide, which is an important solvent in NMR spectroscopy, can be obtained by base-catalysed exchange with D_2O [256] or by thermolysis of [D^9]-trimethylsulfoxonium iodide [257] (yield 80%, with 99–99.2% deuteration).

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The Formation of C–C Bonds with the Aid of α-Halogeno Ethers, Sulfides, and Amines[1]

BY H. GROSS AND E. HÖFT [*]

Dedicated to Professor Alfred Rieche on the occasion of his 65th birthday

α-Halogeno ethers, sulfides, and amines are reactive compounds which can be used for the formation of new C–C bonds, either as nucleophilic or as electrophilic reagents, or by α-elimination. The use of these compounds in the synthesis of many classes of organic compounds is reviewed.

α-Halogeno ethers, sulfides, and amines can be formally derived from, and are generally prepared from, carbonyl compounds. Whereas α-halogeno ethers and sulfides may be regarded as homopolar compounds as indicated in formula *(1a)*, the α-halogeno amines, according to *Böhme*[2], exist largely as resonance-stabilized carbenium-immonium salts corresponding to formula *(2b)*.

$$\underset{(1)}{R\text{-}Z\text{-}\overset{Hal}{\overset{|}{C}}H\text{-}R^1} \rightleftharpoons [R\text{-}Z\text{-}\overset{\oplus}{C}H\text{-}R^1 \longleftrightarrow \underset{(2)}{R\text{-}\overset{\oplus}{Z}=CH\text{-}R^1}]\,Hal^{\ominus}$$

(a), Z = O, S
(b), Z = N-R^2

All compounds of the types *(1)* and *(2)* are much more reactive than simple alkyl halides. α-Halogeno ethers have been widely used in preparative chemistry[3–7]. The *N*- and *S*-analogues have recently also been studied by several research groups, and particularly by *Böhme* and his co-workers.

The present review deals with methods for the formation of C–C bonds with the aid of α-halogeno ethers and sulfides derived from oxo compounds, carboxylic acids, or carbonic acid, whereas the only *N*-analogues considered are those derived from oxo compounds. Reviews on α-halogenated amino compounds in higher oxidation states (carbonamide chlorides, carbamide chlorides, *etc.*) have already been published[8,9].

For earlier work and for the preparation of α-halogeno ethers and sulfides, the reader is referred to the articles mentioned in[3–7]. Information about the preparation of the *N*-derivatives may be obtained from the original publications[9,10].

A. α-Halogeno Ethers, Sulfides, and Amines as Electrophiles

The earliest known reactions of the halogen derivatives *(1a)* and *(2b)* leading to the formation of new C–C bonds were those involving the addition of a nucleophile to the carbenium-onium ion. This leads, formally, in accordance with equation (a), to a product

$$R\text{-}Z\text{-}\underset{R^1}{\overset{|}{C}}H\text{-}Hal + \overset{\ominus}{\overset{|}{C}}\text{-} \rightarrow R\text{-}Z\text{-}\underset{R^1}{\overset{|}{C}}H\text{-}\overset{|}{C}\text{-} + Hal^{\ominus} \quad (a)$$

in which the group R–Z–CHR¹ remains intact. Sometimes, *e.g.*, on reaction with aromatic nucleophiles, products with other structures can be formed.

1. Reactions with Cyanides

The active halogen compounds react with cyanides according to Scheme (b) to form nitriles.

$$R\text{–}Z\text{–}CH_2Cl \xrightarrow[-Cl^{\ominus}]{CN^{\ominus}} R\text{–}Z\text{–}CH_2\text{–}CN \quad (b)$$

The reaction of alkali-metal cyanides with chloromethyl aryl ethers in aqueous acetone gives good

[*] Doz. Dr. H. Gross and Dr. E. Höft
Institut für organische Chemie der Deutschen Akademie der Wissenschaften zu Berlin
An der Rudower Chaussee
X 1199 Berlin-Adlershof (Germany)

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yields of aryloxyacetonitriles *(3)*, R = aryl[11]; benzene[12] and dimethylformamide[13] have been recommended as solvents for the reaction with chloroalkyl alkyl ethers. Chloromethyl alkyl ethers react with heavy-metal cyanides such as AgCN[14], $Hg_2(CN)_2$[15] or $Cu_2(CN)_2$[16], even in nonpolar solvents, to form α-alkoxynitriles *(3)* in yields of up to 80 %.

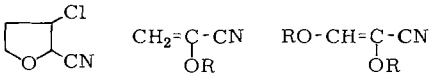
$RO-CHR^1-CN$ *(3)* $\qquad$ $C_2H_5O-CH(CN)-CO_2C_2H_5$ *(4)*

R = Aryl, alkyl
R^1 = H, alkyl

Ethyl ethoxychloroacetate reacts similarly in xylene to give ethyl ethoxycyanoacetate *(4)*[17]. 2-Cyano-1,4-dioxane[18] and 2-cyanotetrahydropyran[19] can be prepared in an analogous manner. Bis(cyanomethyl) ether *(5)*[13] can be obtained from bis(chloromethyl) ether, but in α,β'-dihalogeno ethers only the α-halogen atom undergoes substitution, with formation of *(6)*[20,21]. Thus 3-chloro-2-cyanotetrahydrofuran *(7)* is obtained from 2,3-dichlorotetrahydrofuran[22,23],

$NC-CH_2-O-CH_2-CN$ *(5)* $\qquad$ $Hal-CH_2-CH_2-O-CHR-CN$ *(6)*, R = H, CH_3

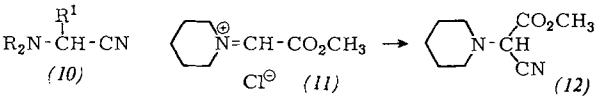
while the reaction of α,β-dibromodiethyl ether or 1,2-diethoxy-1,2-dichloroethane with $Cu_2(CN)_2$ and subsequent dehydrohalogenation leads to the unsaturated



(7) $\qquad$ *(8)* $\qquad$ *(9)*

α-alkoxynitriles *(8)*[24] and *(9)*[25]. *S*-Cyanomethyl thioacetate can be obtained from *S*-chloromethyl thioacetate[26].

According to *Böhme*[2,27,28], α-aminonitriles *(10)* can be prepared in very good yields by the reaction of α-halogeno amines with anhydrous hydrogen cyanide. *N*-(Methoxycarbonylmethylene)piperidinium chloride *(11)* reacts in a similar manner to give the piperidinocyanoacetate *(12)*[29].

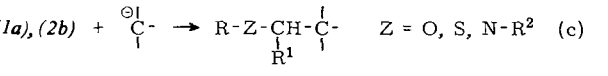


(10) $\qquad$ $Cl^{\ominus}$ *(11)* $\qquad$ *(12)*

R, R^1 = Alkyl

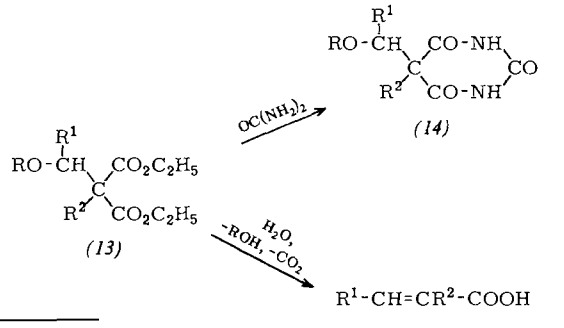
2. Reactions with Compounds Containing Active Methylene Groups

Alkoxymethyl, alkylthiomethyl, and dialkylaminomethyl groups can be introduced into compounds containing active methylene groups by reaction of their alkali metal salts with compounds of the type *(1a)* or *(2b)*.



(1a), (2b) $\qquad$ Z = O, S, $N-R^2$ (c)

Reaction (c) has been known for some time, *e.g.* in the reaction of α-halogeno ethers with sodiomalonic esters[3,30,31], and has recently been extensively used[12,32–37] *e.g.* for the preparation of alkoxyalkylmalonates *(13)* (R, R^1, R^2 = alkyl, or R^1, R^2 = H;



(13) $\qquad$ *(14)*

$R^1-CH=CR^2-COOH$

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[16] *H. R. Henze* and *N. E. Rigler,* J. Amer. chem. Soc. *56*, 1350 (1934); *J. J. Spurlock* and *H. R. Henze,* J. org. Chemistry *4*, 234 (1939); *H. R. Henze, V. B. Duff, W. H. Matthews, J. W. Melton,* and *E. O. Forman,* J. Amer. chem. Soc. *64*, 1222 (1942).

[17] *A. Bendich* and *G. C. Clements,* J. Amer.. chem. Soc. *75*, 4075 (1953).

[18] *B. A. Nelson, R. C. Minsek, J. I. Simon,* and *D. L. Underwood,* J. Amer. chem. Soc. *77*, 1695 (1955).

[19] *R. Zelinski* and *K. Yorka,* J. org. Chemistry *23*, 640 (1958).

[20] *F. Bottari* and *B. Macchia,* Gazz. chim. ital. *92*, 165 (1962); Chem. Zbl. *1964*, 10-0827.

[21] *J. H. Clark* and *H. R. Henze,* J. org. Chemistry *2*, 508 (1938).

[22] *W. Reppe et al.,* Liebigs Ann. Chem. *596*, 86, 113 (1955).

[23] *H. Normant,* C. R. hebd. Séances Acad. Sci. *229*, 1348 (1949).

[24] *T. Cuvigny* and *H. Normant,* C. R. hebd. Séances Acad. Sci. *237*, 815 (1953).

[25] *H. Baganz* and *J. Pflug,* Chem. Ber. *90*, 386 (1957).

[26] *H. Böhme* and *A. Dick,* Arch. Pharmaz. *294*, 475 (1961).

[27] *H. Böhme, W. Lehners,* and *G. Keitzer,* Chem. Ber. *91*, 340 (1958).

[28] *H. Böhme, H. Ellenberg, O.-E. Herboth,* and *W. Lehners,* Chem. Ber. *92*, 1608 (1959).

[29] *H. Gross* and *J. Gloede,* unpublished.

[30] *A. J. Hill* and *DeWitt T. Keach,* J. Amer. chem. Soc. *48*, 257 (1926).

[31] *S. M. McElvain* and *H. Burkett,* J. Amer. chem. Soc. *64*, 1831 (1942).

[32] *A. W. Bogatski,* Ž. obšč. Chim. *30*, 3500 (1960); Chem. Abstr. *55*, 19780h (1961); *A. V. Bogatski, N. A. Goryatshuk, O. I. Tischenko,* and *A. A. Kiryakova,* Ž. obšč. Chim. *33*, 42 (1963); Chem. Abstr. *59*, 435e (1963); *A. V. Bogatski* and *S. D. Yablonovskaya,* Ž. obšč. Chim. *32*, 3886 (1962); Chem. Zbl. *1965*, 4-0902; *A. V. Bogatski,* Ukrainskij chim. Ž. *31*, 1186 (1965).

[33] *O. S. Stepanova* and *L. Ya. Glinskaya,* Ž. obšč. Chim. *34*, 1467 (1964); Chem. Zbl. *1966*, 28-0805.

[34] *A. V. Bogatski, S. A. Andronati,* and *N. L. Garkovik,* Ukrainskij chim. Ž. *31*, (11) 1186 (1965); Chem. Abstr. *64*, 12542g (1966).

[35] *A. V. Bogatski, D. B. Furman* and *L. N. Kolodnitzkaya,* Ž. org. Chim. *2*, 59 (1966); Chem. Abstr. *64*, 14125 (1966).

[36] *O. Ss. Stepanowa, O. I. Tischenko, Zh. I. Bezgudova, G. I. Goryaschina,* and *A. I. Drosdovskaya,* Ž. vses. chim. Obšč. im. D. I. Mendeleeva *10*, (6) 704 (1965); Chem. Abstr. *64*, 9587e (1966).

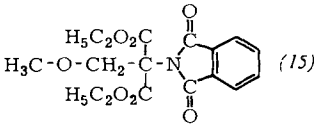
[37] *M. Renard* and *G. Dony,* Ind. chim. belge *16*, 479 (1951); Chem. Abstr. *46*, 10108c (1952).

cf. Table 1). These can be converted into substituted barbiturates *(14)* [32, 36–38] or hydrolysed to give the free dicarboxylic acids, from which substituted acrylic acids can be obtained by partial decarboxylation and elimination of alcohol [33,39].

Table 1. Diethyl alkoxylmalonates *(13)* synthesized.

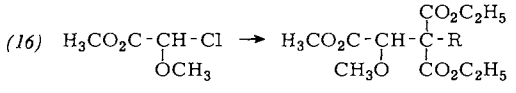
R	R^1	R^2	Yield (%)	Ref.
C_2H_5	H	C_2H_5	67–77	[39]
C_6H_5–CH_2	H	C_2H_5	56	[30]
C_2H_5	H	n-C_7H_{15}	86	[33]
i-C_4H_9	CH_3	C_2H_5	53	[34]
CH_3	CH_3	C_4H_9	61	[32]
C_2H_5	CH_3	CH_2=CH–CH_2	83	[31]
C_2H_5	CH_3	CH_3–$CH(C_3H_7)$–	84	[31]
CH_3	CH_3	$(C_6H_5)_2CH$	78	[35]
CH_3	C_2H_5	C_3H_7	63–71	[36]
CH_3	CO_2CH_3	H	65	[41]
CH_3	CO_2CH_3	Phthalimido	82	[41]
CH_3	H	Phthalimido	83	[40]

Diethyl phthalimidomalonate reacts with chloromethyl methyl ether to give diethyl methoxymethylphthalimidomalonate *(15)* [40].



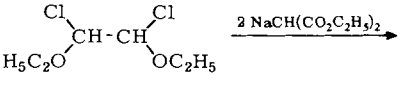
(15)

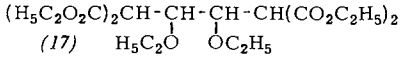
Methyl chloromethoxyacetate *(16)* reacts similarly to form esters of tricarboxylic acids [41].



(16)

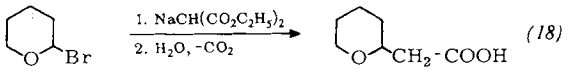
1,2-Diethoxy-1,2-dichloroethane and diethyl sodiomalonate react to form tetraethyl 2,3-diethoxybutane-1,1,4,4-tetracarboxylate *(17)*, and hence, *e.g.* by elimination of alcohol, give tetraethyl buta-1,3-diene-1,1,4,4-tetracarboxylate [4, 42].





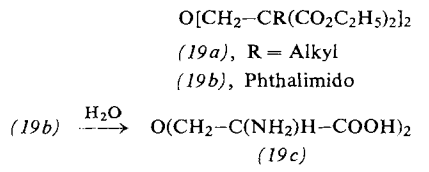
(17)

2-Tetrahydropyranylacetic acid *(18)* has been prepared from 2-bromotetrahydropyran by reaction with diethyl sodiomalonate, hydrolysis, and partial decarboxylation [43].



(18)

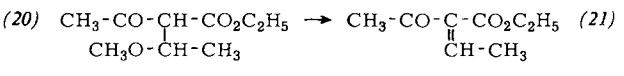
The reaction of bis(halogenomethyl) ether with diethyl alkylmalonates leads to tetraethyl 3-oxapentane-1,1,5,5-tetracarboxylate *(19a)* [44]; diethyl phthalimidosodiomalonate gives the bisphthalimido compound *(19b)*, which yields 2,4-diamino-3-oxapentane-1,1,5,5-tetracarboxylic acid *(19c)* on hydrolysis [45].



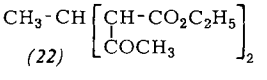
(19a), R = Alkyl
(19b), Phthalimido

(19c)

Other CH acids, such as β-keto esters, react analogously to the malonates. With acetoacetic ester, competition occurs between *O*- and *C*-alkylation [3]. According to more recent investigations [46], the reaction of α-chloroethyl methyl ether and lithioacetoacetic ester leads only to the *C*-alkylation product *(20)*, which loses methanol to form α-ethylideneacetoacetic ester *(21)*. Diethyl 1,3-diacetyl-2-methylglutarate *(22)* was also isolated; this product was presumably formed by Michael addition of acetoacetic ester to *(21)*.



(20) *(21)*



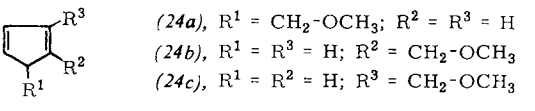
(22)

In the case of benzoylacetates or esters of higher α-acetylcarboxylic acids, the product corresponding to *(20)* is stable [46]; this is also true of cyclic β-keto esters, from which the alkoxymethyl and acetoxymethyl derivatives *(23)* have been obtained [47].



(23)

Cyclopentadienylsodium reacts with chloromethyl methyl ether to form the isomeric methoxymethylcyclopentadienes *(24a)* to *(24c)* [48], the main product, particularly at low temperatures, being *(24a)*.



(24a), R^1 = CH_2-OCH_3; R^2 = R^3 = H
(24b), R^1 = R^3 = H; R^2 = CH_2-OCH_3
(24c), R^1 = R^2 = H; R^3 = CH_2-OCH_3

[38] *O. S. Stepanova, L. A. Semenyuk, A. I. Drosdovskaya,* and *Ye. A. Yatzenko,* Ukrainskij chim. Ž. *29*, 1115 (1963); Chem. Zbl. *1965*, 45-0982; *A. V. Bogatski, N. A. Gorjatshuk,* and *G. I. Parnak,* Ž. obšč. Chim. *32*, 1498 (1962); Chem. Abstr. *58*, 4414f (1963).

[39] *O. S. Stepanova,* and *Ye. A. Yatzenko,* Ž. vses. chim. Obšč. im. D. I. Mendeleeva *8*, 114 (1963); Chem. Zbl. *1966*, 27-0799.

[40] *S. Maeda, M. Terumi,* and *T. Suzuki,* Bull. Inst. physic. chem. Res. (Tokyo) *19*, 267 (1940); Chem. Abstr. *34*, 6931 (1940).

[41] *H. Gross* and *J. Freiberg,* Chem. Ber. *99*, 3260 (1966).

[42] *H. Baganz* and *R. Müller,* Chem. Ber. *94*, 2132 (1961).

[43] *J. Colonge, J. Dreux,* and *M. Coblentz,* C. R. hebd. Séances Acad. Sci. *250*, 3202 (1960).

[44] *M. Kh. Berkhamof,* Materialy Nauchn.-Konf. Aspirantov, Aserb. Gos. Univ. *1964*, 90; Chem. Abstr. *64*, 15735g (1966).

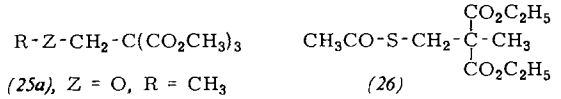
[45] *H. Zahn, R. Dietrich,* and *W. Gerstner,* Chem. Ber. *88*, 1737 (1955).

[46] *T. I. Temnikova* and *V. V. Takhistov,* Ž. org. Chim. *2*, 1168 (1966).

[47] *H. Böhme, K. Kreitz,* and *E. Nürnberg,* Arch. Pharmaz. *292*, 456 (1959); *H. Böhme* and *K. Kreitz, ibid 291*, 566 (1958).

[48] *G. Kresze, G. Schulz,* and *H. Walz,* Liebigs Ann. Chem. *666*, 45 (1963); French Pat. 1250688 (Dec. 8th, 1959), Imperial Chemical Industries Ltd.; Chem. Zbl. *1964*, 39-2409.

Trimethyl alkoxymethyl- or acetoxymethylmethane tricarboxylates *(25a)* and *(25b)* can be obtained from trimethyl sodiomethanetricarboxylate and chloromethyl methyl ether or chloromethyl acetate, respectively [49].



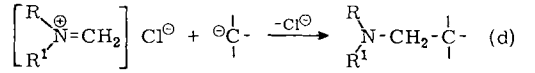
(25a), Z = O, R = CH_3
(25b), Z = O, R = CH_3CO
(25c), Z = S, R = C_6H_5

(26)

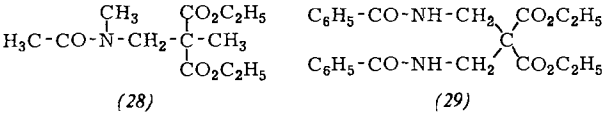
Chloromethyl thioethers and compounds having active methylene groups also react according to equation (c). Thus trimethyl sodiomethanetricarboxylate gives the methylthio compound *(25c)* [49], while acetoacetic esters give the *S*-analogue of *(20)* [50]. Diethyl acetylthiomethylmethylmalonate *(26)* can be obtained from *S*-chloromethyl thioacetate and methyl malonate [47].

Böhme found that compounds containing active methylene groups are aminomethylated by α-halogeno amines *(27)*, R, R^1 = alkyl, in accordance with equation (c) or (d) [51]. This provides a route to dialkyl-

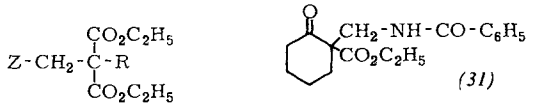
spondingly substituted amides or diacylamides ("amidomethylation"). Thus the compounds *(28)* to *(31)* can be obtained in this way. These reactions are particularly useful for the amidomethylation of β-diketones, which cannot be accomplished by the usual methods.



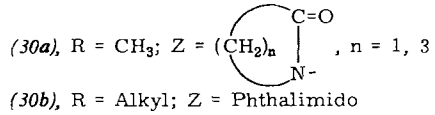
(27), R,R^1 = H, Alkyl, Acyl



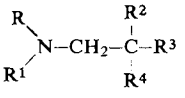
(28) *(29)*



(31)



(30a), R = CH_3; Z = , n = 1, 3
(30b), R = Alkyl; Z = Phthalimido
(30c), R = CH_3; Z = Succinimido

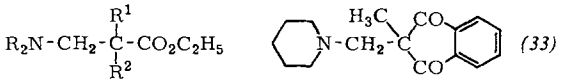
Table 2. *N*-Substituted carbonamides and dicarbonimides synthesized. 

R	R^1	R^2	R^3	R^4	Yield (%)	Ref.
H	C_6H_5–CO	C_2H_5	$CO_2C_2H_5$	$CO_2C_2H_5$	72	[52]
H	C_6H_5–CO	CH_2–NH–CO–C_6H_5	CO_2CH_3	CO_2CH_3	81	[52]
H	C_6H_5–CO	CH_3	$CO_2C_2H_5$	CN	48	[52]
H	C_6H_5–CO	C_6H_5	CO–CH_3	CN	79	[52]
H	Cl_3C–CO	C_6H_5	CN	CO–CH_3	57	[52]
H	C_6H_5–CO	H	CO–CH_3	CO–C_6H_5	51	[52]
CH_3–CO	CH_3	$CO_2C_2H_5$	CH_3	$CO_2C_2H_5$	68	[53]
C_6H_5–CO	CH_3	CO–CH_3	CH_3	$CO_2C_2H_5$	28	[53]
CH_3–CO	n-C_3H_7	$CO_2C_2H_5$	CH_3	$CO_2C_2H_5$	38	[53]
o-OC–C_6H_4–CO		$CO_2C_2H_5$	$CO_2C_2H_5$	C_2H_5	67	[54]
o-OC–C_6H_4–CO		$CO_2C_2H_5$	CO–CH_3	CH_3	63	[54]
o-OC–C_6H_4–CO		CN	CO–CH_3	C_6H_5	72	[54]
OC–CH_2–CH_2–CO		$CO_2C_2H_5$	$CO_2C_2H_5$	CH_3	47	[54]

aminomethyl compounds, which can be obtained only with difficulty, or not at all, by the usual aminomethylation reactions. Similarly, *N*-halogenomethylamides, *(27)* with R = H, alkyl; R^1 = acyl [52,53], halogenomethyldiacylimides, *(27)* with R = R^1 = acyl [54], or *N*-chloromethyllactams [57] give corre-

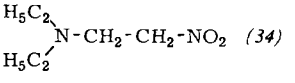
Table 2 shows a selection of possible preparations. *(30a)* and *(30b)* can be converted into barbituric acid derivatives by reaction with urea.

Diethyl piperidinomethylmalonate *(32a)* was obtained *e.g.* from *N*-chloromethylpiperidine and diethyl sodioethylmalonate [51]. *(32b)* to *(34)* have been prepared in a similar manner from compounds containing active methylene groups [51].



(33)

(32a), R_2 = -$(CH_2)_5$-; R^1 = $CO_2C_2H_5$; R^2 = C_2H_5
(32b), R = C_2H_5; R^1 = $COCH_3$; R^2 = CH_3



(34)

This principle can also be used for the synthesis of α-substituted α-amino acids. The halogeno amine compounds, *e.g.* *(35)*, which can be readily prepared

[49] *H. Böhme* and *L. Häfner*, Chem. Ber. *99*, 879 (1966).

[50] *H. Böhme* and *E. Mundlos*, Chem. Ber. *86*, 1414 (1953).

[51] *H. Böhme*, *E. Mundlos*, and *G. Keitzer*, Chem. Ber. *91*, 656 (1958).

[52] *H. Böhme*, *R. Broese*, *A. Dick*, *F. Eiden*, and *D. Schünemann*, Chem. Ber. *92*, 1599 (1959).

[53] *H. Böhme*, *H. Dick*, and *G. Driesen*, Arch. Pharmaz. *294*, 312 (1961).

[54] *H. Böhme*, *R. Broese*, and *F. Eiden*, Chem. Ber. *92*, 1258 (1959).

[55] *H. Gross*, *J. Gloede*, and *J. Freiberg*, Liebigs Ann. Chem., *702*, 68 (1967); *H. Gross* and *J. Gloede*, Angew. Chem. *78*, 823 (1966); Angew. Chem. internat. Edit. *5*, 837 (1966).

[56] *H. Gross*, *J. Gloede*, *J. Freiberg*, *G. Ollmann*, and *W. Bürger*, unpublished.

[57] *H. Böhme*, *G. Driesen*, and *D. Schünemann*, Arch. Pharmaz. *294*, 344 (1961).

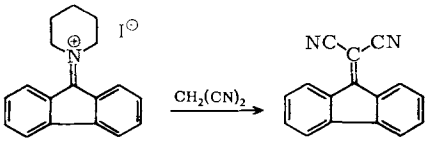
from dichloroacetic acid[55], react with active methylene groups in accordance with equation (d), to give α-substituted α-amino acid derivatives; for example, reaction with *(35)* leads to *(36)*[55,56].



(35) $Cl^{\ominus}$ Z = OCH_3, Piperidino

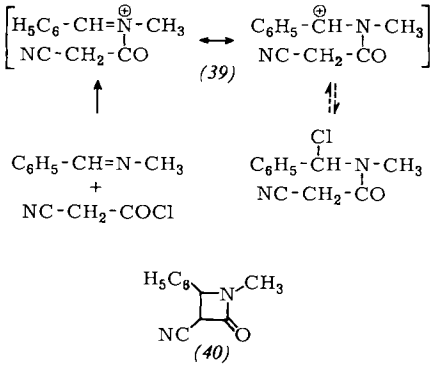
(36), R = *p*-C_3H_7O-C_6H_4-CO-CH_2-, C_6H_5-CH=CH-CO-CH_2-, *N*-(*p*-CH_3-C_6H_4)-pyrrolyl

N-(9-Fluorenylidene)piperidinium iodide *(37)*, which may be regarded as an α-halogeno amine, reacts with malonodinitrile to give 9-fluorenylidenemalonodinitrile *(38)* in 62 % yield[58].



(37) *(38)*

The formation of the azetidinone *(40)* can also be formulated as proceeding *via* an intermediate "α-halogeno amine"[59]: methylphenylmethyleneamine reacts with cyanoacetyl chloride to form an adduct *(39)*, which cyclizes in the presence of triethylamine to give 3-cyano-1-methyl-4-phenylazetidin-2-one *(40)*.



(39)

(40)

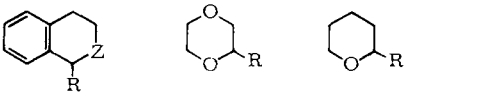
3. Reactions with Grignard Compounds

Substituted ethers, thioethers, and amines can be obtained by reaction with Grignard compounds in accordance with equation (e) (cf.[3,60]). Of the many possible preparative uses, only a few will be mentioned here; for further examples, the reader is referred to the original literature[12,61–63].

(1a), *(2b)* $\xrightarrow{R^2MgX}$ R–Z–CHR^1–R^2 (e)

Z = O, S, NR^3

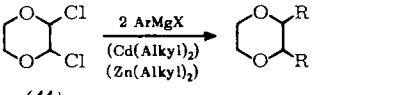
The halogen atom in 1-halogenoisochromans[64], 1-halogenoisothiochromans[65], 2-chloro-1,4-dioxane[66,67], or 2-chlorotetrahydropyran[68–71] can be replaced smoothly by alkyl or aryl groups, with formation of *(41)*, *(42)*, or *(43)*.



(41) *(42)* *(43)*

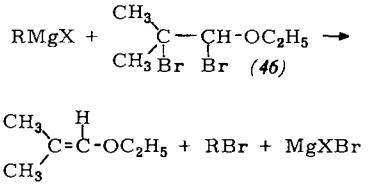
Z = O, S R = Alkyl, Aryl, C≡CH

2,3-Diaryl-1,4-dioxanes *(45)* have been obtained in very good yields from 2,3-dichloro-1,4-dioxane[67,72,73].



(44) *(45)*, R = Aryl, Alkyl

In the reaction of α,β-dihalogeno ethers, *e.g. (46)*, or 2,3-dichlorodioxane *(44)*, particularly with alkylmagnesium halides or organolithium compounds, the nucleophilic substitution is occasionally accompanied by dehalogenation to form the vinyl ethers[67,73,74];



(46)

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[59] *H. Böhme, S. Ebel*, and *K. Hartke*, Chem. Ber. *98*, 1463 (1965).

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[66] *R. K. Summerbell* and *H. E. Lunk*, J. org. Chemistry *23*, 499 (1958).

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[71] *N. I. Shuikin, I. F. Belskii, R. A. Kharakhanov, B. Kozma*, and *M. Bartok*, Acta Univ. Szegediensis, Acta physica chem. [N.S.] *9*, 37 (1963); Chem. Zbl. *1965*, 17-0948.

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[73] *R. K. Summerbell, W. M. Smedley, D. M. Jerina*, and *D. R. Berger*, J. org. Chemistry *27*, 4078 (1962); *R. K. Summerbell, A. L. Burlingame, D. R. Dalton*, and *C. K. Dalton*, J. org. Chemistry *27*, 4365 (1962).

[74] *B. T. Gillis* and *K. F. Schimmel*, J. org. Chemistry *25*, 2187 (1960).

this reaction can be utilized *e.g.* for the preparation of *p*-dioxene [67]. Phenyl-lithium reacts with 2,3-dichloro-1,4-dioxane to give the unstable 2-phenyldioxene. Unsaturated ethers can be obtained by the use of alk-1-enylmagnesium halide [75–77]. The reaction of α,β-dibromodiethyl ether with vinylmagnesium chloride yields 4-bromo-3-ethoxybut-1-ene *(47)* [78, 79].

$$CH_2{=}CH{-}\underset{\displaystyle OC_2H_5}{\underset{|}{CH}}{-}CH_2Br \quad (47)$$

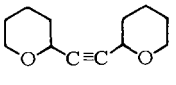
The reaction of α,β′-dihalogeno ethers, for instance *(48)*, with *e.g.* propenylmagnesium halide leads to crotyl β-halogenoethyl ether *(49)*; the crotyl vinyl ether formed on dehydrohalogenation of *(49)* can then rearrange to give the unsaturated aldehyde *(50)*. This very flexible synthesis has been used for the preparation of a series of γ,δ-unsaturated aldehydes [80].

$$CH_3{-}CH{=}CH{-}MgHal + ClCH_2{-}O{-}CH_2{-}CH_2Br \longrightarrow$$
(48)

$$CH_3{-}CH{=}CH{-}CH_2{-}O{-}CH_2{-}CH_2Hal \longrightarrow$$
(49)

$$CH_3{-}CH{=}CH{-}CH_2{-}O{-}CH{=}CH_2 \longrightarrow CH_2{=}CH{-}C(CH_3)H{-}CH_2{-}CHO$$
(50)

Alk-1-ynylmagnesium halides also react with α-halogeno ethers [3]. The reaction of ethynylmagnesium bromide with 2-chlorotetrahydropyran yields 2-tetrahydropyranylacetylene *(43)*, R = C≡CH [69, 70], while ethynylenebis(magnesium bromide) gives bis-(2-tetrahydropyranyl)acetylene *(51)* [70].



(51)

$$HC{\equiv}C{-}(CH_2)_4{-}C{\equiv}C{-}CH_2{-}OCH_3$$
(52a)

$$CH_3O{-}CH_2{-}C{\equiv}C{-}(CH_2)_4{-}C{\equiv}C{-}CH_2{-}OCH_3$$
(52b)

Alkali-metal acetylides react in a similar manner. For example, the mono- and diethers *(52a)* and *(52b)* have been obtained from the α-mono- and α,ω-disodium compounds of 1,7-octadiyne [81]. Hex-1-ynyl-lithium reacts with chloromethyl methyl ether to give hept-2-ynyl methyl ether [82]. Compounds of this type (see Table 3), including the acetylene ethers *(53)* obtained from alk-1-ynyl- or arylethynylmagnesium halides [77, 83] or from lithium derivatives of alkylacetylenes [84] and α-chloro ethers, have been used for further syntheses. For example, *(53)* can rearrange to allenes *(54)* [83, 84], which give unsaturated carbonyl compounds *(55)* on hydrolysis [83].

$$R{-}C{\equiv}CR^1H{-}OR^2 \longrightarrow R{-}CH{=}C{=}CR^1{-}OR^2 \longrightarrow R{-}CH{=}CH{-}CO{-}R^1$$
(53) *(54)* *(55)*

Table 3. Alkoxyalkylacetylenes *(53)*, allenes *(54)*, and α,β-unsaturated carbonyl compounds *(55)* synthesized.

R	R^1	Yield (%) *(53)*	*(54)*	*(55)*	Ref.
i-C_3H_7	H	85	80		[84]
t-C_4H_9	H	83	82		[84]
t-C_4H_9	H	81	96		[84]
c-C_4H_9	H	90	85		[84]
c-C_5H_{11}	H	92	90		[84]
C_6H_5	H	71		50	[83]
C_6H_5	CH_3	70		67	[83]
C_6H_5	C_3H_7	70		55	[83]
C_6H_5	C_6H_5	55			[83]

Ethyl 1-(bromomethyl)pent-4-en-2-ynyl ether *(56)* has been prepared from but-3-en-1-ynylmagnesium halide and α,β-dibromodiethyl ether.

$$CH_2{=}CH{-}C{\equiv}C{-}\underset{\displaystyle OC_2H_5}{\underset{|}{CH}}{-}CH_2Br \quad (56)$$

Further reactions of α-halogeno ethers with alkenyl- and alkynylmagnesium halides are to be found in the original literature [86–90].

In contrast to the behavior of α,β-dichloroethers, both halogen atoms can be substituted in 1,2-diethoxy-1,2-dichloroethane or in 2,5-dichlorotetrahydrofuran, as well as in *(44)*. It is possible in this way to prepare ethers such as *(57a)* [91] or *(57b)* [4, 92] and 2,5-dialkyl- and 2,5-diaryltetrahydrofurans [93]. Bis(chloromethyl) methylene diether *(58a)* reacts with Grignard compounds to give methylene diethers *(58b)* [94].

$$R{-}C{\equiv}C{-}\underset{\displaystyle OR^1}{\underset{|}{CH}}{-}\underset{\displaystyle OR^1}{\underset{|}{CH}}{-}C{\equiv}C{-}R \qquad R{-}CH_2{-}O{-}CH_2{-}O{-}CH_2R$$

(57a), R = H — *(58a)*, R = Cl

(57b), R = $CH_3O{-}CH{=}CH$ — *(58b)*, R = Alkyl, Aryl

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[90] *R. Zelinski* and *J. Louvar*, J. org. Chemistry *23*, 807 (1958).

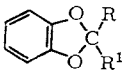
[91] *R. Epsztein* and *S. Holand*, C. R. hebd. Séances Acad. Sci. *250*, 2910 (1960).

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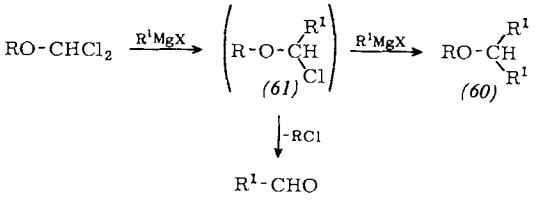
[93] *H. Gross*, Chem. Ber. *95*, 83 (1962).

[94] *W. Siedel* and *F. Winkler*, German Pat. 870108 (Aug. 30th, 1944); Chem. Abstr. *50*, 4197 f (1956).

Both halogen atoms can also be substituted in α,α-dihalogenated ethers; 2,2-disubstituted benzodioxoles *(59a)* have been prepared in this way from pyrocatechol dichloromethylene ether. Benzodioxoles such as *(59c)* are obtained from 2-chloro-2-phenylbenzodioxole *(59b)* [95]. Dichloromethyl alkyl ethers react with Grignard compounds to form ethers of secondary alcohols *(60)* [96–98].

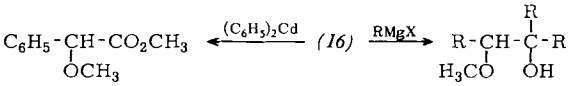


(59a), R = R^1 = Alkyl, Aryl
(59b), R = Cl, R^1 = C_6H_5
(59c), R = CH_3, R^1 = C_6H_5



Aldehydes can be obtained in low yields as by-products, probably as a result of the elimination of R–Cl from *(61)* [98].

The reaction of Grignard compounds with methyl chloromethoxyacetate *(16)* leads not only to substitution of the halogen, but also to addition to the methoxy carbonyl group with formation of glycol monomethyl ethers *(62)*; with diphenylcadmium, on the other hand, the only reaction is replacement of the halogen and formation of methyl *O*-methylmandelate [41].



(62)

An interesting variant of the reaction of α,β-dihalogeno ethers with Grignard compounds is *Boord*'s synthesis of unsaturated compounds (see Table 4 and [116–118]).

The initially formed β-bromo ether *(63)* can be converted either into the olefin *(64a)* by treatment with

Table 4. Olefins, vinyl ethers, and unsaturated alcohols having the general formula *(64c)* synthesized by *Boord*'s method from α,β-dihalogenated ethers.

R	R^1	R^2	Yield (%)	Ref.
n-C_4H_9	H	H	78	[101]
$(CH_3)_2CH-(CH_2)_2$	H	H	90	[100]
$C_{14}H_{29}$	H	H	62	[106]
C_6H_5	H	H	89	[105]
H	CH_3	n-C_4H_9	66	[103]
H	H	$CH_2=CH-CH_2$	72–76	[107]
CH_3	H	i-C_4H_9	91	[103]
CH_3	H	$CH_2=CH-CH_2$	67	[107]
CH_3	CH_3	n-C_3H_7	75	[103]
H	C_2H_5	OC_2H_5	65	[110]
H	C_6H_5	OC_2H_5	62	[110]
i-C_5H_{11}	H	OC_4H_9	70	[109]
C_2H_5	C_2H_5	OCH_3	79	[110]
$HO-(CH_2)_2$	C_2H_5	H	81	[113]
$HO-(CH_2)_2$	$CH_3-CH_2-CH(CH_3)-CH_2$	H	78	[111]
$HO-(CH_2)_3$	CH_3	H	82	[113]
$HO-(CH_2)_3$	n-C_5H_{11}	H	60	[114]
$HO-(CH_2)_3$	$C_5H_{11}-C\equiv C$	H	50	[112, 115]
$HO-(CH_2)_3$	$C_6H_5-C\equiv C$	H	50	[112]

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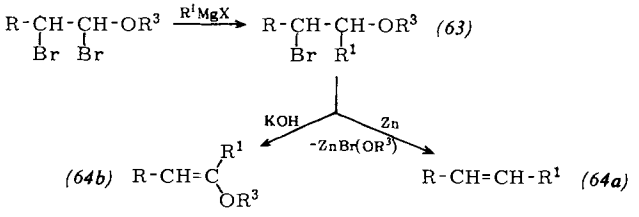
[114] *R. C. Brandon*, *J. M. Derfer*, and *C. E. Boord*, J. Amer. chem. Soc. *72*, 2120 (1950).

[115] *A. Meisters* and *P. C. Wailes*, Austral. J. Chem. *13*, 347 (1960); Chem. Abstr. *55*, 2470h (1961).

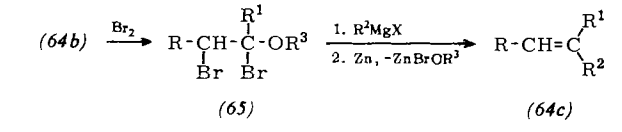
[116] *D. C. Rowlands*, *K. W. Greenlee*, *I. M. Derfer*, and *C. E. Boord*, J. org. Chemistry *17*, 807 (1952).

[117] *B. B. Elsner* and *E. R. Wallsgrove*, J. Instn. Petroleum Technologists *35*, 259 (1949); Chem. Abstr. *43*, 7898f (1949).

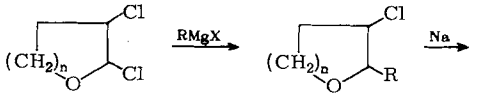
[118] *H. Seifert*, Mh. Chem. *79*, 198 (1948).



Mg or Zn, or into the vinyl ether *(64b)* by reaction with KOH. *(64b)* reacts with bromine to form the dibromo ether *(65)*, which can be converted by a similar reaction sequence into the olefin *(64c)*. This method has been used for the preparation of monoolefins containing up to 20 C-atoms [99–106] and (using unsaturated Grignard compounds) of diolefins [107] and vinyl ethers *(64b)* [108–110].



A similar reaction with cyclic α,β-dihalogeno ethers yields unsaturated alcohols, *e.g. (66)*.



$$NaO\text{-}(CH_2)_{n+1}\text{-}CH{=}CH\text{-}R \longrightarrow HO\text{-}(CH_2)_{n+1}\text{-}CH{=}CH\text{-}R \quad (66)$$

The cleavage of the β-halogeno ether, which has been carried out for a number of examples with $n = 1$ [111,112] and $n = 2$ [113,114] proceeds more readily with sodium, and is not stereospecific; *(66)* is generally obtained as a *cis-trans* mixture.

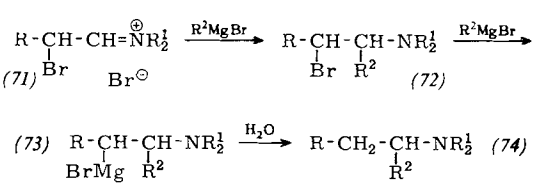
Chloromethyl sulfides react with Grignard compounds, in accordance with equation (e), to form thioethers *(67)* [119], while α-halogeno amines give trialkylamines *(68)* (for R, R^1, R^2, R^3 = alkyl, aryl, or R^3 = H, see [2,27,28,120]).

$RS{-}CHR^1{-}R^2$ *(67)* $\qquad$ $RR^1N{-}CHR^3R^2$ *(68)*

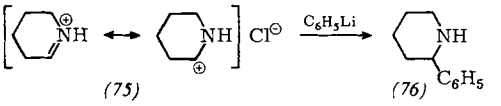
The reaction of allylmagnesium halides with chloromethyldialkylamines leads to almost quantitative yields of γ,δ-unsaturated amines *(69)*, which add HCl to form γ-chloro-*N*-alkylamines *(70)* [121].

$$R_2N{-}CH_2{-}CH_2{-}CH{=}CH_2 \xrightarrow{HCl} R_2N{-}CH_2{-}CH_2{-}CHCl{-}CH_3$$
(69) $\qquad$ *(70)*

α-Dibromoalkylamines *(71)*, which can be obtained by the addition of bromine to enamines, react with Grignard compounds to form α-branched β-bromoalkylamines *(72)*; reaction with a further molecule of alkylmagnesium bromide followed by the elimination of alkyl bromide gives *(73)*, which affords the amine *(74)* on hydrolysis [122].



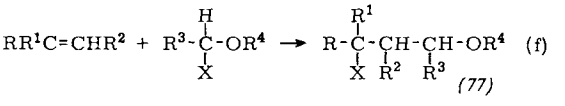
Piperidine hydrochloride *(75)* reacts with phenyllithium to form 2-phenylpiperidine *(76)* in approximately 50 % yield [28].



4. Reactions with Unsaturated Compounds

a) Reactions with Olefins

The addition of α-halogeno ethers to unsaturated compounds has frequently been used to establish new C–C bonds [7,123,124]. This addition is catalysed by $HgCl_2$, $ZnCl_2$, $BiCl_3$, or $AlCl_3$, and proceeds as shown in equation (f), in agreement with the Markovnikov rule.



Some γ-halogeno ethers *(77)* obtained in this way are listed in Table 5; for further examples, see [125,140–150].

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Table 5. γ-Halogeno ethers obtained from olefins *(77)*.

R	R^1	R^2	R^3	R^4	X	Yield (%)	Ref.
CH_3	CH_3	H	H	CH_3	Cl	60	[124]
CH_3	CH_3	CH_3	C_6H_5	CH_3	Cl	65	[124]
CH_3	H	H	H	C_3H_7	Cl	53	[126]
C_2H_5	H	H	H	c-C_6H_{11}	Cl	67	[127]
C_2H_5	H	H	H	C_2H_5	Br	71	[128]
C_2H_5	H	H	H	C_2H_4Cl	Cl	50	[129]
C_3H_7	H	H	H	C_6H_{11}	Cl	51	[129]
CH_3	CH_3	H	H	C_2H_4Br	Cl	48	[130]
Cl	Cl	Cl	H	CH_3	Cl	78	[131]
C_6H_5	H	H	H	CH_3	Cl	75	[132]
CH_3	CH_3	H	CH_3	C_2H_5	Cl	62	[96]
H	H	$OCO-CH_3$	C_6H_5	CH_3	Cl	70	[133]
H	H	CH_2Cl	H	CH_3	Cl	94	[134]
H	H	$CH_2OCO-CH_3$	CH_3	CH_3	Cl	57	[135]
C_6H_5	H	H	CH_2Cl	C_2H_5	Cl	50	[96]
CH_3	H	H	CH_2Br	C_4H_9	Br	50	[136]
$(CH_2)_8CO_2C_2H_5$	H	H	CH_3	CH_3	Cl	70	[135]
C_6H_5	H	H	CH_3	C_4H_9	Cl	60	[137]
CH_3	CH_3	Cl	H	C_3H_7	Cl	77	[138]
H	$(CH_2)_4$		CH_2Cl	C_2H_5	Cl	37	[133]
H	$(CH_2)_4$		H	CH_3	Cl	37	[139]

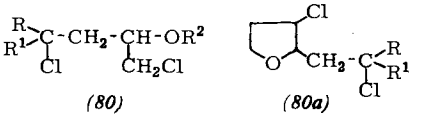
α,α'-Dihalogeno ethers, *e.g.* bis(chloromethyl) ether, may be added to propylene and isobutylene in the presence of $ZnCl_2$ to form *(78a)* and *(78b)* [151].

$(Cl-CRR^1-CH_2-CH_2)_2O$ $(XCH_2-CXH-CH_2-CH_2)_2O$

(78a), $R = CH_3$; $R^1 = H$ *(79a)*, X = Cl

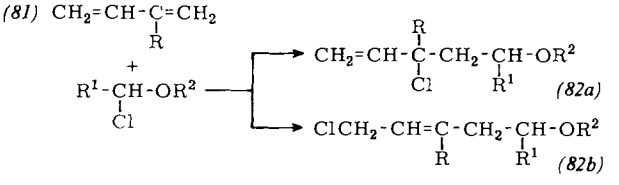
(78b), $R = R^1 = CH_3$ *(79b)*, X = Br

The reaction with chlorinated ethylenes [131,142] or with allyl chloride [133] to form *(79a)* takes place only in the presence of $AlCl_3$, whereas bis(bromomethyl) ether reacts with allyl bromide/$ZnBr_2$ to give *(79b)* [152]. Bis(chloromethyl) ethers of glycol, of 2,3-butanediol, and of 1,2-cyclohexanediol also give good yields of the expected addition products with 2 moles of propylene or butylene [151,153]. α,β-Dihalogeno ethers add to monoolefins to form dihalogeno ethers having the structure *(80)* [96,136]; for example, 2,3-dichlorotetrahydrofuran gives *(80a)* [147,154,155].



(80) *(80a)*

Reaction with conjugated diolefins *(81)* proceeds particularly readily [124] as 1,2- or 1,4-addition. A mixture of the two products is obtained in most cases.



(82a) *(82b)*

Pudovik [156] found that butadiene initially gives mainly 1,2-adducts. However, since these readily isomerize under the conditions of the reaction to form the 1,4-adducts, the proportion of the latter present toward the end of the reaction is always higher. Similar results were obtained in the reaction of various α-chloro ethers with butadiene, isoprene, and chloro-

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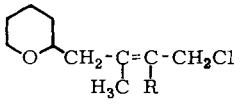
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Table 6. Products of the addition of α-halogeno ethers to conjugated olefins.

R	R^1	R^2	Yield (%) (82a)+(82b)	Yield (%) (82b)	Ref.
H	C_6H_5	CH_3		65	[124]
H	H	CH_3	70		[124]
H	H	n-C_3H_7	85		[157]
H	H	c-C_6H_{11}	77.5		[157]
H	H	CH_2–CH_2Cl	82		[157]
Cl	C_2H_5	CH_3	70		[158]
Cl	CH_2–CH_2Cl	CH_3	40		[158]
H	C_3H_7	CH_3	60		[158]
CH_3	C_2H_5	CH_3		77	[159]
CH_3	C_6H_5	C_2H_5		70	[159]

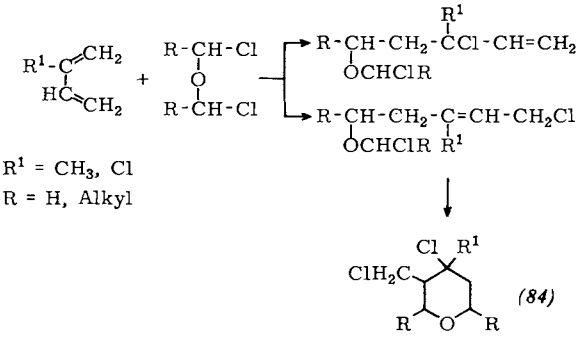
prene (see Table 6 and [141, 160–165]); cyclic dienes give analogous products [124, 166]. 2-Chlorotetrahydropyran reacts with isoprene or 2,3-dimethylbutadiene to give good yields of the 1,4-adducts *(83a)* and *(83b)* [167].



(83a), R = H

(83b), R = CH_3

Tetrahydropyran derivatives *(84)* are obtained from bis(α-chloroalkyl) ethers and chloroprene or isoprene [168] in good yields. α,β-Dichlorodiethyl ether and butadiene [165] or chloroprene [162] also give mainly

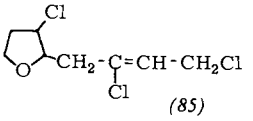


R^1 = CH_3, Cl

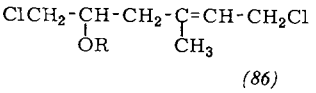
R = H, Alkyl

(84)

the 1,4-adducts, together with small quantities of 1,2-products, whereas the addition of 2,3-dichlorotetrahydrofuran to chloroprene leads exclusively to the 1,4-adduct *(85)* (yield 80 %) [155, 169]. Part of the side chain of vitamin A was synthesized by the addition of α,β-dichloroethyl alkyl ether to isoprene in the presence of $TiCl_4$ to form *(86)* [170].

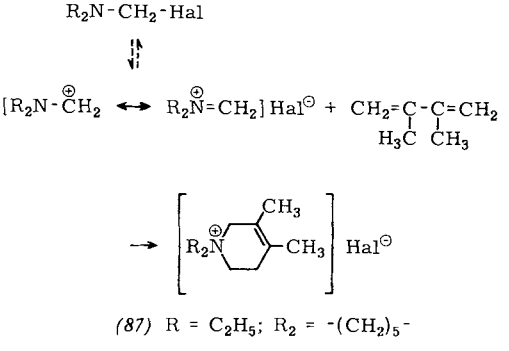


(85)



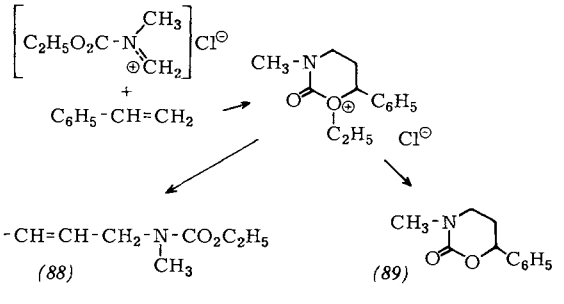
(86)

α-Halogenated amines, such as halogenomethyldiethylamine or *N*-bromomethylpiperidine, react with 2,3-dimethylbutadiene (at room temperature or when heated in methylene chloride) to give a Δ^3-piperidinium halide *(87)* by a reaction resembling the Diels-Alder synthesis [171].



(87) R = C_2H_5; R_2 = $-(CH_2)_5-$

Another reaction of this type is the addition of ethyl *N*-chloromethyl-*N*-methylcarbamate to styrene in the presence of boron trifluoride; this reaction probably leads first to an oxonium salt, which decomposes into *(88)* (65 %) and *(89)* (8–10 %). When the benzyl ester of the same carbamic acid is used, the 1,3-oxazine is formed in 65 % yield [172].



(88)

(89)

b) Reactions with Acetylene and Vinylacetylene

α-Halogenomethyl alkyl ethers add to acetylene in the presence of $AlCl_3$ to give the 3-chloroallyl alkyl ether *(90)*.

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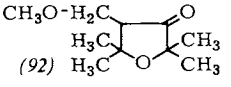
[171] *H. Böhme, K. Hartke,* and *A. Müller,* Chem. Ber. *96*, 607 (1963).

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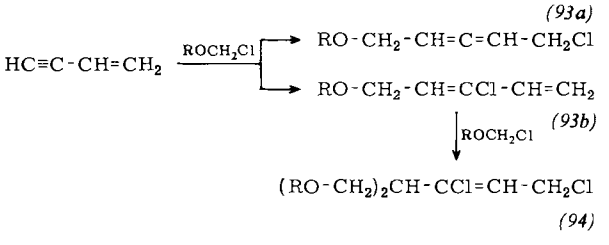
$$HC\equiv CH + ROCH_2Cl \xrightarrow{AlCl_3} RO-CH_2-CH=CHCl + ClCH_2-CH=CHCl$$
(90)

With chlorodimethyl ether, 1,3-dichloroprene is obtained as well as *(90)*, R = CH_3 [173]. The addition of chloromethyl alkyl ethers to tetramethylbutynediol leads to 3-chloro-2,5-dihydroxy-4-methoxymethyl-2,5-dimethylhex-3-ene *(91)*, which gives the furanone derivative *(92)* on treatment with sulfuric acid [174].

$$(CH_3)_2C(OH)-C\equiv C-C(OH)(CH_3)_2 \xrightarrow{CH_3OCH_2Cl} (CH_3)_2C(OH)-C(Cl)=C(CH_2-OCH_3)-C(OH)(CH_3)_2$$
(91)

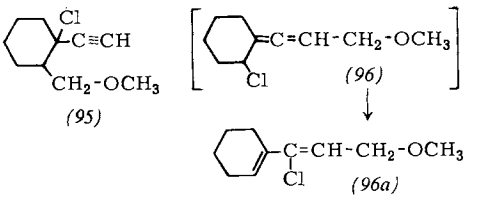

(92)

Dykstra [175] and *Vartanyan* [7] have found that in the presence of $BiCl_3$ [175,176] or $ZnCl_2$ [177], α-chloro ethers add to vinylacetylene in the 1,4-position to give *(93a)*, which then undergoes partial isomerization into *(93b)*. The latter compound can add another mole of chloro ether to form *(94)* [177].


(93a) *(93b)* *(94)*

Similar reactions have been carried out with propyl- [177], 1-chloro-1-methylethyl- [178], and allylvinylacetylene [179] and similar compounds [180]. In most cases these reactions also proceed *via* 1,4-addition. The products can isomerize in various ways.

The addition of monochlorodimethyl ether to Δ^1-cyclohexenylacetylene yields a mixture of the cyclohexane derivatives *(95)* and *(96a)* (molar ratio 62:38). The compound *(96a)* is probably also formed by isomerization of the 1,4-addition product *(96)* [181].


(95) *(96)* *(96a)*

α-Chloromethyl alkyl ethers add to divinylacetylene in the 1,2-positions to give *(97a)* [182]. The addition to isopropenylvinylacetylene takes place selectively at the double bond having the highest electron density;

$$RO-CH_2-CH_2-CR^1Cl-C\equiv C-CH=CH_2$$
(97a), $R^1 = H$ *(97b)*, $R^1 = CH_3$

the product is *(97b)* [183]. 2,3-Dichlorotetrahydrofuran and isopropenylvinylacetylene give a product analogous to *(97b)* [155].

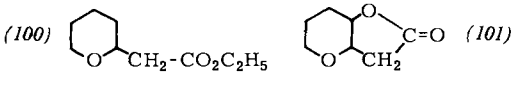
c) Reactions with Ketenes

The reaction of α-chloro ethers with ketenes leads to β-alkoxycarbonyl chlorides *(98)*. Monochlorodimethyl ether gives low yields [184].

$$RO-CHR^1-Cl + CH_2=C=O \longrightarrow RO-CHR^1-CH_2-COCl$$
(98)

Better results are obtained with α-chloro-β,β-diphenyldiethyl ether and 2-chlorotetrahydropyrans [186,187]; the resulting acyl chlorides were converted directly into β-ethoxy-γ,γ-diphenylbutanoic acid *(99)* and ethyl 2-tetrahydropyranylacetate *(100)*. The reaction of ketene with 3-acetoxy-2-chlorotetrahydropyran gives a product that yields perhydrofuro[3,2-*b*]pyran-2-one

$$(C_6H_5)_2CH-CH(OC_2H_5)-CH_2-COOH$$
(99)


(100) *(101)*

(101) directly on distillation [185]. Addition of α,β-dichlorodiethyl ether [187] and 2,3-dichlorotetrahydrofuran [188] to ketene and subsequent alcoholysis yields the esters *(102)* and *(103)*, respectively, while 2,5-di-

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[176] *S. I. Sadychsade*, *A. S. Zhikhmamedbekova*, *S. D. Yultshevskya*, *S. Kh. Salakhova*, and *A. S. Rsajeva*, Azerbajžanskij chim. Ž. *1963*, 37; Chem. Zbl. *1965*, 40-0805.

[177] *S. A. Vartanyan* and *A. O. Tossunyan*, Izvest. Akad. Nauk Arm. SSR, chim. Nauki *15*, 337 (1962); Chem. Abstr. *59*, 3755e (1963).

[178] *S. A. Vartanyan*, *A. O. Tossunyan*, and *L. G. Mesropyan*, Ž. obšč. Chim. *33*, 62 (1963); Chem. Abstr. *59*. 6241g (1963).

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[184] *H. P. Staudinger* and *K. H. W. Tuerck*, Brit. Pat. 539163 (Aug. 29th, 1941); Chem. Abstr. *36*, 3509 (1942); US-Pat. 2316465 (June 27th, 1941); Chem. Abstr. *37*, 5734 (1943).

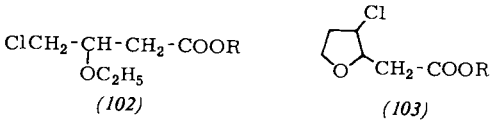
[185] *C. D. Hurd* and *R. D. Kimbrough jr.*, J. Amer. chem Soc. *82*, 1373 (1960).

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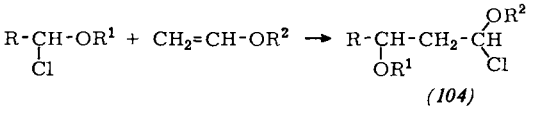
chlorotetrahydrofuran gives the corresponding bifunctional acyl chloride [189].



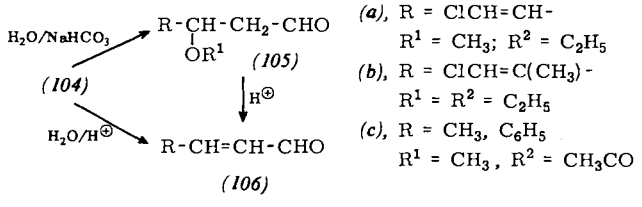
(102) *(103)*

d) Reactions with Vinyl Ethers, Enamines, Ketene Acetals

Olefins with *O* and *N* groups on the double bond react with α-halogeno ethers [cf. eq. (f)] to give very reactive addition products, which, in many cases, react further without being isolated. The addition of α-chloro ethers to vinyl ethers proceeds, even in the absence of catalysts, to give *e.g. (104a)* and *(104b)*.



(104)

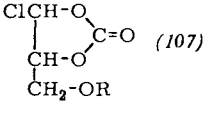


(105) *(106)*

(a), R = ClCH=CH-, $R^1 = CH_3$; $R^2 = C_2H_5$
(b), R = ClCH=C(CH_3)-, $R^1 = R^2 = C_2H_5$
(c), R = CH_3, C_6H_5, $R^1 = CH_3$, $R^2 = CH_3CO$

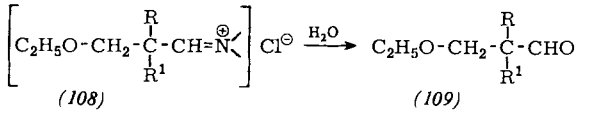
The primary products *(104a)* and *(104b)*, which are obtained in 80–92 % yield, give *(105a)* and *(105b)* on hydrolysis with aqueous $NaHCO_3$ [190], while hydrolysis in acidic solution is accompanied by elimination of methanol and formation of *(106a)* and *(106b)* [191].

Vinyl acetate reacts similarly in the presence of $HgCl_2$ [133] or $ZnCl_2$ [192]. Hydrolysis of the primary product *(104c)*, which is obtained in good yields, again leads to the elimination of an alkoxy group and formation of the unsaturated aldehyde. 2-Oxo-1,3-dioxole and α-chloromethyl alkyl ethers react to form the glyceraldehyde derivative *(107)* [133].



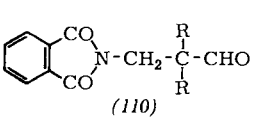
(107)

The reaction of chloromethyl ethyl ether with enamines in acetonitrile leads initially to immonium salts *(108)*, which give β-ethoxyaldehydes *(109)* on hydrolysis [193].

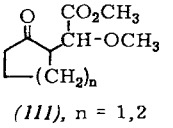


(108) *(109)*

Enamines derived from indanones have been alkylated in a similar manner [194]. *N*-(Bromomethyl)phthalimide and enamines give good yields of β-phthalimidoaldehydes *(110)* [193], while methyl chloromethoxyacetate *(16)* reacts in a similar manner with *N*-cyclopent-1-enyl- or *N*-cyclohex-1-enylmorpholine to form methyl methoxy-(2-oxocycloalkyl)acetates *(111)* [41].

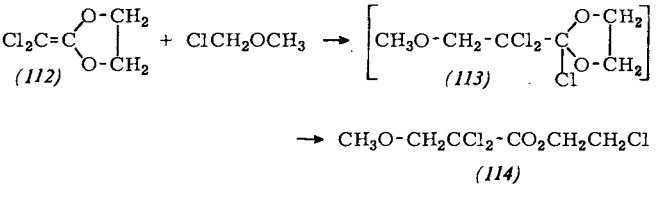


(110)



(111), n = 1,2

The addition of chlorodimethyl ether to 2-(dichloromethylene)-1,3-dioxolane derivative *(112)* probably leads first to the unstable dioxolane derivative *(113)*, which, however, rearranges to give the ester *(114)* [195].



(112) *(113)* *(114)*

5. Reactions with Aromatic and Heterocyclic Compounds

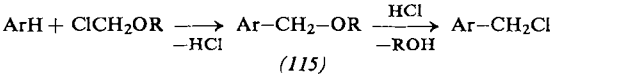
In the presence of Friedel-Crafts catalysts, compounds of the type *(1a)* and *(2b)* react with simple and condensed aromatic compounds, phenols, phenol ethers, and heteroaromatic compounds, sometimes in excellent yields.

a) Formation of Benzyl Compounds

α-Halogeno ethers, sulfides, and amines react with aromatic compounds, primarily in accordance with equation (g).

$$ArH + Cl{-}CHR^1{-}X{-}R \rightarrow Ar{-}CHR^1{-}X{-}R \qquad (g)$$
$$X = O, S, NR^2$$

Chloromethyl alkyl ethers give benzyl ethers *(115)* (Ar = C_6H_5; R = CH_3, C_4H_9) under mild conditions (−40 to −20 °C in $CS_2/AlCl_3$) in yields of up to 37 %, together with benzyl chloride [196].



(115)

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Above 0 °C, the benzyl ethers are evidently unstable under the conditions of the reaction; consequently, the reaction with chloromethyl alkyl ethers always proceeds as a chloromethylation [197, 198].

The symmetrical dichloro- or dibromodimethyl ethers can be used in the same way for halogenomethylation [197, 199–202]. CS_2 has been used as solvent, and the

$$2\,ArH + (XCH_2)_2O \xrightarrow[-H_2O]{} 2\,Ar{-}CH_2X$$

catalyst in this case was $SnCl_4$ [203]. No catalyst is required in acetic [198] or sulfuric acid [200, 201]; zinc chloride was added for the reaction in concentrated hydrochloric acid [202].

Halogenoalkylation with α-halogeno ethers often presents certain advantages over earlier methods with respect to both yields and procedures; some examples are given in Table 7.

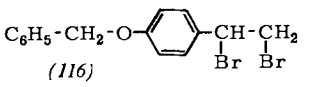
Table 7. Chloromethylated aromatic compounds prepared by halogenoalkylation with CH_3OCH_2Cl (I) or $ClCH_2O{-}CH_2Cl$ (II).

Benzyl chlorides prepared	Yield (%)	Chloro ether	Ref.
2,4-Dimethyl-	50–60	I	[198]
2,4,6-Trimethyl-	80–85	I	[198]
2,4,6-Triisopropyl-	90	I	[203]
2-Methyl-5-nitro-	100	II	[204]
4-Ethyl-3-nitro-	57	I	[205]
2-(β-Chloroethyl)-5-nitro-	65	II	[200]
3-Formyl-2-hydroxy-5-nitro-	90	I	[206]
2-Methoxy-5-nitro-	74, 90	II	[207, 202]
4-Methoxy-3-nitro-		II	[202]
3-Chlormethyl-2-methyl-5-nitro-	43	II	[204]
3-Formyl-4-hydroxy-5-methoxy-	28	II	[208]
4-Acetamido-		II	[201]

The reaction with monochlorodimethyl ether has recently been more widely used for the chloromethylation of styrene-divinylbenzene polymers; depending on the reaction conditions, it is possible to obtain polymers of various degrees of chloromethylation [209–221], which react with amines to give strongly basic ion-exchange resins. Polymers with lower degrees of chloromethylation are specially used for automatic peptide synthesis by *Merrifield*'s method [222]. Investigations have also been carried out on the chloromethylation of benzanthrones [223–225] and triaryltriazines [226].

The reaction of aromatic compounds with α,β-dibromodiethyl ethers proceeds as a dibromoethylation. Phenyl benzyl ether gave a 55 % yield of *p*-(α,β-dibromoethyl)phenyl benzyl ether *(116)* [227].

$$C_6H_5{-}CH_2{-}O{-}C_6H_5 \xrightarrow[-C_2H_5OH]{C_2H_5O{-}CHBr{-}CH_2Br}$$



(116)

Friedel-Crafts reactions of α-halogeno ethers with benzene derivatives can give benzyl ethers as the principal products if the ether grouping is sterically or electronically stabilized. For example, chloromethyl β-phenylethyl ether *(117)*, $n = 2$, undergoes intramolecular reaction in the absence of catalysts to form isochroman *(118)*, $n = 2$, in a yield of more

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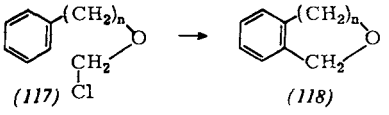
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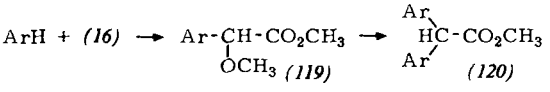
[227] *P. Bapséres* and *R. Quelet*, Bull. Soc. chim. France *1953*, C 50.

than 90 %[228]. Isochromans having substituents in the benzene nucleus or in the heterocycle have been prepared in a similar manner[229,230]; in the presence of $AlCl_3$, chloromethyl γ-phenylpropyl ether *(117)*, $n = 3$, gives homoisochroman *(118)*, $n = 3$[231].



(117) *(118)*

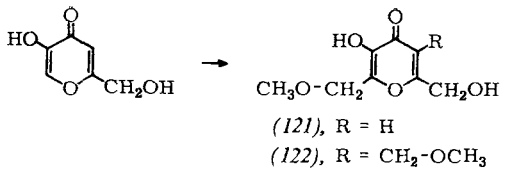
In the reaction of methyl chloromethoxyacetate *(16)* with benzene derivatives, the corresponding methyl *O*-methylmandelates *(119)* can be isolated in yields of up to 86 %[41]. With an excess of the aromatic component, the methyl diarylacetate *(120)* can be obtained



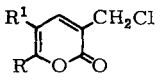
(119) *(120)*

in one step after prolonged reaction. Bromination of *(119)* leads smoothly to methyl arylglyoxylate[232].

α- and γ-Pyrones react with monochlorodimethyl ethers to form the methoxymethyl derivatives. Thus kojic acid gives the 6-methoxymethyl *(121)* or the 3,6-bis(methoxymethyl) compound *(122)*, depending on the amount of chloro ether used, whereas chroman-2-one gives 3-methoxymethylchromanone[233]. The reaction of α-pyrones with a mixture of monochloro- and symmetrical dichlorodimethyl ethers yields 3-chloromethyl-α-pyrones *(123)*[234].

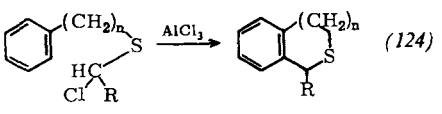


(121), R = H
(122), R = CH_2-OCH_3



(123), R = CH_3
R^1 = CH_3, C_3H_7

thioisochromans *(124)*, *e.g.* with R = H, CH_3, C_6H_5; $n = 2$, can be obtained from α-chloroalkyl β'-phenylethyl sulfides/$AlCl_3$ in good yield[65]. Homoisothiochromans *(124)*, $n = 3$, are obtained in the same way from α-chloroalkyl γ-phenylpropyl sulfides[236].



(124)

α-Halogeno amines or α-halogeno amides can react with aromatic compounds, in some cases in the absence of a catalyst, also in accordance with equation (g). *N*-Chloromethyldialkylamines react both with sodium phenoxides or *N,N*-dialkylaniline hydrochlorides[237] and with furans[238] to form dialkylaminomethylated aromatic compounds *(125)*. α-Halogeno amines such as *(35)* can be used in accordance with equation (g) for the synthesis of *N*-alkylated amino-acid derivatives (see Table 8).

Table 8. Dialkylaminomethylated aromatic compounds synthesized. Ar–CH(R)–N(R^1)(R^2) *(125)*

Ar	R	R^1	R^2	Yield (%)	Ref.
C_6H_5	H	CH_3	CH_3CO	68	[240]
p-$(CH_3)_2N$–C_6H_4	H	CH_3	CH_3	71	[237]
p-$(CH_3)_2N$–C_6H_4	H	CH_3	$CH_2C_6H_5$	47	[237]
o-HO–C_6H_4	H	CH_3	CH_3	35	[237]
4-Hydroxy-3-methoxy-carbonyl-phenyl	H	C_2H_5	C_2H_5	40	[237]
2-Furyl	H	$(CH_2)_2$–O–$(CH_2)_2$		91	[238]
5-Methylfur-2-yl	H	$(CH_2)_5$		91	[238]
p-$(CH_3)_2N$–C_6H_4	CO_2CH_3	$(CH_2)_5$		45	[56]
1-(*p*-Tolyl)pyrrol-2-yl	$CONC_5H_{10}$	$(CH_2)_5$		55	[56]
C_6H_5	H	OC–C_6H_4–CO		94	[241]
5-Chloro-2-hydroxyphenyl	H	OC–C_6H_4–CO		70	[244]

Chloromethyl thioethers react with benzene/$AlCl_3$ in accordance with equation (g) to give benzyl methyl sulfides in moderate yield[235]. On the other hand,

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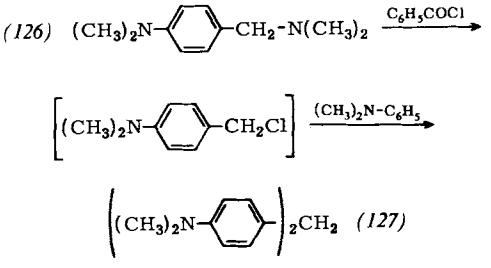
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[243] *S. E. Smirnova-Samkova*, *K. A. Kornev*, and *G. A. Chernevskaya*, Ukrainskij chim. Ž. *29*, 459 (1963); Chem. Abstr. *59*, 6281 b (1963).

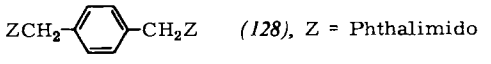
[244] *M. Yamaguchi*, J. chem. Soc. Japan, Pure Chem. Sect. *73*, 393 (1952); Chem. Abstr. *47*, 10497 d (1953).

The reaction of dimethyl-*p*-dimethylaminobenzylamine *(126)* and benzoylchloride leads to *p*-dimethylaminobenzyl chloride, which cannot be isolated, but reacts as a phenylogous α-halogeno amine with *N,N*-dimethylaniline to give bis(*p*-dimethylaminophenyl)-methane *(127)* [239].



(126) $(CH_3)_2N-C_6H_4-CH_2-N(CH_3)_2$ $\xrightarrow{C_6H_5COCl}$ $[(CH_3)_2N-C_6H_4-CH_2Cl]$ $\xrightarrow{(CH_3)_2N-C_6H_5}$ $[(CH_3)_2N-C_6H_4]_2CH_2$ *(127)*

$AlCl_3$ is recommended as the catalyst for the reaction of α-halogeno amides with aromatic compounds to form α-arylalkylamides *(125)*, R = alkyl, R^1 = acyl, R^2 = H [240]. *N*-Bromomethylphthalimide reacts with benzene in boiling benzene/$ZnCl_2$ to give *N*-benzylphthalimide in 94 % yield [241], while the reaction of *N*-chloromethylphthalimide with benzene, xylene, biphenyl, or naphthalene in nitromethane/Zn Cl_2 leads to the introduction of two phthalimidomethyl groups and formation of *e.g. (128)* in yields of up to 95 % [242, 243].

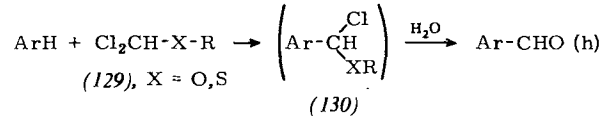


$ZCH_2-C_6H_4-CH_2Z$ *(128)*, Z = Phthalimido

For further reactions of *N*-chloromethylphthalimide with aromatic compounds [244, 245] and of 1,4-bis (chloromethyl)piperazine-2,5-dione [246] with benzene to form 1,4-dibenzylpiperazine-2,5-dione, see the original literature. Some of the amines and amides prepared are listed in Table 8.

b) Synthesis of Aldehydes

When dichloromethyl alkyl ether *(129)*, X = O, react with aromatic compounds in the presence of Friedel-Crafts catalysts ($AlCl_3$, $SnCl_4$, $TiCl_4$), only one chlorine atom is replaced by the aromatic group, as indicated in equation (h). Hydrolysis of the primary product



ArH + $Cl_2CH-X-R$ → $[Ar-CH(Cl)-XR]$ $\xrightarrow{H_2O}$ Ar-CHO (h)

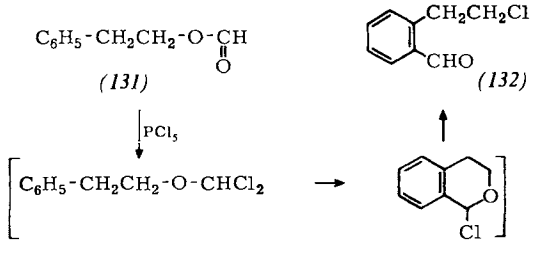
(129), X = O,S — *(130)*

(130), which cannot be isolated, leads to good yields of the corresponding aldehyde [247]. Similarly, dichloromethyl methyl sulfide *(129)*, X = S, can be used for the formylation of aromatic compounds [248]. Table 9 lists a number of the aldehydes prepared by this method.

Table 9. Aldehydes obtained from aromatic compounds by formylation with α,α-dichloro ethers or α,α-dichloro thioethers RX—$CHCl_2$.

Aldehyde	RX	Yield (%)	Ref.
Cuminaldehyde	CH_3O	69	[247]
2,4,6-Trimethylbenzaldehyde	CH_3O	85	[247]
Biphenyl-4-carbaldehyde	C_4H_9O	64	[247]
4-Phenylmethylbenzaldehyde	CH_3O	64	[98]
α-Naphthaldehyde	CH_3O	80	[247]
Fluorene-2-carbaldehyde	C_4H_9O	62	[247]
Anthracene-9-carbaldehyde	CH_3O	92	[247]
Pyrenecarbaldehyde	C_4H_9O	88	[247]
4-Methoxybenzaldehyde	CH_3S	94	[235]
2-Methoxy-5-nitrobenzaldehyde	CH_3O	62	[247]
2-Methoxy-1-naphthaldehyde	CH_3S	94	[235]
Veratraldehyde	CH_3S	87	[235]
4-Hydroxybenzaldehyde	CH_3S	83	[235]
4-Hydroxy-3-methoxybenzaldehyde	CH_3S	91	[235]
2,4-Dihydroxybenzaldehyde	CH_3O	68	[248]
Orcylaldehyde	CH_3S	84	[235]
2,4,6-Trihydroxybenzaldehyde	CH_3S	73	[235]
Ferrocenecarbaldehyde	C_2H_5O	72	[249]
Coronenecarbaldehyde	C_4H_9O	77	[250]
Thiophene-2-carbaldehyde	CH_3O	90	[247]
1-Formylcolchicine	CH_3O	80	[251]

The final product of the reaction of β-phenylethyl formate *(131)* with PCl_5 is *o*-(β-chloroethyl)benzaldehyde *(132)* [252]. The reaction probably proceeds *via* dichloromethyl β-phenylethyl ether, which first undergoes an intramolecular Friedel-Crafts reaction to give 1-chloroisochroman; the latter subsequently rearranges to *(132)* [228, 253].



$C_6H_5-CH_2CH_2-O-CH(=O)$ *(131)* → PCl_5 → $[C_6H_5-CH_2CH_2-O-CHCl_2]$ → 1-Chloroisochroman → *(132)* o-$(CH_2CH_2Cl)C_6H_4CHO$

α-Halogeno amines such as *N,N*-dimethylformamide dichloride can be used for the formylation of aromatic compounds. These reactions proceed as Vilsmeier formylations.

c) Synthesis of Carboxylic Acids

In the reactions of trichloromethyl methyl ether *(133)*, X = O, with aromatic compounds in the presence of Friedel-Crafts catalysts, again only one chlorine atom is replaced by the aryl residue. Hydrolysis of the intermediate, which again cannot be isolated, yields an aromatic carboxylic acid [254, 255]. However, the yields

[245] *H. E. Zaugg* and *A. D. Schaefer*, J. org. Chemistry *28*, 2925 (1963).

[246] *E. Cherbuliez* and *E. Feer*, Helv. chim. Acta *5*, 678 (1922); Chem. Zbl. *1923*, 1034; *E. Cherbuliez* and *G. Sulzer*, *ibid. 8*, 567 (1925).

[247] *A. Rieche*, *H. Gross*, and *E. Höft*, Chem. Ber. *93*, 88 (1960).

[248] *H. Gross*, *A. Rieche*, and *G. Matthey*, Chem. Ber. *96*, 308 (1963).

[249] *P. L. Pauson* and *W. E. Watts*, J. chem. Soc. (London) *1962*, 3880.

[250] *H. Reimlinger*, *J. P. Golstein*, *J. Jadot*, and *P. Jung*, Chem. Ber. *97*, 349 (1964).

[251] *G. Muller* and *D. Branceni*, C. R. hebd. Séances Acad. Sci. *255*, 2983 (1962); G. Muller, *A. Blade Font*, and *R. Bardoneschi*, Liebigs Ann. Chem. *622*, 105 (1963).

[252] *H. Laato*, Suomen Kemistilehti B *38*, 157 (1965).

[253] *E. Schmitz*, Chem. Ber. *91*, 1495 (1958).

[254] *H. Gross*, Habilitation Thesis, Humboldt-Universität Berlin, 1963.

[255] *H. Gross*, *J. Rusche*, and *M. Mirsch*, Chem. Ber. *96*, 1382 (1963).

$$ArH + Cl_3C\text{-}X\text{-}CH_3 \longrightarrow$$

(133), X = O,S

$$(Ar\text{-}CCl_2\text{-}X\text{-}CH_3) \xrightarrow{H_2O} Ar\text{-}CO_2H \qquad (i)$$

$$Ar\text{-}C(=O)SCH_3$$

(134)

are very low, owing to a competing reaction of trichloromethyl methyl ether with traces of $AlCl_3$, which results in decomposition into phosgene and methyl chloride [254].

$$Cl_3C\text{–}O\text{–}CH_3 \xrightarrow{AlCl_3} COCl_2 + CH_3Cl$$

Nevertheless, carboxylic acids can be obtained in good yields if trichloromethyl methyl sulfide *(133)*, X = S, is used instead of the ether. Hydrolysis in this case leads first to the thiolester *(134)* of the aromatic carboxylic acid, which can readily be hydrolysed by alkali to obtain the carboxylic acid [235].

Carboxylations of aromatic compounds can be readily accomplished *e.g.* with pyrocatechol dichloromethylene ether *(135)*. Hydrolysis of the ortho acid diester monochloride *(136)* formed in the presence of $AlCl_3$ or $SnCl_4$ affords first the pyrocatechol monoester of the aromatic carboxylic acid, which can be readily hydrolysed with alkali [255]. Alternatively, orthoesters of the type *(138)* can be obtained by treatment of the reaction mixture containing *(136)* with alcohol/pyridine [95].

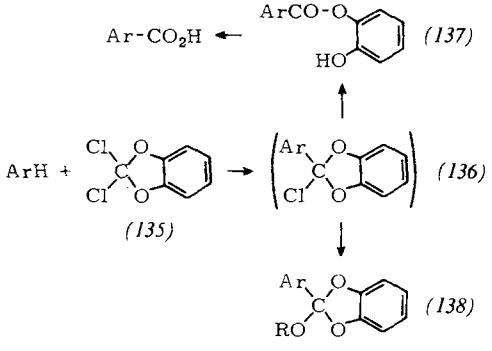


Table 10. Carboxylic acids and carboxylic acid derivatives prepared by reaction of trichloromethyl methyl sulfide *(133)*, X = S, or pyrocatechol dichloromethylene ether *(135)* with aromatic compounds.

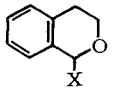
Ar	Yield (%)		
	(134) [235]	*(137)* [255]	Ar—CO_2H [255]
p-Cumenyl		81	84
3,4-Dimethylphenyl		91	90
2,4,6-Trimethylphenyl		87	86
1-Naphthyl	73	96	quant.
9-Anthryl		quant.	89
4-Methoxyphenyl	86	83	98
3,4-Dimethoxyphenyl		88	80
2-Methoxynaphth-1-yl		quant.	96
4-Hydroxyphenyl	63		
3-Chlor-2-hydroxy-4,6-dimethoxyphenyl		96	70
2-Hydroxynaphth-1-yl		91	
2,4-Dihydroxyphenyl	81		
2,3,4-Trihydroxyphenyl	64		
5-Ethoxycarbonylfur-2-yl		92	93

Some examples of the carboxylation of aromatic compounds are shown in Table 10.

In the case of azulenes, one or two carboxyl groups can be introduced in yields of up to 96 %, depending on the reaction conditions and on the amount of *(135)* [256].

6. Reactions with Diazo Compounds

The reaction of α-halogeno ethers and sulfides with diazomethane, diazoacetic ester, or diazo ketones has so far proved unsatisfactory [257]. 1-Bromoisochroman *(139a)* reacts with diazomethane to give 1-bromomethylisochroman *(139b)* in 23 % yield [64].



(139a), X = Br
(139b), X = CH_2Br

On the other hand, vigorous reaction takes place when diazo compounds are mixed with α-halogeno amines. Dialkyl β-chloroethylamine *(140a)* and ethyl α-chloro-β-dialkylaminopropionate *(140b)* have been obtained by reaction of dialkylchloromethylamine with diazomethane and diazoacetic ester, respectively [237].

$$[R_2\overset{\oplus}{N}{=}CH\text{-}R^1]\,Cl^{\ominus} + N_2CH\text{-}R^2 \longrightarrow R_2N\text{-}\underset{\displaystyle CHCl\text{-}R^2}{\overset{\displaystyle R^1}{CH}}$$

(140a), R^1, R^2 = H
(140b), R^1 = H, R^2 = $CO_2C_2H_5$
(140c), R^1 = CO_2CH_3, R^2 = H

The α-halogeno amine *(35)*, Z = OCH_3, reacts with diazomethane to form *(140c)* [258]. *N*-Cylohexylindenepiperidinium chloride and diazomethane give (1-chloromethylcyclohexyl)piperidine [259].

B. α-Halogeno Ethers as Nucleophiles

1. Grignard Compounds from α-Halogeno Ethers

In the reactions described so far, the α-halogeno ethers have always acted as electrophiles. However, after conversion into Grignard compounds, they should also be able to react as nucleophiles. The preparation of Grignard compounds such as *(141)* was recently accomplished by the reaction of α-chloro ethers with magnesium in methylal, $CH_2(OCH_3)_2$, [260] or in tetrahydrofuran [261, 262].

[256] *W. Schroth* and *H. Genzel*, unpublished; *H. Genzel*, Diploma Thesis, Universität Leipzig, 1963.

[257] *M. Kratochvil, J. Jonas*, and *H. Gross*, unpublished experiments.

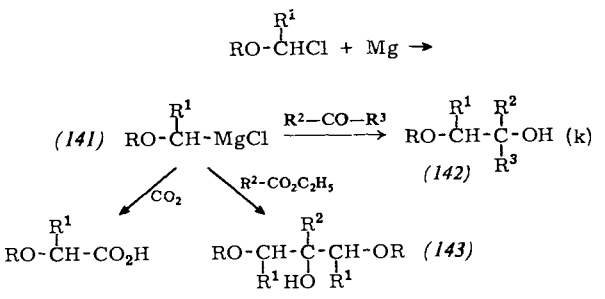
[258] *H. Gross* and *G. Ollmann*, unpublished.

[259] *G. Opitz, A. Griesinger*, and *H. W. Schubert*, Liebigs Ann. Chem. *665*, 91 (1963).

[260] *F. Runge, E. Taeger, Ch. Fiedler*, and *E. Kahlert*, J. prakt. Chem. [4] *19*, 37 (1963).

[261] *H. Normant* and *B. Castro*, C. R. hebd. Séances Acad. Sci. *257*, 2115 (1963).

[262] *H. Normant* and *B. Castro*, C. R. hebd. Séances Acad. Sci. *259*, 830 (1964).



These rather unstable[268] alkoxymethylmagnesium halides *(141)* have been used for the preparation of 1,2-glycol monoalkyl ethers *(142)*, glycerol 1,3-dialkyl ethers *(143)*, and alkoxyacetic acids[261–263] (see Table 11). Tris(ethoxymethyl)carbinol *(144)* was obtained by reaction with diethyl carbonate[261,267], 1-ethoxypentan-2-one *(145)* by reaction with *N,N*-diethylbutyramide, and α-ethoxyacetophenone *(146)* by reaction with benzonitrile[261].

Table 11. Glycol monoalkyl ethers *(142)* formed in accordance with equations (k) and (l).

R	R^1	R^2	R^3	Reaction path	Yield (%)	Ref.
$Cl(CH_2)_2$	H	H	CH_3	(k)	69	[262]
$Cl(CH_2)_2$	H	H	$CH_2=CH$	(k)	46	[262]
$Cl(CH_2)_2$	H	H	n-C_6H_{13}	(k)	63	[262]
CH_3	H	H	*p*-$H_3CO-C_6H_4$	(i)	51	[263]
$C_6H_5CH_2$	H	H	C_6H_5	(k)	80	[262]
$Cl(CH_2)_2$	H	CH_3	CH_3	(k)	80	[262]
C_2H_5	H	CH_3	CH_3	(l)	70	[264]
n-C_4H_9	H	C_2H_5	C_2H_5	(k)	95	[263
C_2H_5	H	CH_3	n-C_5H_{11}	(l)	93	[264]
C_2H_5	H	CH_3	$C_6H_5CH_2$	(l)	70	[264]
$Cl(CH_2)_2$	H	$(CH_2)_5$		(k)	80	[262]
C_2H_5	H	$(CH_2)_4-C(CH_3)_2$		(l)	60	[265]
i-C_3H_7	H	CH_3	C_6H_5	(k)	84	[263]
C_2H_5	H	C_6H_5	Cyclopropyl	(l)	60	[264]
CH_3	H	C_6H_5	C_6H_5	(k)	72	[266]
C_2H_5	CH_3	H	n-C_6H_{13}	(l)	60	[264]
C_2H_5	CH_3	H	$CH_3-CH=CH$	(i)	58	[264]
C_2H_5	CH_3	H	*p*-$(CH_3)_2CH-C_6H_4$	(l)	70	[264]
C_2H_5	C_2H_5	i-C_4H_9	CH_3	(l)	75	[264]

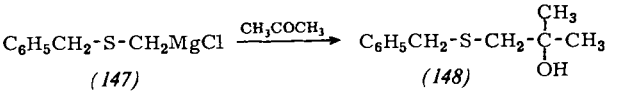
(141) + $O=C(OC_2H_5)_2$ → $(C_2H_5O-CH_2)_3COH$ *(144)*

(141) + $C_3H_7-CO-N(C_2H_5)_2$ → $C_3H_7-CO-CH_2-OC_2H_5$ *(145)*

(141) + C_6H_5-CN → $C_6H_5-CO-CH_2-OC_2H_5$ *(146)*

Lithium may be used instead of magnesium as the "reducing agent" for the α-halogeno ether. Methoxymethyl-lithium, which is obtained from monochloromethyl ether and lithium[266], reacts in the same way as methoxymethylmagnesium chloride with carbonyl compounds and CO_2.

Chloromethyl benzyl sulfide gives the Grignard compound *(147)*, which reacts *e.g.* with acetone to give 1,1-dimethylthioglycol *S*-benzyl ether *(148)*[262].



2. Simultaneous Action of Magnesium and a Ketone on α-Halogeno Ethers

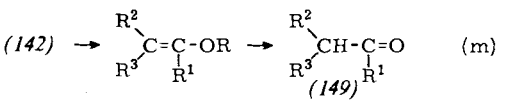
The unstable[268] Grignard compounds of α-halogeno ethers can be prepared only in methylal or tetrahydrofuran. However, α-chloroethers, magnesium, and carbonyl compounds will react directly in ether in a one-step reaction. This leads, in accordance with equation (l), to the same 1,2-glycol monoalkyl ethers *(142)* as are obtained from alkoxymethylmagnesium chloride and carbonyl compounds at low temperatures[264,269]. The glycol ethers *(142)* can be converted into the aldehydes *(149)*, R^1 = H, or ketones

$$R-O-CHR^1-Cl + Mg + R^2-CO-R^3 \xrightarrow{HgCl_2} (142) \qquad (l)$$

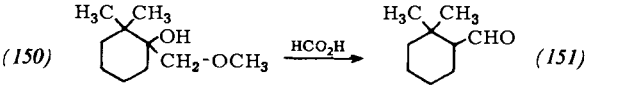
(149), R^1 = alkyl, having one C atom more than the original carbonyl compound, by dehydration and acid hydrolysis of the resulting vinyl ether[264] (see Table 12).

Table 12. Examples of the chain-lengthening of carbonyl compounds to *(149)* in accordance with equations (l) and (m) [264].

R^1	R^2	R^3	Yield (%)
H	n-C_6H_{13}	H	15
H	C_6H_5	H	65
H	CH_3	CH_3	75
H	CH_3	i-C_4H_9	83
H	CH_3	C_6H_5	88
H	i-C_4H_9	i-C_4H_9	90
H	Cyclopropyl	C_6H_5	50
H	C_6H_5	C_6H_5	78
CH_3	C_5H_{11}	CH_3	75
H	$(CH_2)_5$		75
H	$CH-CH_3$		50



Under the same conditions, 2,2-dimethylcyclohexanone gives 2,2-dimethylcyclohexylcarbaldehyde *(151)* *via* the monoether *(150)*[265]. 2-Formyl-1,3,3-trimethylbicyclo[2.2.1]heptane *(152)* has been obtained in a



[263] *E. Taeger, E. Kahlert,* and *H. Walter,* J. prakt. Chem. *[4] 28,* 13 (1965).

[264] *H. Normant* and *C. Crisan,* Bull. Soc. chim. France *1959,* 459, 463.

[265] *M. de Botton,* C. R. hebd. Séances Acad. Sci. *256,* 2186 (1963).

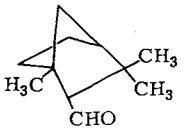
[266] *U. Schöllkopf* and *H. Küppers,* Tetrahedron Letters *1964,* 1503.

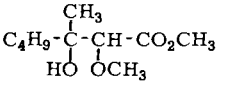
[267] *E. Taeger* and *H. Küchler,* Z. Chem. *6,* 149 (1966).

[268] *E. Taeger* and *Ch. Fiedler,* Liebigs Ann. Chem. *696,* 42 (1966).

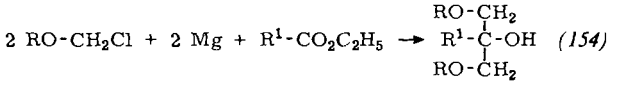
[269] *M. Sommelet,* Ann. Chim. Physique [8] *9,* 484 (1906); Bull. Soc. chim. France [4] *1,* 370 (1907).

similar manner from fenchone [270]. Methyl chloromethoxyacetate *(16)* also undergoes this reaction, and with magnesium and a ketone it gives methyl esters of β-hydroxy-α-methoxycarboxylic acids, *e.g. (153)* [271]. Chloromethyl alkyl ethers also react directly with

(152) 

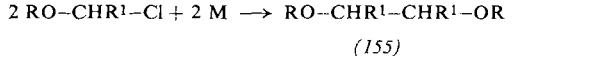
 *(153)*

magnesium and esters in methylal or terahydrofuran to yield bis(alkoxymethyl)carbinols *(154)* [267].

 *(154)*

3. Wurtz Syntheses with α-Halogeno Ethers

The reaction of α-halogeno ethers with metals, which is formally analogous to the Wurtz synthesis, has been little investigated. Equimolar quantities of α-chloroether and sodium give glycol diethers *(155)*, R = CH_3 to C_5H_{11}; R^1 = H, in yields of up to 79 % [130, 272, 273], while with Cu and Fe, derivatives with R = CH_3 to



(155)

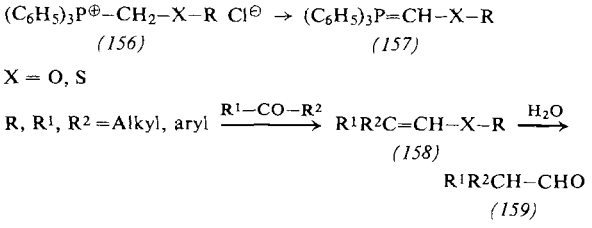
$C_{16}H_{32}$ and R^1 = H to C_3H_7 can be obtained [274]. Diethyl 2,3-diethoxysuccinate *(155)*, R = C_2H_5, R^1 = $CO_2C_2H_5$, has been obtained in the same way by reaction of ethyl ethoxychloroacetate with copper powder [275].

C. Reactions of the α-Halogeno Ethers, Sulfides and Amines Involving α-Elimination

1. Syntheses *via* Phosphorus Ylides

The versatile Wittig olefination process, when applied to compounds of the types *(1a)* or *(2b)*, permits the conversion of carbonyl compounds into vinyl ethers or aldehydes having one C atom more, and into the methyl ketone having two C atoms more than the original compound.

For this reaction, the phosphonium salt *(156)*, X = O, R = aryl (the aliphatic analogues give only low yields [278, 279]), obtained from triphenylphosphine and the α-halogeno ether, is converted into the ylide *(157)*, X = O, by treatment with phenyl-lithium or sodium alkoxide. These ylides react with carbonyl compounds,



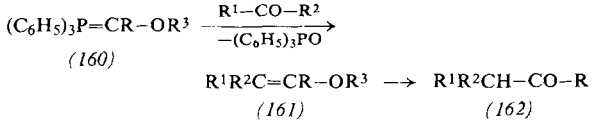
(156) *(157)* *(158)* *(159)*

sometimes in very good yields, to give vinyl ethers or vinyl thioethers *(158)*, which have been hydrolysed in some cases to give aldehydes *(159)* [276–279]. Some of the vinyl compounds prepared are shown in Table 13.

Table 13. Vinyl ethers *(158)*, X = O and vinyl thioethers *(158)*, X = S, prepared.

Starting compound	X	R	Yield (%)	Ref.
Diethylketone	O	*p*-CH_3–C_6H_4	72	[278]
Cyclohexanone	O	*p*-CH_3–C_6H_4	82	[278]
α-Ionone	O	*p*-CH_3–C_6H_4	75	[278]
β-Ionone	O	*p*-CH_3–C_6H_4	73	[278]
Benzaldehyde	O	*p*-CH_3–C_6H_4	75	[278]
Benzaldehyde	S	CH_3	70	[276]
Benzophenone	O	CH_3	82	[276]
Benzophenone	S	CH_3	84	[276]
Cinnamaldehyde	O	CH_3	50	[276]
Fluorenone	O	C_2H_5	66	[276]
Phthalaldehyde	O	*p*-CH_3–C_6H_4	62	[278]
Tigogenone	O	CH_3	85	[277]

Triphenylphosphonium chlorides obtained from α-halogeno derivatives such as ethyl chloromethoxyacetate or α-chloroethyl methyl ether react with bases [$KOC(CH_3)_3$, $NaOC_2H_5$] to give phosphorus ylides *(160)*. With formaldehyde, *(160a)* gives the enol ether of ethyl pyruvate *(161a)* [280], while the reaction of the derivate *(160b)* with aldehydes and ketones has led to the development of a synthesis for vinyl ethers *(161b)* and methyl ketones *(162b)* [281].



(160) *(161)* *(162)*

(a), R = $CO_2C_2H_5$; R^1, R^2 = H; R^3 = CH_3

(b), R = R^3 = CH_3; R^1, R^2 = H, alkyl, aryl

(c), R = CH_3–CO; R^1 = C_6H_5, *o*-O_2N–C_6H_4; R^2 = H; R^3 = CH_3

(d), R = $CO_2C_2H_5$; R^1 = C_6H_5; R^2 = H; R^3 = CH_3

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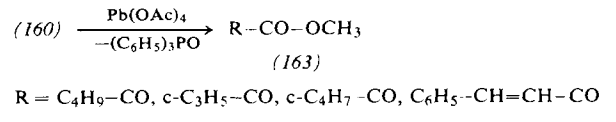
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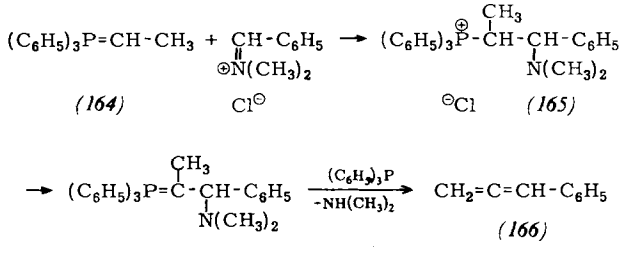
Acylation of ylides of the type *(157)*, X = O, with acyl chlorides or esters leads to acyl derivatives *(160c)*, which can be converted into acylated enol ethers *(161c)* by a Wittig reaction with carbonyl compounds. Hydrolysis *(161c)* gives the dicarbonyl compound *(162c)*. On acylation of *(157)* with formic acid, the same reaction sequence leads to α-keto esters *(162d)* *via* *(161d)* [282]. Finally, α-keto esters *(163)* can be obtained readily from compounds of the type *(160)* by oxidation with lead tetraacetate under mild conditions [283].



(160) $\xrightarrow[-(C_6H_5)_3PO]{Pb(OAc)_4}$ $R-CO-OCH_3$ *(163)*

$R = C_4H_9-CO$, $c\text{-}C_3H_5-CO$, $c\text{-}C_4H_7-CO$, $C_6H_5-CH=CH-CO$

The formation of allenes from α-halogeno amines and alkylidenephosphoranes also proceeds formally by α-elimination [284]. Thus ethylidenetriphenylphosphorane *(164)* and α-chlorobenzyldimethylamine react to form the phosphonium salt *(165)*, which, after loss of the α-proton (by transylidation with a second mole of ylide), undergoes β-elimination to give phenylallene *(166)* in 60 % yield.

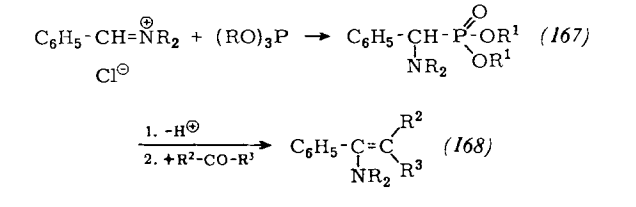


$(C_6H_5)_3P=CH-CH_3$ + $C_6H_5-CH(\oplus N(CH_3)_2)$ → $(C_6H_5)_3\overset{\oplus}{P}-CH(CH_3)-CH(N(CH_3)_2)-C_6H_5$

(164) $Cl^{\ominus}$ $^{\ominus}Cl$ *(165)*

→ $(C_6H_5)_3P=C(CH_3)-CH(N(CH_3)_2)-C_6H_5$ $\xrightarrow[-NH(CH_3)_2]{(C_6H_5)_3P}$ $CH_2=C=CH-C_6H_5$ *(166)*

Enamines can be obtained from α-halogeno amines by the PO-activated olefination discovered by *Horner* [285]. α-Halogenobenzylamines and trialkylphosphines give first the diester *(167)* of the α-(dialkylamino)benzylphosphonic acid, which forms an enamine *(168)* on deprotonation and reaction with carbonyl compounds [286].

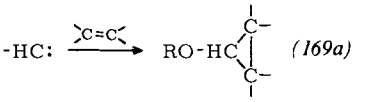


$C_6H_5-CH=\overset{\oplus}{N}R_2$ $Cl^{\ominus}$ + $(RO)_3P$ → $C_6H_5-CH(NR_2)-P(=O)(OR^1)-OR^1$ *(167)*

$\xrightarrow[2.\ +R^2-CO-R^3]{1.\ -H^{\oplus}}$ $C_6H_5-C(NR_2)=C(R^2)(R^3)$ *(168)*

2. Syntheses of Cyclopropane Derivatives [*]

α-Elimination of HCl from α-halogeno ethers in the presence of olefins yields alkoxycyclopropanes *(169a)*.



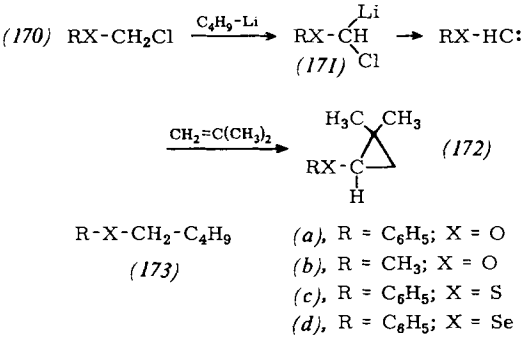
$RO-CH_2Cl$ $\xrightarrow{-HCl}$ $RO-HC:$ $\xrightarrow{>C=C<}$ $RO-HC(-C-)(-C-)$ *(169a)*

It is not yet certain whether this reaction, which was studied by *Schöllkopf* [287], proceeds *via* alkoxycarbenes or whether metalated intermediates react as "carbenoids" [288].

Alkoxycyclopropanes can be obtained in various ways from α-halogeno ethers. As was shown in Section A.3, α-halogeno ethers react with organometallic compounds by nucleophilic substitution. Under certain structural conditions, however, the H_α atom of the halogeno ether can be acidic, so that metalation can take place in the α-position. These two reactions can compete with each other.

For example, chloromethyl phenyl ether *(170)* can be metalated with butyl-lithium to give phenoxychloromethyl-lithium *(171a)*, which reacts further with isobutylene to form 2,2-dimethyl-1-phenoxycyclopropane *(172a)* [287]. The reaction with chloromethyl phenyl sulfide *(170c)* also proceeds *via* the lithium compound with formation of 2,2-dimethyl-1-phenylthiocyclopropane *(172c)* [289–291], while the reaction with chloromethyl methyl ether *(170b)* leads to 1-methoxy-2,2-dimethylcyclopropane *(172b)* [289, 292, 293]. Finally, the analogous phenylselenocyclopropane derivative *(172d)* can be prepared from chloromethyl phenyl selenoether *(170d)*, with potassium t-butoxide as the base in this case [294].

Since the acidity of the α-hydrogen atom increases in the order *(170b)* < *(170a)* < *(170c)*, α-chloromethyl aryl sulfides should be more easily metalated than α-chloromethyl methyl ether. In agreement with this, the yield of cyclopropane derivative is highest with *(170c)* (up to 90 % when potassium t-butoxide is



(170) $RX-CH_2Cl$ $\xrightarrow{C_4H_9-Li}$ $RX-CH(Li)(Cl)$ *(171)* → $RX-HC:$

$\xrightarrow{CH_2=C(CH_3)_2}$ $RX-C(H)(-C(CH_3)_2-)$ *(172)*

$R-X-CH_2-C_4H_9$ *(173)*

(a), R = C_6H_5; X = O
(b), R = CH_3; X = O
(c), R = C_6H_5; X = S
(d), R = C_6H_5; X = Se

[282] *E. Zbiral*, Tetrahedron Letters *1965*, 1483.

[283] *E. Zbiral* and *E. Werner*, Tetrahedron Letters *1966*, 2001.

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[*] We thank Prof. *U. Schöllkopf* for reading this part of the manuscript.

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[289] *U. Schöllkopf*, *A. Lerch*, *W. Pitteroff*, and *G. J. Lehmann*, Angew. Chem. *73*, 765 (1961).

[290] *U. Schöllkopf* and *G. J. Lehmann*, Tetrahedron Letters *1962*, 165.

[291] *U. Schöllkopf*, *G. J. Lehmann*, *J. Paust*, and *H. D. Härtl*, Chem. Ber. *97*, 1527 (1964).

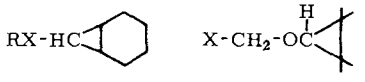
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used)[290,292]. On the other hand, the nucleophilic substitution of the halogen atom is easiest in α-chloromethyl alkyl ethers. The side reaction, *i.e.* the nucleophilic substitution of the chlorine atom by the alkyl residue, is most prominent for these compounds. The reaction of *(170b)* with n-butyl-lithium proceeds almost exclusively by substitution with formation of *(173b)*, whereas with the bulky t-butyl-lithium, metalation occurs and *(172b)* is obtained in a yield of 32 %. Direct nucleophilic substitution with n-butyl-lithium has also been observed for *(170a)* [formation of *(173a)*]; however, this occurs only to a small extent, since the nucleophilic reaction is more difficult than for *(170b)* and the α-hydrogen atom is acidic[292,293]. The lower the electron density on the olefin, the more pronounced does the competitive nucleophilic reaction become[295].

As was found with *cis*- and *trans*-butene, the reaction proceeds stereospecifically as a *cis*-addition[295]. With cyclohexene, *(170a)* to *(170c)* give 7-substituted norcaranes *(174)*[292,295], the product always being a mixture of the *endo*- and *exo*-forms.



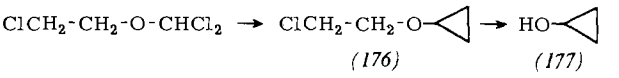
(174), R = Alkyl, Aryl
X = O,S

(175a), X = Cl
(175b), X = CH_3O

The *exo* form always predominates (*cis*:*trans* = 1.8:1 to 7:1) since the transition state leading to the *exo* compound is energetically more favorable. This is also shown by comparison of the isomer mixtures obtained in the reaction of chloromethyl methyl ether and chloromethyl isopropyl ether with cyclohexene. The *exo*:*endo* ratio was 7:1 for the bulky isopropyl derivative, and only 4.5:1 for the methyl derivative[292]. On the other hand, the phenoxycarbene is more reactive, and hence less selective, than the methoxycarbene, so that in this case an *exo*:*endo* ratio of only 1.8:1 is obtained[292,296]. 2,2-Diethoxy-1-phenylthiocyclopropanone can be obtained from *(170c)* with ketene acetal as the olefin[290].

A convenient route to alkoxycyclopropanes is the reaction of methyl-lithium with dichloromethyl alkyl ethers and olefins in the presence of lithium iodide. The reaction probably proceeds *via* chloroiodomethyl alkyl ethers, which react immediately with methyl-lithium to form the alkoxychloromethyl-lithium. The subsequent reaction then proceeds as a stereospecific *cis* addition[296,297]. When chloromethyl dichloromethyl ether is used, only the dichloromethyl group reacts; the reaction leads to chloromethyl cyclopropyl ether *(175a)*, which can be converted into the acetal *(175b)* by treatment with $NaOCH_3$[296].

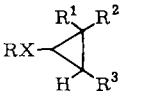
Cyclopropanole *(177)* has been synthesized from β-chloroethyl dichloromethyl ether and ethylene. β-Chloroethoxycyclopropane *(176)* was first prepared,



(176) *(177)*

and this was then converted into *(177)* by elimination of HCl and hydrolysis of the resulting cyclopropyl vinyl ether, or by reaction with butyl-lithium to form cyclopropanol-lithium and subsequent hydrolysis[298]; the latter represents the superior method.

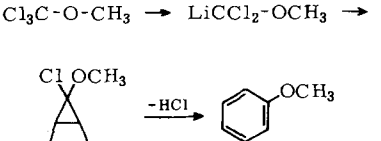
Table 14. Alkoxy-, alkylthio-, and alkylselenocyclopropanes synthesized.



R	X	R^1	R^2	R^3	Yield (%)	Ref.
CH_3	O	CH_3	CH_3	H	32	[292]
n-C_6H_{13}	O	CH_3	CH_3	H	79	[296]
n-C_6H_{13}	O	H	$CH=CH_2$	H	76 [a]	[296]
C_2H_5	O	CH_3	CH_3	H	75	[287,292,295]
CH_3	O	H	OC_2H_5	H	51 [a]	[296]
CH_3O-CH_2	O	CH_3	CH_3	H	41	[296]
$Cl-CH_2-CH_2$	O	CH_3	CH_3	H	78	[298]
H	O	CH_3	CH_3	H	87	[298]
i-C_3H_7	O	H	$(CH_2)_4$		55 [a]	[293]
CH_3	O	H	$(CH_2)_6$		43 [a]	[296]
H	O	H	$(CH_2)_4$		94 [a]	[298]
n-C_6H_{13}	O	H	$O-(CH_2)_3$		48 [a]	[296]
C_6H_5	S	C_2H_5O	C_2H_5O	H	80	[290, 291]
C_6H_5	S	CH_3	CH_3	H	90	[290, 291]
C_6H_5	S	H	$CH=CH-CH_2-CH_2$		60	[291]
C_6H_5	Se	CH_3	CH_3	H	70	[294]
C_6H_5	Se	H	$CH=CH-CH_2-CH_2$		68 [a]	[294]

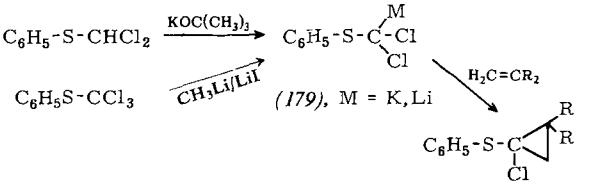
[a] As a mixture of stereoisomers.

α-Elimination of two atoms of chlorine from trichloromethyl methyl ether with methyl-lithium in cyclopentadiene yields anisole (21 %). The reaction presumably involves initial formation, *via* methoxydichloromethyl-lithium, of 6-chloro-6-methoxybicyclo-[3.1.0]hex-2-ene *(178)*, which then loses HCl, with ring expansion to form anisole[296].



(178)

Finally, substituted cyclopropanes of the type *(180)* can be obtained by metalation of oligochloromethyl phenyl sulfides[296,299]. Dichloromethyl phenyl sulfide



(179), M = K, Li

(180a), R = CH_3
(180b), R = OC_2H_5

[295] *U. Schöllkopf, A. Lerch,* and *J. Paust*, Chem. Ber. *96*, 2266 (1963).

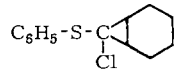
[296] *U. Schöllkopf* and *J. Paust*, Chem. Ber. *98*, 2221 (1965).

[297] *U. Schöllkopf* and *J. Paust*, Angew. Chem. *75*, 670 (1963).

[298] *J. Paust* and *U. Schöllkopf*, Angew. Chem. *77*, 262 (1965); *U. Schöllkopf, J. Paust, A. Al-Alzrak,* and *H. Schumacher*, Chem. Ber. *99*, 3391 (1966).

[299] *U. Schöllkopf, F. P. Woerner,* and *E. Wiskott*, Chem. Ber. *99*, 806 (1966).

and potassium t-butoxide presumably give phenylthiodichloromethylpotassium *(179)*, which reacts, either *via* chlorophenylthiocarbene or *via* the carbenoid, with isobutylene to form *(180a)* (yield 50 %) and with ketene acetal to form *(180b)* (yield 40–60 %). Cyclohexene presumably gives a mixture of the *exo* and *endo* forms of 7-chloro-7-phenylthionorcarane



(181)

(181) [296, 299]. Similarly, trichloromethyl phenyl sulfide reacts with methyl-lithium *via (179)*, M = Li, to form the cyclopropane derivative 1-chloro-2-methyl-1-phenylthiocyclopropane *(180a)* [296, 299].

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COMMUNICATIONS

Tetrakis[(alkali-metalphenylphosphino)methyl]-methanes and their Conversion into Metal-Containing and Metal-Free Spiroheterocycles [1]

By *J. Ellermann* and *F. Poersch*

Since reaction of the potassium cyanometalates(0) $K_6[Cr(CN)_6]$ and $K_4[Ni(CN)_4]$ with tetrakis[(diphenylphosphino)methyl]methane *(1)* [2] does not, like that of the isoelectronic metal carbonyls $Cr(CO)_6$ and $Ni(CO)_4$, yield spiro-heterocyclic complex compounds [3,4], but instead leads to their conversion into tetrakis[(potassiumphenylphosphino)methyl]methane [5], the direct preparation of compound *(2a)* and the analogous sodium derivative *(2b)* appeared to be of interest.

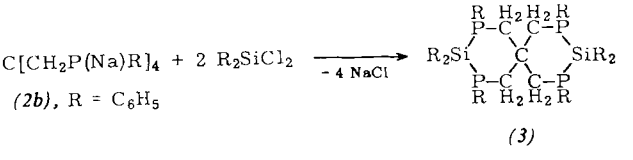
With this object we treated the phosphine *(1)* with potassium or sodium in liquid ammonia in the molar ratio 1:8 at −33 °C with vigorous stirring (reaction in dioxane [6] is extremely slow). A color change from blue through green accompanies formation of the orange-yellow compounds *(2a)* and *(2b)*, respectively. The C_6H_5M formed simultaneously undergoes ammonolysis in the liquid ammonia [7] to benzene and alkali-metal amide, the latter being subsequently

$$\underset{(1)}{C[CH_2P(C_6H_5)_2]_4} + 8\,M \xrightarrow[-33\,^\circ C]{NH_3} \underset{\substack{(2a),\ M=K\\(2b),\ M=Na}}{C[CH_2P(M)C_6H_5]_4} + 4\,C_6H_5M$$

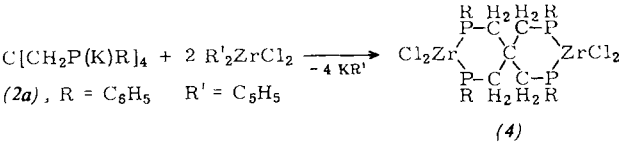
decomposed to NH_3 and alkali-metal bromide by an equimolar amount of NH_4Br [2]. After evaporation of the ammonia and benzene at room temperature, compounds *(2a)* and *(2b)* are separated from MBr by extraction with tetrahydrofuran, precipitated by petroleum ether (after concentration of the extract), filtered off, washed with petroleum ether, and dried in a high vacuum.

Compounds *(2a)* and *(2b)* are extremely sensitive to air and moisture and must be kept under argon; they dissolve readily in THF and ethanol but only slightly in benzene and are insoluble in aliphatic hydrocarbons. Because of the very high solubility in THF the yields are only *ca.* 75 to 80 % although, as is shown by determination of the alkali-metal bromides the conversion was almost quantitative. Elemental analysis, osmometric determination of molecular weights in THF, and IR spectra, which show only vibrations of the neopentane skeleton and of the $>P-C_6H_5$ group [3] [ν(P–Na) ≈ 860 cm^{-1}; ν(P–K) ≈ 410 cm^{-1} (?)], prove the structure of solvent-free products *(2a)* and *(2b)*. If the compounds are allowed to stand for about one hour in THF, the measured molecular weights are high; this is ascribed to formation of adducts (1:1 to 1:4) with the solvent. These products are unambiguously non-electrolytes according to conductivity measurements in THF.

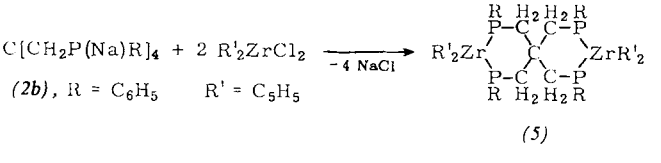
By virtue of their neopentane skeletons, compounds *(2a)* and *(2b)* behave preferentially as doubly bidentate reagents, so that treatment with 2 mols of an organo-non-metallic or organometallic dihalide leads to synthesis of covalent spiroheterocyclic products containing the non-metal or metal. In this way reaction of compound *(2b)* with dichloro(diphenyl)-silane [8] in THF at 60 °C in a sealed tube leads to a decrease in the intensity of color and formation, simultaneously, of a gelatinous NaCl precipitate and THF-soluble, pale pink 2,3,3,4,8,9,9,10-octaphenyl-2,4,8,10-tetraphospha-3,9-disilaspiro[5.5]undecane *(3)*, which can be filtered from NaCl and precipitated with petroleum ether. Its composition and structure are proved by elemental analysis, molecular-weight determination, and the IR spectrum. This product *(3)*, m.p. 126 °C, is readily soluble in THF, dioxane, or ethanol, but barely soluble in aromatic or aliphatic hydrocarbons.



(2b), R = C_6H_5 *(3)*



(2a), R = C_6H_5 R' = C_5H_5 *(4)*



(2b), R = C_6H_5 R' = C_5H_5 *(5)*

Reaction of dichlorodi-(π-cyclopentadienyl)zirconium [9] with compound *(2a)* leads to formation of cyclopentadienylpotassium (crystallizes out at *ca.* 20 °C) and pale brown 3,3,9,9-tetrachloro-2,4,8,10-tetraphenyl-2,4,8,10-tetraphospha-3,9-dizirconaspiro[5.5]undecane *(4)*, but that with *(2b)* leads to separation of NaCl and formation of yellowish-white 3,3,9,9-tetra-(π-cyclopentadienyl)-2,4,8,10-tetraphenyl-2,4,8,10-tetraphospha-3,9-dizirconaspiro[5.5]undecane *(5)*. The KC_5H_5 and NaCl, respectively, are formed quantitatively The product *(4)* can be isolated only in about 10 % yield on addition of petroleum ether, although *(5)* is obtained in almost quantitative yield.

Product *(4)*, which crystallizes with 1 mol of THF, was characterized by elemental analysis, product *(5)* [m.p. 270 °C (decomp.)] by elemental analysis, molecular-weight determination, and IR spectrum which shows the typical absorption of π-bonded C_5H_5 groups [10] as well as vibrations

of the neopentane skeleton and P–C_6H_5 groups[2,3]. Both compounds are readily soluble in THF or ethanol but insoluble in benzene or petroleum ether.

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[*] Dr. J. Ellermann
F. Poersch
Institut für Anorganische Chemie,
Universität Erlangen-Nürnberg
8520 Erlangen (Germany)
Fahrstrasse 17

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KP_{15}, a New Potassium Polyphosphide

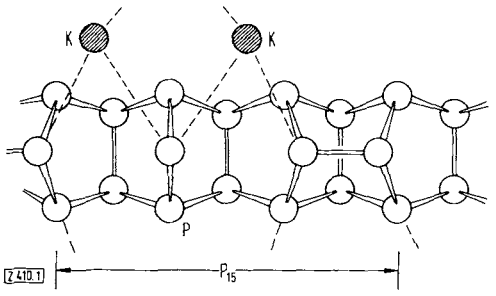
By *H. G. von Schnering* and *H. Schmidt* [*]

After a detailed study of the reaction conditions in the system K/P, red needles of a compound could be prepared that had been observed previously[1–4] but had not been accurately characterized. Elemental analysis and determination of the structure showed that it was potassium polyphosphide KP_{15}.

Preparation and Properties: Potassium and red phosphorus are heated at 650 °C in a sealed quartz ampoule (length 20 cm; temperature gradient 650/200 °C); the yield depends on the K:P ratio, 5 to 20 atoms-% of K being favorable; traces of water favor the deposition appreciably (chemical transport by way of phosphines?). KP_{15} is deposited at 300–320 °C as transparent, ruby, flat needles; it is odorless and is stable indefinitely in air. It is not attacked by H_2O and only slowly by concentrated oxidizing acids. Samples are decomposed for analysis by bromine-nitric acid in a sealed tube at 120 °C.

Structure: KP_{15} crystallizes in the triclinic form [$a = 23.74$, $b = 9.69$, $c = 7.21$ Å, $\alpha = 116.7°$, $\beta = 97.5°$, $\gamma = 90.0°$; space group $P\bar{1}$; $Z = 4$] with marked twinning parallel to (100). Studies of single crystals show the structure contains phosphorus units in the form of infinite tubes, unidimensional along [010], of pentagonal cross-section, and divisible into P_{15} units (see Figure). Of the 15 P atoms only one is bound to two other P atoms ($>P^{\ominus}$), the others being bound to three other P atoms ($>P$). Each potassium atom unites four $(P_{15})_{\infty}$ units to each other, so that a two-dimensional framework parallel to (100) results. Each potassium atom has 6 near neighbors (2 P< at 3.48 Å; 4 P< at 3.24 or 3.37 Å). If these linkages are also taken into account, then the P_{15} unit contains P atoms linked in three different ways: (I) K–P<K, (II) K–P<, (III) :P<; (I) and (II) have a tetrahedral and (III) a pyramidal structure. The P–P distances are 2.18 to 2.30 Å; the bond angles at the phosphorus are between 93 and 112 °. If the peculiar relation of (I) to the K–P distances [d(K–P<) > d(K–P<)] is considered, the view that K^+ and P_{15}^- ions exist becomes tenable.

The structures of KP_{15} and of $HgPbP_{14}$[4] (here P< is replaced by Pb and one P–P bridge is missing) shows that P_5 units play a part in such polyphosphides (see Figure). Mention should also be made of the compounds KP_{10}[1] and TlP_5[5], whose structures are not yet known. *Thurn* and *Krebs*[6] have demonstrated recently that such tubular phosphorus units are in fact structural elements of violet phosphorus.



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[*] Prof. Dr. H. G. von Schnering
and Dipl.-Chem. H. Schmidt
Anorganisch-Chemisches Institut der Universität
Hindenburgplatz 55
44 Münster (Germany)

[1] *H. D. Korte*, Dissertation, Universität Münster, 1960.

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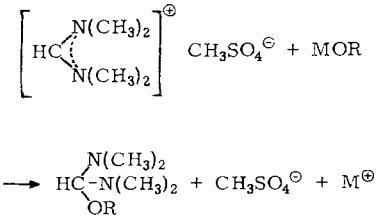
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Stability of Aminal Esters and their Reactions with Aromatic Aldehydes

By *H. Bredereck, G. Simchen, H. Hoffmann, P. Horn*, and *R. Wahl* [*]

Since the synthesis of bis(dimethylamino)methoxymethane *(1a)*[1], we have prepared further aminal esters *(1)*[2–4] by treating *N,N,N',N'*-tetramethylformamidinium methyl sulfate[1] with sodium or potassium alkoxide (molar ratio 1:1) in ether or cyclohexane at room temperature. After filtration and distillation of the solvent under vacuum, the aminal esters *(1)* were obtained. Their purity was established by NMR spectrometry.



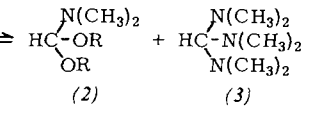
(1) M = Na, K

R	Yield (%)	Content of *(1)* in equil. mixture (%) [a]
(1a) CH_3	62 [1]	62–64
(1b) $C_2H_5C_3H_7$	60 [2]	62–66
(1c) iso-C_3H_7	45 [2]	54
(1d) t-C_4H_9	68 [3,4]	32–33

[a] After standing at room temperature; the content of *(1)* was determined by NMR spectrometry.

If the aminal esters are warmed to 100 °C or allowed to stand for about a week at room temperature, partial dismutation into *N,N*-dimethylformamide acetals *(2)* and tris(dimethylamino)methane *(3)* occurs [2].

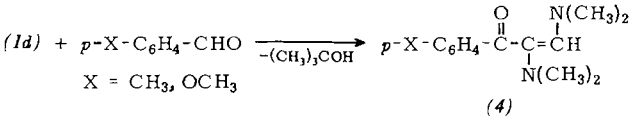
When allowed to stand for several hours, equimolar mixtures of *(2)* and *(3)* undergo the reverse reaction to give the corresponding aminal esters *(1)* [2]. Pure aminal ester has not been isolated from such equilibrium mixtures.



(2) *(3)*

The reaction of bis(dimethylamino)-t-butoxymethane *(1d)* with aromatic aldehydes adopts a surprising course. If the reaction components (molar ratio 3:1) are warmed for 3–4 h at 110–140 °C, t-butyl alcohol distils off, the reaction being analogous to that of CH-acidic compounds [4,6].

In the case of reactions with *p*-tolualdehyde or *p*-anisaldehyde, contrary to expectation, 1,2-bis(dimethylamino)vinyl aryl ketone may be isolated in 30 % yield by fractional distillation of the reaction mixture.



(4)

The structure of the product *(4a)* [*(4)* with X = CH_3, m.p. 114 °C] was proved by independent synthesis from dimethylaminomethyl *p*-tolyl ketone and bis(dimethylamino)-t-butoxymethane *(1d)* [5]. The structure *(4b)* [*(4)* with X = OCH_3, m.p. 85–87 °C] follows from comparison of the NMR spectra with that of *(4a)*.

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[*] Dr. H. Bredereck, Dr. G. Simchen,
Dipl.-Chem. H. Hoffmann, Dipl.-Chem. P. Horn, and
Dipl.-Chem. R. Wahl
Institut für Organische Chemie der Technischen Hochschule
Azenbergstr. 14/16
7 Stuttgart (Germany)

[1] *H. Bredereck, F. Effenberger*, and *G. Simchen*, Chem. Ber. *98*, 1078 (1965); Angew. Chem. *74*, 353 (1962); Angew. Chem. internat. Edit. *1*, 331 (1962).

[2] *H. Hoffmann*, unpublished.

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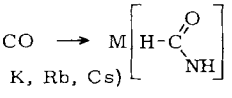
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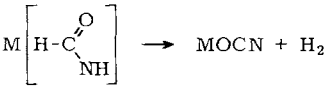
Carbonylation of Metal Amides to Metal Formamides

By *R. Nast* and *P. Dilly* [*]

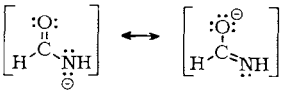
Sodium and potassium formamide have hitherto been accessible only by treatment of formamide with the corresponding metal amide in liquid ammonia [1]. We have found that solutions or suspensions of alkali-metal amides in liquid ammonia react in general with gaseous CO at normal pressure and about −45 °C, giving the alkali-metal formamide in quantitative yield:



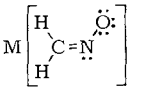
Pure gaseous CO is passed with a streaming velocity of at least 25 l/h, with rigid exclusion of moisture, through a solution of about 25 mmoles of MNH_2 (M = K, Rb, or Cs) in *ca.* 100 ml of liquid ammonia at about −45 °C for 2 h. The alkali-metal formamide is precipitated as a pure, colorless crystalline powder either at once or on concentration of the solution. Even $NaNH_2$, which is sparingly soluble in liquid ammonia, can be carbonylated quantitatively in this way since sodium formamide is more soluble than $NaNH_2$ in NH_3. The streaming velocity of CO should not be lower than the value given above, since prolonged action of an excess of $NH_2^{\ominus}$ dehydrogenates the alkali-metal formamide to the corresponding cyanate:



The alkali-metal formamides are very hygroscopic and are hydrolysed by water to formamide and by an excess of caustic alkali to formates. The ν_{CO} frequencies that appear in their IR spectra at 1580–1590 cm^{-1} ("amide-I bands") are substantially independent of the alkali-metal ion and are at about 100 cm^{-1} lower than for free formamide [2]. This indicates marked contribution of the polar carbonyl



structure to the bond structure of the formamide anion. The presence of the isomeric alkali formoximates can thus be excluded.



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[*] Prof. Dr. R. Nast and Dipl.-Chem. P. Dilly
Institut für Anorganische Chemie der Universität
Papendamm 6
2 Hamburg 13 (Germany)

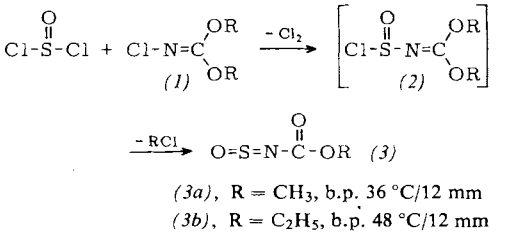
[1] *E. C. Franklin*, J. Amer. chem. Soc. *55*, 4915 (1933).

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Synthesis of *N*-Sulfinylurethanes

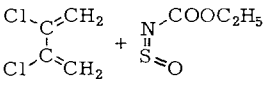
By *H.-H. Hörhold* [*]

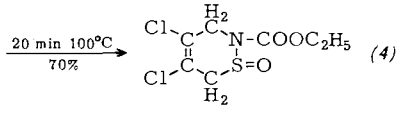
We have found that *N*-sulfinylurethanes can be synthesized in *ca.* 50 % yield by treating *N*-chloroiminocarbonic esters *(1)* with thionyl chloride. The reaction begins below 0 °C with evolution of chlorine and continues with elimination of alkyl chloride when the temperature is raised. It is thus assumed that the thermally unstable (chlorosulfinylimino)-carbonic esters *(2)* occur as intermediates.



(3a), R = CH_3, b.p. 36 °C/12 mm
(3b), R = C_2H_5, b.p. 48 °C/12 mm

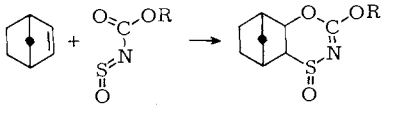
Compounds *(3a)* and *(3b)* are colorless liquids, and extremely sensitive to moisture. Their structures are proved by their compositions, their molecular weights (138 for *(3b)*, cryoscopically in benzene), hydrolysis to sulfur dioxide and the corresponding alkylurethanes, and their IR spectra, measured in the gas phase and showing the characteristic bands for the O=S=N group (1135 cm^{-1}, 1250 cm^{-1}, 1290 cm^{-1}, the last perhaps ν_{C-O}) and the C=O group (1790 cm^{-1}). In *N*-sulfinylurethanes, as in *N*-(benzenesulfonyl)sulfinylimines[1], the S=N double bond is activated for addition reactions. Reaction with 1,3-dienes readily gives 1:1 adducts, such as *(4)*, in which the alkoxycarbonyl group is retained.





(4): $\nu_{C=O}$ = 1735 cm^{-1}, m.p. 92–93 °C colorless crystals

A 1:1 adduct is formed surprisingly easily from *(3)*, R = C_2H_5, and norbornene; after heating equimolar quantities of these compounds in anhydrous ether for 1 h, the adduct crystallizes in *ca.* 80 % yield as colorless crystals of m.p. 79–81 °C. The IR spectrum (KBr) shows no absorption in the region of C=O bands but a strong band at 1600 cm^{-1} ($\nu_{C=N}$). Thus it follows that the carbonyl group has been involved in the addition reaction whose formulation as a 1,4-addition is probable:



Ethyl N-sulfinylurethane (3b):

70 g of diethyl *N*-chloroiminocarbonate is added, over a period of 1 h, to 160 ml of $SOCl_2$ with stirring and cooling (0 °C). The chlorine liberated is removed from the reaction mixture in a stream of dry argon. When evolution of chlorine ceases the mixture is stirred for a further 2 h at room temperature and the excess of $SOCl_2$ is distilled off in a vacuum at 30 °C (maximum bath temperature). The oily colorless residue is then further heated in a vacuum by placing the distillation flask in a preheated bath (120–130 °C). Ethyl *N*-sulfinyl urethane *(3b)* distils over and is collected in a cooled receiver. After repeated distillation at 12 mm the ethyl *N*-sulfinylurethane is obtained as a colorless liquid (yield 25–35 g). Compound *(3a)* is obtained analogously as a colorless liquid in 41 % yield.

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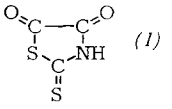
[*] Dr. H.-H. Hörhold
Institut für Organische Chemie und Biochemie der Universität
Humboldtstr. 10
X 69 Jena (Germany)

[1] *G. Kresze et al.*, Angew. Chem. *74*, 135 (1962); Angew. Chem. internat. Edit. *1*, 89 (1962).

2-Thioxo-1,3-thiazolidine-4,5-dione [1]

By *V. Hahnkamm* and *G. Gattow*[*]

Whereas the wine-red 2-thioxo-1,3-dithiolane-4,5-dione[2] is formed on treatment of trithiocarbonic acid $SC(SH)_2$ with oxalyl chloride, 2-thioxo-1,3-thiazolidine-4,5-dione *(1)* (which crystallizes in orange needles) was obtained for the first time by a similar reaction of dithiocarbamic acid[3].



A dilute solution of $(COCl)_2$ in $CHCl_3$ is added in excess, with exclusion of air and moisture, to a suspension of $SC(SH)(NH_2)$ or $NH_4[SC(S)(NH_2)]$ in $CHCl_3$; the reaction, which involves evolution of HCl or formation of NH_4Cl, respectively, is complete after the reactants have been stirred in a stream of N_2 for 5 h. The product *(1)* is obtained by distillation of $CHCl_3$ from the filtrate and is purified by recrystallization from petroleum ether (yield, about 60 %).

Compound *(1)* (m.p. 119 ± 1 °C, d_4^{25} = 1.795 ± 0.005 g/cm^3) is very soluble in water and alcohols, moderately soluble in $CHCl_3$, benzene, and ether, but only sparingly soluble in aliphatic hydrocarbons. Its mass spectrum shows, besides fragments, a strong peak at *m/e* = 147 [theoretical for the molecular weight of *(1)*, 147.18].

Compound *(1)* reacts acid in water and forms colored soluble complexes or precipitates with numerous heavy-metal ions, *e.g.*, with Fe^{3+} a pale red complex, with Ni^{2+} a deep red complex, with Cu^{2+} a red-brown precipitate, with Pb^{2+} an orange-yellow precipitate, and with Tl^{+} a pale brown precipitate.

IR spectrum of *(1)*: 3250 (m), 1742 (s), 1490 (w), 1426 (s), 1303 (m), 1220 (s), 1100 (w), 1075 (s), 974 (w), 948 (m), 748 (m), 637 (m), 552 (w), 530 (w), 485 (m) cm^{-1} [4].

X-Ray studies by use of rotating-crystal, equator Weissenberg, and equi-inclination Weissenberg photographs showed that *(1)* is monoclinic with *Z* = 4 formula units in the elementary cell; *a* = 9.30 ± 0.05, *b* = 5.08 ± 0.03, *c* = 11.35 ± 0.06 Å, β = 93.5 ± 0.5 °; X-ray density d_R = 1.82$_6$ g/cm^3. The space group C_{2h}^5–$P2_1/a$ (No. 14) follows from the extinctions [(*h*0*l*) only with *h* = 2*n*, and (0*k*0) only with *k* = 2*n*]; $C_{2h}^{1,2,4}$, $C_2^{1,2}$, and $C_s^{1,2}$ are also possible.

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[*] Dipl.-Chem. V. Hahnkamm and Prof. Dr. G. Gattow
Institut für Anorganische Chemie und Kernchemie
der Universität
Joh.-Joachim-Becher-Weg 24
65 Mainz (Germany)

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[3] Cf. Part XXV, cited in [1].

[4] s = strong, m = medium, w = weak.

Six Oxidation States of the Iron-Phthalocyanine Complex

By *R. Taube* and *H. Drevs*[*]

The iron-phthalocyanine complex [FePc] is of particular interest because, *inter alia*, of the great similarity of the structure of this complex to that of the biochemically important heme. We have found that iron(II) phthalocyanine[1], and also other metal phthalocyanines, can be reduced in tetrahydrofuran (THF) in four stages:

$$[FePc] + n\,e^- \rightarrow [FePc]^{n-}.$$

Only the first two reduction states have hirtherto been isolated, and closely studied, as crystalline lithium salts containing tetrahydrofuran, Li[FePc]·4.5 THF *(1)* and Li_2[FePc]·5.5 THF *(2)* [2]. We have now obtained the third and the fourth reduction states in pure crystalline form.

In order to prepare the third reduction state, pure recrystallized *(2)* in boiling THF was treated with a solution of dilithiobenzophenone in THF in the molar ratio 1:3. The third reduction state precipitates immediately. The dry compound forms dark olive-green crystals of composition Li_3[FePc]·8THF *(3)*, which are very slightly soluble in THF but somewhat more soluble in dimethylformamide (DMF), to give intensely reddish-violet solutions.

The fourth reduction state was obtained in the same manner, by treatment of *(2)* with dilithiostilbene, as violet crystals of composition Li_4[FePc]·9 THF *(4)*.

The compound dissolves in THF to form an intensely bluish-green solution. It dissolves also in DMF but then rapidly decomposes with development of a violet color.

The salts *(3)* and *(4)* are oxidized in air, with loss of tetrahydrofuran, *(4)* occasionally becoming incandescent. On oxidation of *(3)* and *(4)* with iodine in THF in the absence of air, 2.95 and 3.91 atoms, respectively, of iodine are consumed and [FePc] is formed. The electrolytic character of compounds *(3)* and *(4)* could be proved by transfer experiments in DMF or THF. Magnetic measurements by Gouy's method at temperatures between 83 and 293 °K substantiated the applicability of the Curie-Weiss law, $\chi_M = C/T + \theta$.

Values found were[3]:

for *(3)*: $\theta = 35$ °K, $\chi_g(293\ °K) = 1.44\times10^{-6}$ cm³/g, $\mu'_{eff} = 2.60$ B.M. [4]

for *(4)*: $\theta = 12$ °K, $\chi_g(293\ °K) = 3.08\times10^{-6}$ cm³/g, $\mu'_{eff} = 3.43$ B.M. [4]

It follows that *(3)* and *(4)* are formed from *(2)* by stepwise addition of electrons to the iron-phthalocyanine complex. If we include FePcCl, which has been described by *Barrett et al.* [5], and whose structure as iron(III) phthalocyanine chloride we finally proved [6], we now know six iron-phthalocyanine complexes of differing total electron numbers.

Model calculations by the simplified LCAO–MO method [7] lead to the following electron configurations, which agree with the observed magnetic moments in respect of the number (*n*) of unpaired electrons:

Formula	Electron configuration	*n*	$\mu_{eff.}$ (293 °K) [8]
[FePc]Cl	$(b_{2g})^2(6e_g)^2(2a_{1g})^1$	3	4.35 B.M. [6]
[FePc]	$(b_{2g})^2(6e_g)^3(2a_{1g})^1$	2	3.90 B.M. [9]
Li[FePc]·4.5 THF	$(b_{2g})^2(6e_g)^4(2a_{1g})^1$	1	2.12 B.M. [2]
Li_2[FePc]·5.5 THF	$(b_{2g})^2(6e_g)^4(2a_{1g})^2$	0	0.31 B.M. [2]
Li_3[FePc]·8 THF	$(b_{2g})^2(6e_g)^4(2a_{1g})^2(7e_g)^1$	1	2.46 B.M.
Li_4[FePc]9 THF	$(b_{2g})^2(6e_g)^4(2a_{1g})^2(7e_g)^2$	2	3.36 B.M.

Greatly simplifying, one can regard the electrons in the molecular orbitals $2a_{1g}$, $6e_g$, and b_{2g} as d-electrons of the central atom and the electrons in the $7e_g$ orbitals as π-electrons of the phthalocyanine [7]. One can then describe the stepwise addition of electrons to the iron-phthalocyanine complex $[FePc]^+$ as a lowering of the oxidation state of the central atom from +3 to 0, which is followed by an increase in the negative charge on the phthalocyanine from −2 to −3 and −4 in the complexes *(3)* and *(4)*, respectively. The reducibility of the phthalocyanine, which theoretically corresponds to occupation of its lowest antibonding π-orbitals $6e_g$ [7], is proved by the existence of electron-rich lithium [10] and zinc phthalocyanines [11].

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[*] Doz. Dr. R. Taube and Dipl.-Chem. H. Drevs
Institut für Anorganische Chemie der Universität
Soldtmannstr. 16
X 22 Greifswald (Germany)

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1-Hexadecene, an Intermediate in the Microbial Oxidation of n-Hexadecane *in vivo* and *in vitro* [1]

By *F. Wagner, W. Zahn*, and *U. Bühring* [*]

Primary alcohols, aldehydes, and carboxylic acids have been identified as intermediates in microbial oxidation of higher n-alkanes [2]; these intermediates contain the same number of carbon atoms as the original n-alkane. There is, however, little agreement about the first step in enzymic attack on an n-alkane; hydroxylation [3], hydroperoxidation, and dehydrogenation to the 1-alkene have been considered, but neither an alkyl hydroperoxide [2] nor an n-alkene [2,4] could be isolated and unambiguously characterized.

We have, for the first time, been able to isolate and identify 1-hexadecene as intermediate after cultivation of *Micrococcus cerificans, Mycobacterium phlei, Nocardia sp., Pseudomonas sp.*, or *Rhodotorula sp.* in an inorganic salt solution with alkene-free n-hexadecane [5] as sole source of carbon.

After aerobic cultivation of *Nocardia* sp. for 26 h in 6 liters of inorganic salt solution [5a] containing 100 g of purified n-hexadecane, we obtained 170 g of wet bacterial mass (*ca.* 60 % water content) after centrifugation and washing during the logarithmic growth phase. This material was extracted with acetone and then diethyl ether. The residue obtained on concentration of the united extracts was chromatographed on a silica gel column (diam. 4 cm, length 20 cm). Petroleum ether (b.p. 60–80 °C) eluted a mixture of n-hexadecane and 1-hexadecene, which was separated chromatographically by means of the mercury-hexadecene adduct; the adduct was cleaved by methanolic HCl [7]. After further chromatographic purification on silica gel thin-layer plates [6], 7 mg of pure 1-hexadecene was obtained. This was identified by IR-spectroscopic, gas-chromatographic, and thin-layer chromatographic comparison with an authentic specimen. The terminal double bond of the 1-hexadecene was also authenticated by oxidation with $KMnO_4$, in acetone containing acetic acid, to yield pentadecanoic acid which was identified by gas chromatography after esterification with diazomethane.

We also obtained 1-hexadecene (0.01 mg) when a crude enzyme extract [6a] from *Nocardia* sp. (1 g of protein in 75 ml of 0.1 M phosphate buffer of pH = 7.0) was stirred for 2 h at 30 ° with 1.5 g of *n*-hexadecane. It was isolated and chromatographically identified as above.

The role of 1-hexadecene as intermediate in the microbial oxidation of *n*-hexadecane is explained by the fact that it is easily oxidized further *in vivo* and *in vitro*.

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[*] Dr. F. Wagner, Dipl.-Chem. W. Zahn, and cand. chem. U. Bühring
Institut für Biochemie und Biotechnologie
der Technischen Hochschule
Azenbergstr. 14
7 Stuttgart (Germany)

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[5] 100 ml Hexadecane purum (olefin content *ca.* 0.001 %; Fa. Fluka, Buchs, Switzerland) was shaken with a 1 % methanolic solution (100 ml) of mercury(II) acetate for 15 h at room temperature. After separation from the methanolic phase, the hexadecane phase was washed with water, placed on a silica gel column (diam. 4 cm, length 20 cm), and eluted with petroleum ether (500 ml; b.p. 40–60 °C). The eluate was freed from petroleum ether in a vacuum. The residue consisted of hexadecane containing less than 0.0001 % of alkene, as shown by chromatographic determination of the Hg adduct with diphenylcarbazone [6].

[5a] Composition: NH_4NO_3, 2 g/l; KH_2PO_4, 1 g/l; K_2HPO_4, 2 g/l; $Na_2HPO_4 \cdot 12\,H_2O$, 2 g/l; $MgSO_4 \cdot 7\,H_2O$, 0.2 g/l.

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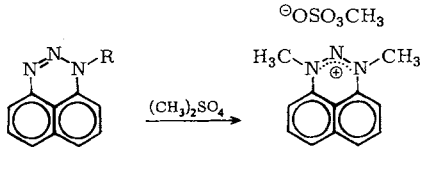
[6a] Preparation: A 20 g (wet weight) cell was broken at −25 °C by means of an X-Press (Biox Company, Sweden) and extracted three times with 25 ml of 0.1 M phosphate buffer (pH = 7.0). The extract was centrifuged (20000 *g*) for 20 min at +4 °C. The supernatant fraction was the crude enzyme extract.

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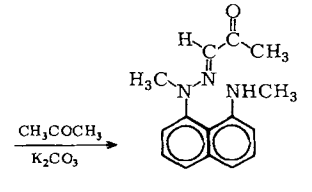
A Novel Ring Fission of a 1,3-Dimethyl-1*H*-naphtho[1,8-*de*]-1,2,3-triazinium Salt

By *H. Beecken*[*]

If methylation of 1*H*-naphtho[1,8-*de*]-1,2,3-triazine *(1)* with dimethyl sulfate is carried out, not in alcoholic alkali[1], but in acetone containing potassium carbonate[2], then the two known methyl derivatives – the orange *(2)* and the blue 2-methyl isomer – are accompanied by larger amounts of 1,3-dimethyl-1*H*-naphtho[1,8-*de*]-1,2,3-triazinium methyl sulfate *(3)* and a pale yellow compound *(4)*, the relative yields depending on the excess of methylating agent and on the reaction time.



(1), R = H *(2)*, R = CH_3 *(3)*



(4)

On thin-layer chromatography on silica gel G (solvent: benzene/ethyl acetate 14:1 v/v) the products give R_F values: 0.01 *(3)*, 0.30 *(4)*, 0.45 *(2)*, and 0.56 (blue isomer).

The compound *(4)* is better obtained by starting from pure *(3)*, which is obtained in 96.5 % yield from *(2)* and dimethyl sulfate in boiling benzene [2].

(3): brown-violet crystals, m.p. 263–265 °C (from acetonitrile; decomp.), λ_{max} (in methanol) = 503, 332, 318, 306, 227 mμ with log ε = 3.13, 3.86, 3.85, 3.77, 4.89. The structure of *(3)* follows from the bathochromic shift of the longest wavelength band in comparison with *(2)* [in methanol, *(2)* has λ_{max} = 454, 337, 276, 230 mμ with log ε = 2.99, 4.07, 3.59, 4.63; in methanolic hydrochloric acid *(1)* absorbs at λ_{max} = 505, 332, 318, 305 (sh), 224 mμ with log ε = 2.99, 3.83, 3.79, –, 4.79], and also from the fact that, under the same conditions, the blue 2-methyl isomer gives no quaternary salt with dimethyl sulfate, and from studies[3] of quaternary salt formation in the naphtho[1,2-*d*]triazole system.

The hydrazone *(4)*, pale yellow prisms, m.p. 111 °C (from benzene/petroleum ether), is obtained together with *(2)* when *(3)* is boiled in acetone in the presence of anhydrous potassium carbonate. The product *(4)* is separated as a more slowly migrating zone from *(2)* by chromatography on aluminum oxide (activity II, neutral; eluent, petroleum ether/benzene 1:1.3 v/v). Its structure is proved by elemental analysis, the UV spectrum [λ_{max} (in methanol) = 343, 296, 253, 228, 208 mμ with log ε = 4.05, 4.28, 4.30, 4.33, 4.63], the IR spectrum [in KBr; ν_{N-H} = 3460 cm^{-1}, $\nu_{C=O}$ = 1678 cm^{-1}, $\nu_{C=N}$ = 1660 cm^{-1}], and the mass spectrum [*m/e* = 255 (calc. mol. wt. 255.3), 240 (weak), 212 (medium), 199/197 (medium), 185 (strongest peak; corresponds to cleavage of the N–N bond)]. The NMR spectrum confirms this structure.

The formation of *(4)* from *(3)* can be explained in either of two ways involving attack by a hydroxide ion: (i) attack on N atom 2 of the cation of *(3)*; the resulting *N*-hydroxy compound opens to a nitrosoamine that condenses with acetone to give the hydrazone *(4)*; or (ii) hydroxide ions produce acetone anions that are then bound to N atom 2; the intermediate is stabilized by ring opening with formation of a conjugated C=N double bond and proton shift.

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[*] Dr. H. Beecken
Farbenfabriken Bayer A.G.
509 Leverkusen-Bayerwerk (Germany)

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ESR Spectrum of a Non-Degenerate State of the Benzene Radical Anion

By *W. Köhnlein, K. W. Böddeker*, and *U. Schindewolf*[*]

Benzene radical anions, $C_6H_6^-$, are obtained on reduction of benzene with alkali metals in solvent systems which dissolve the metals with formation of solvated electrons (*e.g.* tetrahydrofuran [THF], dimethoxyethane [DME]). The ESR spectrum of this anion[1] consists of a septet with binomial distribution of intensities and a hyperfine splitting of 3.75 gauss.

While investigating the temperature dependence of formation of the benzene radical anion in THF/DME with liquid K/Na alloy, we observed that the ESR septet found at low temperatures (below about −20 °C) (Fig. 1) gives way on warming to a new spectrum (Fig. 2) with 15 lines at the same *g*-value.

The new spectrum consists of a triplet, the lines of which are each split further into a quintet. The hyperfine splitting of the triplet (6.5 gauss) is about four times that of the quintets (1.7 gauss). Both triplet and quintet again show binomial distribution of intensities. Parallel to the change of the ESR

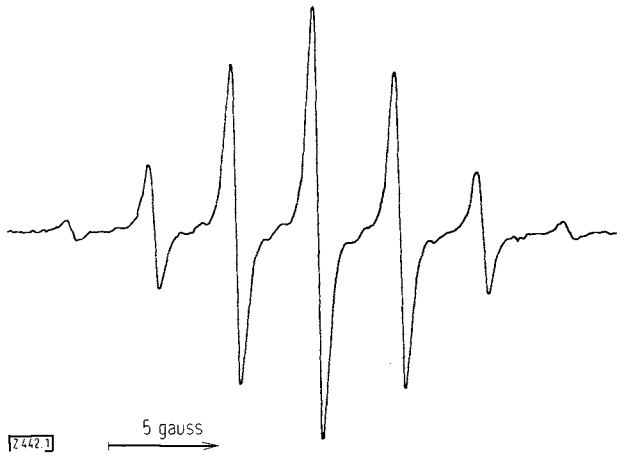


Fig. 1. ESR spectrum of the benzene radical anion in THF/DME at −30 °C in the presence of alkali metal.

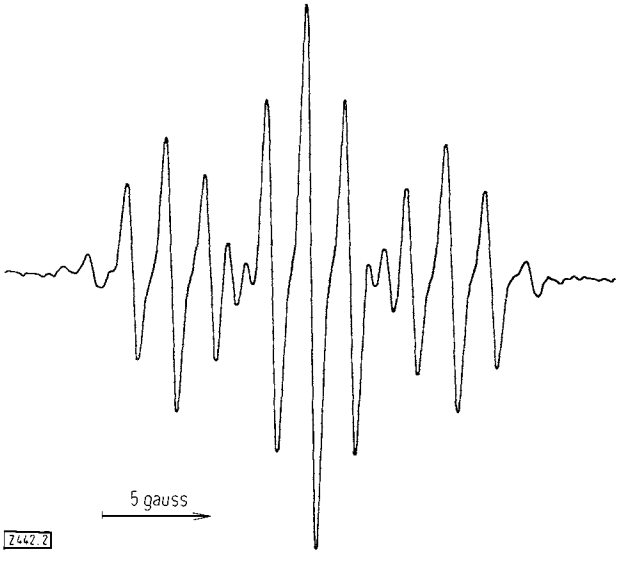
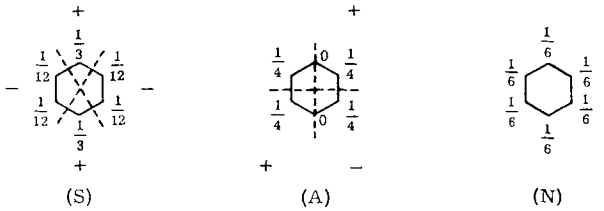


Fig. 2. ESR spectrum of the benzene radical anion in THF/DME at −30 °C after warming to 0 °C and recooling in the absence of alkali metal.

signal the color of the solution changes from deep green to brown-yellow. On cooling in the presence of alkali metal, the color of the solution changes to green again and the original 7-line spectrum is observed. In the absence of metal, however, the brown-yellow solution and its 15-line spectrum persist when the system is cooled.

According to the Hückel-MO theory, the ground state of the benzene radical anion consists of two degenerate states which differ in the distribution of spin density of the unpaired electron about the six C-atoms; the electronic wave functions of the two states are, respectively, symmetrical (S) and antisymmetrical (A) with respect to a plane of symmetry through opposite C-atoms perpendicular to the plane of the ring[2]. (The numbers on the formulae represent the spin densities at the C-atoms; + and − refer to the sign of the electronic wave functions.)



In the normal form of the undisturbed benzene radical anion, (N), resulting from mixing of the two degenerate states, the spin densities are evenly distributed and the ESR spectrum shows the well known septet.

Through perturbation of the symmetry the degeneracy can be removed. For example, in the radical anions of monodeutero benzene[3] and mono- and *p*-dialkylbenzene[4] state (A) is occupied preferentially; correspondingly, the ESR spectra of these anions basically consist of a quintet, with further hyperfine splitting depending on the system considered.

The 15-line spectrum reported here may be interpreted as resulting from the removal of degeneracy in favor of state (S) through interactions with alkali metal ions. Corresponding to the distribution of electron spin densities, the ESR spectrum of this state is expected to show a triplet with a further quintet splitting of the three lines; the triplet hyperfine splitting should be four times larger than the quintet splitting.

The spectra were recorded on an ESR spectrometer AEG 20–X. Samples were prepared by distilling the reagents (25 mg K plus 15 mg Na; 4 ml THF [Merck, for chromatography], 2 ml DME [Merck, for synthesis], and 0.5 ml benzene [Merck, for gas chromatography]; all reagents purified by distillation or drying over $LiAlH_4$) into the reaction vessel sealed to a vacuum line and furnished with a suitable side arm for recording the spectra.

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[*] Dr. W. Köhnlein
Institut für Strahlenchemie,
Kernforschungszentrum Karlsruhe
Present address: Institut für Strahlenbiologie der Universität
Hittorfstr. 17
44 Münster (Germany)

Dr. K. W. Böddeker and Doz. Dr. U. Schindewolf
Institut für Kernverfahrenstechnik der Technischen
Hochschule und des Kernforschungszentrums
Postfach 947
75 Karlsruhe (Germany)

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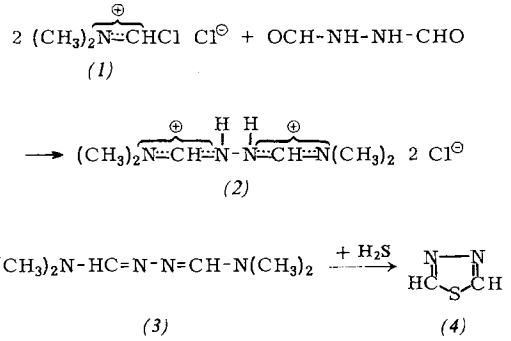
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A Simple Synthesis of 1,3,4-Thiadiazole

By *B. Föhlisch, R. Braun*, and *K. W. Schultze*[*]

1,3,4-Thiadiazole *(4)* was first synthesized by *Goerdeler, Ohm*, and *Tegtmeyer*[1], who used a four-stage process that started from thiosemicarbazide. *Jensen* and *Pedersen*[2] obtained the heterocycle from hydrazine and potassium dithioformate.

Our synthesis, by which quite large amounts of thiadiazole can be obtained, starts from *N,N*-dimethylformamide azine dihydrochloride *(2)*, which is obtained in 80–90 % yield



from dimethylformamidoyl chloride *(1)*[3] and *N,N'*-diformylhydrazine or hydrazine dihydrochloride. Sodium ethoxide converts compound *(2)* into the free dimethylformamide azine *(3)*; this reacts with H_2S at room temperature with loss of dimethylamine and formation of 1,3,4-thiadiazole *(4)* in 80 % yield. When treated with H_2S in methanol in the presence of 2 molar equivalents of sodium methoxide, the hydrochloride *(2)* gives *(4)* directly.

The ^1H–NMR spectrum of *(4)* in $DCCl_3$ shows a singlet at $\tau = 0.72$, $J_{^{13}C-H} = 213.5$ Hz.

Synthesis of (2):

Phosgene[5] (0.02 mole) is added dropwise to a solution of *N,N'*-diformylhydrazine[4] (8.8 g, 0.1 mole) in anhydrous dimethylformamide (100 ml) and methylene chloride (100 ml) at 0 °C (evolution of gas). The mixture is boiled for 20 h under reflux, and the precipitate is filtered off and purified by means of boiling chloroform. Yield, 18.6 g (86 %) of a colorless crystalline powder, m.p. 240–242 °C (decomp.).

Synthesis of (3):

An ice-cooled suspension of 10 g of *(2)* in ethanol (50 ml) is treated with 2 molar equiv. of sodium ethoxide solution. The sodium chloride is centrifuged off, the ethanol removed in a vacuum, and the residue crystallized from benzene, Yield, 6.3 g (95 %) of colorless plates, m.p. 75–76 °C. Dipicrate, yellow needles, m.p. 196–197 °C (from ethanol).

1,3,4-Thiazodiazole (4):

An ice-cooled solution of compound *(3)* (15 g) in methanol (75 ml) is saturated with H_2S. The reaction mixture is kept overnight at room temperature and the product *(4)* is subsequently isolated by vacuum-distillation. Yield, 7.3 g (80 %) of a colorless crystalline mass, b.p. 80 °C/11 mm, m.p. 42–43 °C (lit.[1], b.p. 82–83.5 °C/13 mm, m.p. 42–43 °C).

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[*] Dr. B. Föhlisch, cand. chem. R. Braun, and
Dipl.-Chem. K.W. Schultze
Institut für Organische Chemie der Technischen Hochschule
Azenbergstr. 14–16
7 Stuttgart N (Germany)

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Synthesis of Nucleoside Diphosphates by means of Di-(2,2,2-trichloroethyl) Phosphorochloridate

By *F. Eckstein* and *K. H. Scheit*[*]

Phosphoric acid diester chlorides whose ester groups can be removed by Pd/H[1], alkali[2], or bromine[3] have been used for the preparation of nucleoside phosphates. We have found that the readily accessible[4] di-(2,2,2-trichloroethyl) phosphorochloridate (m.p. 37–42 °C) is excellently suited for phosphorylation of nucleosides because of the simple isolation of the nucleoside di-(2,2,2-trichloroethyl) phosphate and the mildness of the conditions needed for removal of the trichloroethyl groups.

We condensed some protected nucleosides with the diester chloride (1.2 equiv.) in pyridine (0 °C, 12 h). Evaporating the pyridine, taking up the residue in chloroform, and extracting the solution with aqueous $NaHCO_3$ gave the nucleoside di-(2,2,2-trichloroethyl) phosphate. On treatment with Zn/Cu in dimethylformamide (50 °C, 1 h)[5] or with Zn dust in 80 % acetic acid (room temp., 1 h) the triester was cleaved mainly to nucleoside phosphate with a small amount of nucleoside 2,2,2-trichloroethyl hydrogen phosphate (see Table). The nucleoside phosphates were isolated by chromatography an DAEA-cellulose. They did not contain inorganic phosphate as impurity.

The triesters are hydrolysed by concentrated ammonia solution (2 h) to nucleoside 2,2,2-trichloroethyl hydrogen phosphate (80 %) and nucleoside (20 %).

^{32}P-labeled nucleoside phosphates should also be readily preparable by this method.

Starting material	Yield (%) of triester	Reduction with Zn/Cu in DMF Yield [a] (%) of	
		nucleoside phosphate	nucleoside trichloroethyl phosphate
5'-Tritylthymidine	95	95 [b]	5 [b]
3'-Acetylthymidine	80	82 [c]	10
3'-Acetyl-2'-deoxyuridine [d]	62 [e]	71 [f]	9
2',3'-Isopropylideneuridine	95	72	9
2',3'-Isopropylideneinosine	80 [g]	86	14

[a] Determined spectrophotometrically after separation by paper chromatography.

[b] After removal of the trityl group.

[c] + 8 % of deacetylated product.

[d] M.p. 171–174 °C.

[e] M.p. 126–127 °C.

[f] + 20 % of deacetylated product.

[g] M.p. 164–165 °C.

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[*] Dr. F. Eckstein and Dr. K. H. Scheit
Max-Planck-Institut für experimentelle Medizin
Abteilung Chemie
Hermann-Rein-Str. 3
34 Göttingen (Germany)

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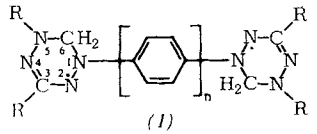
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Bisverdazyls $N^1,N^{1'}$-Linked by Aromatic Systems[1]

By *F. A. Neugebauer, H. Trischmann*, and *M. Jenne*[*]

Whereas in solution and in the solid state the bisverdazyl *(1a)* exists in temperature-dependent equilibrium with the "electron-isomeric" diamagnetic form *(2a)*[2], the bisverdazyl *(1b)* occurs in the solid state up to 77 °K as a diradical ($\mu/\mu B = 2.43$). However, as shown by the absorption spectrum (298 °K; shoulder at 500 nm; 98 °K, maximum 500 nm), *(1b)* also exists in a temperature-dependent equilibrium with the double zwitterion *(2b)*. The diamagnetic form *(2c)* of the next homologue can be detected in solution only at low temperature (98 °K, shoulder at 790 nm).



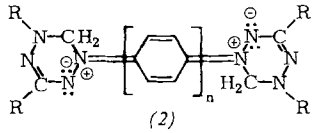
(1)

R = C_6H_5

(a), n = 2

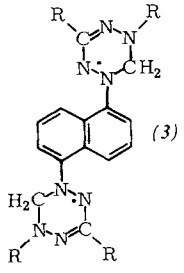
(b), n = 3

(c), n = 4

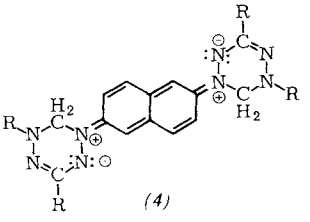


(2)

The 1,5-bisverdazylnaphthalene *(3)* remains a diradical in the solid state and in solution up to 77 °K. It has a typical verdazyl absorption spectrum [maximum in dioxane: 713 nm (ε = 7700), 420 (14900), 270 (14900)].



(3)



(4)

However, 2,6-bisverdazylnaphthalene, like *(1a)*, is in temperature-dependent equilibrium with the quinonoid double zwitterion *(4)*, almost entirely in the diamagnetic form at low temperatures. The biradical concentration in the solid state is 36 % at 348 °K, 27 % at 298 °K, 11.5 % at 195 °K, and 6.1 % at 90 °K. The energy of conversion of the "electron-isomers" into each other between 348 and 298 °K is *ca.* 1.8 kcal/mole. The bisverdazyls *(1)* and *(4)* are examples (to be added to porphyrindine[3] and homologues of Chichibabin's hydrocarbon[4]) of compounds with an even total number of electrons that occur in diamagnetic and paramagnetic "electron-isomeric" forms[5].

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[*] Dr. F. A. Neugebauer, H. Trischmann, and M. Jenne
Max-Planck-Institut für Medizinische Forschung
Institut für Chemie
Jahnstr. 29
69 Heidelberg (Germany)

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Preparation of Tetrachlorodicyanophosphates and the Existence of Tetrachlorodifluorophosphates

By *H. W. Roesky*[*]

Although the hexachlorophosphate ion, $[PCl_6]^-$, and the hexafluorophosphate ion, $[PF_6]^-$, have long been known, it has hitherto proved impossible to prepare mixed hexahalogeno- or hexapseudohalogeno-phosphates.

For the synthesis of the tetrachlorodicyanophosphate ion, $[PCl_4(CN)_2]^-$, phosphorus pentachloride was treated with potassium cyanide (molar ratio 1:5) in anhydrous acetonitrile. Reaction occurred exothermally on vigorous stirring. The mixture was heated for 30 min at 40–50 °C and then filtered. An excess of a 1 % aqueous solution of tetrabutylammonium chloride solution was added to the filtrate and the resulting precipitate filtered off and reprecipitated from acetone/water. 2 g of PCl_5 gave 0.6 g of $(CH_3CH_2CH_2CH_2)_4N^+[PCl_4(CN)_2]^-$, m.p. 142 °C. Under the same conditions tetrapropylammonium chloride gave $(CH_3CH_2CH_2)_4N^+[PCl_4(CN)_2]^-$, m.p. 157 °C. These products are white solids that, when moist, slowly evolve HCN. The IR spectrum contains the bands between 700 and 420 cm^{-1} expected for $[PCl_4(CN)_2]^-$; these are the vibrations to be ascribed to ν(P–C), ν(P–Cl), and δ(PCN). Unambiguous assignment and determination of structure are possible only after measurements of the Raman spectrum. In the case of D_{4h} symmetry an alternative selection rule would apply. Provisional assignments are ν(PCN) 655(s), ν(PCl) 480(vs), δ(PCN) 435(vs) cm^{-1}. Assignment of ν(CN) to 2200(w) cm^{-1} is certain[1].

Phosphorus dichloride trifluoride, PCl_2F_3[2], reacts with CsF in dry acetonitrile at room temperature:

$$2\ PCl_2F_3 + 2\ CsF \rightarrow Cs^+[PF_6]^- + Cs^+[PCl_4F_2]^-$$

It was impossible to separate the cesium hexafluorophosphate completely from the cesium tetrachlorodifluorophosphate[3]. The tetrachlorodifluorophosphate is extraordinarily sensitive to moisture and decomposes the acetonitrile with development of a brown color. Provisional assignment of IR bands: ν(P–F) 760, ν(P–Cl) 455 cm^{-1}.

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[*] Dr. H.W. Roesky
Anorganisch-Chemisches Institut der Universität
Hospitalstr. 8–9
34 Göttingen (Germany)

[1] s = strong, vs = very strong, w = weak.

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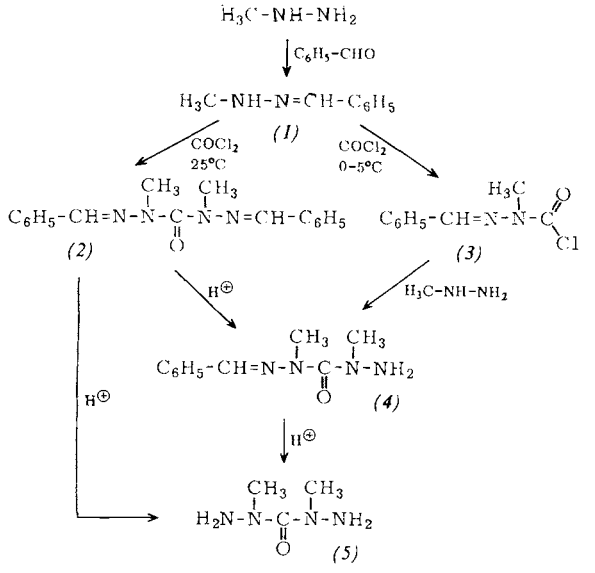
[3] The hexafluorophosphate, which is sparingly soluble in acetonitrile, is filtered off. The filtrate decomposes to a slight extent with formation of more hexafluorophosphate.

2,4-Dimethyl Carbonohydrazide

By *L. Raphaelian, H. Hooks,* and *G. Ottmann*[*]

Several methods have been described[1] for the preparation of 1,5-disubstituted carbonohydrazides but 2,4-dialkylcarbonohydrazides and 2,4-diarylcarbonohydrazides are apparently unknown. We have now prepared 2,4-dimethylcarbonohydrazide *(5)* from methylhydrazine and phosgene.

The primary amino group of methylhydrazine was blocked by conversion to the 1-benzylidene derivative *(1)*, which was then treated with phosgene. Depending on the conditions, this reaction afforded either 1,5-bis(benzylidene)-2,4-dimethylcarbonohydrazide *(2)* or 2'-benzylidene-1'-methylchloroformohydrazide *(3)*[2]. Compound *(2)* is obtained by slow addition of the stoichiometric amount of phosgene to a slurry of *(1)* or its hydrochloride in ether at 25–35 °C. *(3)* is formed exclusively (94 % yield) when a large excess of phosgene is added rapidly at 0–5 °C. Compound *(2)* is converted to *(5)* by transhydrazinolysis with 2,4-dinitrophenylhydrazine or by hydrolysis with 25 to 37 % hydrochloric acid. 20 % acid favors formation of 1-benzylidene-2,4-dimethylcarbonohydrazide *(4)* m.p. 139.5–140.5 °C, as well as *(5)*.



2'-Benzylidene-1'-methylchloroformohydrazine *(3)*, which can be recrystallized from ethanol, reacts readily with methyl hydrazine to form an oily mixture; hydrolysis of this product gave pure *(5)* in 23 % yield.

The reaction of methylhydrazine with phosgene in ether gave *(5)* in less than 2% yield. Attempts to synthesize *(5)* by the reaction of diethyl carbonate with methylhydrazine were unsuccessful and gave only ethyl 2-methylcarbazinate [3].

Procedure:

Phosgene (175 g) is passed into a stirred slurry of 473 g of benzaldehyde methylhydrazone in 6 liter of ether for 8 h at a temperature of 25–30 °C (external cooling). After standing at room temperature for 15 to 18 h, the precipitate is separated and washed with water to remove the hydrochloride of compound *(1)*. The water insoluble portion is dried and recrystallized from heptane to afford 465 g (89 % yield) of 1,5-bis(benzylidene)-2,4-dimethylcarbonohydrazide *(2)*, m.p. 159–160 °C.

A mixture of 226 g of *(2)*, 335 g of 2,4-dinitrophenylhydrazine, 5 liter of ethyl alcohol, and 165 ml of concentrated hydrochloric acid is refluxed for 48 to 72 h, and benzaldehyde dinitrophenylhydrazone is removed by filtration. The filtrate is evaporated to dryness *in vacuo* and extracted with water. The aqueous solution is neutralized, the water is evaporated, and the dry residue recrystallized from ether or acetonitrile to afford pure 2,4-dimethyl carbohydrazide, m.p. 65 °C.

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[*] Dr. L. Raphaelian, H. Hooks, and Dr. G. Ottmann
Olin Mathieson Chemical Corporation, Chemicals Division
275 Winchester Ave.
New Haven, Conn. 06504 (U.S.A.)

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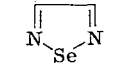
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1,2,5-Selenadiazole

By *L. M. Weinstock*, *P. Davis*, *D. M. Mulvey*, and *J. C. Schaeffer* [*]

3,4-Dicyanoselenadiazole [1] and 4-amino-1,2,5-selenadiazole-3-carboxylic acid [2] are known. We have now synthesized the previously unknown parent compound 1,2,5-selenadiazole *(1)*.



(1)

The synthesis of *(1)* is analogous to the recently reported one-step preparation of 1,2,5-thiadiazole [3]. Ethylenediamine dihydrochloride was allowed to react with selenium monochloride (molar ratio 1 : 8) in dimethylformamide, first for 1 h at −20 °C and then for 6 h at 0 °C. Subsequent steam distillation of the reaction mixture afforded 7 % of 1,2,5-selenadiazole.

IR-Spectrum (liquid film): 3030 (w), 1359 (s), 1230 (s), 1005 (m), 878 (s), 725 (s) cm^{-1} [4].

The 12 eV mass spectrum of 1,2,5-selenadiazole displays a signal at *m/e* 134 corresponding to $^{12}C_2H_2{}^{14}N_2{}^{80}Se$. Four satellite molecular peaks at *m/e* 136, 132, 131, and 130 appear in proportion to the relative isotopic abundances of Se^{82}, Se^{78}, Se^{77}, and Se^{76}. In the 70 eV mass spectrum, $HCNSe^+$, HCN^+, and Se^+ appear as the major fragmentation products, analogous to the fragmentation of 1,2,5-thiadiazole [5].

The properties of 1,2,5-selenadiazole are compared with those of 1,2,5-oxadiazole (furazan) [6] and 1,2,5-thiadiazole [3, 7]. The data indicate that 1,2,5-selenadiazole, like 1,2,5-thiadiazole and selenophene, is a thermally stable, aromatic ring system.

	1,2,5-Oxadiazole[6]	1,2,5-Thiadiazole [7]	1,2,5-Selenadiazole
B.p. (°C)	98	94	138
M.p. (°C)	−28	−50.1	20.5–21
d (g/ml) (t)	1.168 (20 °C)	1.268 (25 °C)	2.10 (24 °C)
n_D	1.4077 (20 °C)	1.5150 (25 °C)	1.6158 (24 °C)
λ_{max} (mμ) [solvent]	only end absorption [H_2O]	253 7800 [CH_3OH]	285 6300 [CH_3OH]
τ [a]	1.34	1.24 [6]	0.72
$J_{^{13}C-H}$ (Hz)	199	192 [6]	188
Mass spectrum: major fragmentation products	$HCNO^+$, HCN^+ $C_2H_2N^+$, NO^+	$HCNS^+$, HCN^+, S^+ [5]	$HCNSe^+$, HCN^+, Se^+

[a] Solvent: CCl_4; tetramethylsilane as internal standard.

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[*] Dr. L. M. Weinstock, Mr. P. Davis, Dr. D. M. Mulvey, and Mr. J. C. Schaeffer
Merck Sharp and Dohme, Research Laboratories
Rahway, New Jersey 07065 (U.S.A.)

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[4] w = weak, m = medium, s = strong.

[5] *F. H. Marquardt*, Ph. D. Thesis, Indiana University, 1960; Dissertation Abstr. *21*, 3272 (1961).

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Bis-(1,5-cyclooctadiene)platinum(0)

By *J. Müller* and *P. Göser* [*]

If $CODPtCl_2$ [1] (COD = 1,5-cyclooctadiene) is treated with an excess of iso-C_3H_7MgBr in ethereal solution, under N_2 at −40 °C, and in the presence of COD, a dark yellow solution results when the mixture is stirred for 3 h. After methanolysis at −50 °C, removal of the solvent by distillation, and crys-

tallization of the residue from hexane at a low temperature, an almost colorless, well-crystallizing, light-sensitive compound CODPt(iso-C_3H_7)$_2$ *(1)* can be isolated in 40% yield (m.p. 54–56 °C).

If a solution of this product *(1)* in COD at 20 °C under N_2 is irradiated for 22 h with UV light (Hg high-pressure lamp Hanau Q 81), subsequent distillation of the COD in a high vacuum and chromatography of the residue on neutral Al_2O_3 ("Woelm", 7% H_2O) with n-hexane as eluent gives a colorless solution from which, on cooling to −78 °C, colorless diamagnetic $(COD)_2Pt(0)$ *(2)* [m.p. 110–111 °C (decomp.)] crystallizes in 22% yield.

Compound *(2)* is the first purely olefinic complex of zerovalent platinum. For comparison we prepared the known[2] yellow nickel complex $(COD)_2Ni$ *(3)* [m.p. 140–142° (decomp.)] in 13% yield by treating anhydrous $NiCl_2$ under N_2 with an excess of iso-C_3H_7MgBr and COD in ether and irradiating the resulting dark brown solution with UV light for 8 h. The compounds *(2)* and *(3)* have similar properties but *(2)* is more resistant to atmospheric oxidation.

In the ^1H–NMR spectrum of *(2)* in C_6H_6, two signals (intensity ratio, 1:2) appear at $\tau = 5.82$ (olefinic protons) and $\tau = 7.81$ (methylene protons).

The corresponding signals of *(3)* are at $\tau = 5.64$ and 7.84. The signal of *(2)* at $\tau = 5.82$ shows two satellites ($J = 55$ Hz) caused by ^1H-^{195}Pt coupling; the corresponding satellites of the methylene protons signal are poorly resolved.

The mass spectrum of *(3)* (Atlas mass spectrometer CH4, ion source TO4, 50 eV) shows mainly the ions $(COD)_2Ni^+$ (relative intensity $I_r = 27.9$), $CODNi^+$ ($I_r = 100.0$), $C_4H_6Ni^+$ ($I_r = 65.9$), and Ni^+ ($I_r = 8.2$). Under similar conditions the complex *(2)* gives an appreciably more complicated mass spectrum; the principal ions $(COD)_2Pt^+$ and $CODPt^+$ are accompanied by several groups of less intense peaks arising mainly by successive loss of C_2 and C_3 units from the molecular ion. The mass spectrum of the free ligand, which is liberated on thermal decomposition of the complex, is also detectable with both *(2)* and *(3)*.

The IR spectrum of *(2)*, which contains many lines, is characterized by the following bands (KBr): 2994, 2907, 2853, 2801, 1471, 1458, 1445, 1392, 1361, 1323, 1299, 1230, 1203, 1171, 1151, 1085, 1068, 1000, 990, 954, 879, 860, 845, 820, 813, 803, 779, 760, and 673 cm^{-1}.

Attempts to prepare di(norbornadiene)platinum(0) have so far failed. Treatment of nor-$C_7H_8PtCl_2$[3] with an excess of iso-C_3H_7MgBr in ether under N_2 at −40 °C gave almost an 80% yield of well-crystalline yellow nor-C_7H_8Pt(iso-C_3H_7)$_2$, but UV irradiation of this material in norbornadiene did not give the desired purely olefine complex.

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[*] Dr. J. Müller and Dipl.-Chem. P. Göser
Anorganisch-Chemisches Laboratorium der
Technischen Hochschule
Arcisstr. 21
8 München (Germany)

[1] *J. Chatt, L. M. Vallarino,* and *L. M. Venanzi,* J. chem. Soc. (London) *1957*, 2496.

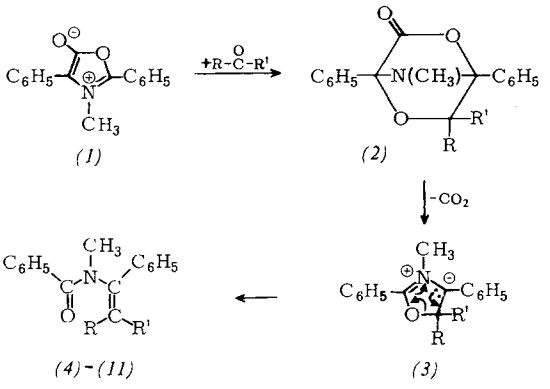
[2] *B. Bogdanović, M. Kröner,* and *G. Wilke,* Liebigs Ann. Chem. *699*, 1 (1966).

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1,3-Cycloadditions of Mesoionic Oxazolones to Carbonyl Compounds

By *R. Huisgen* and *E. Funke*[*]

The mesoionic oxazolone *(1)* is a very active azomethine ylide; its 1,3-adducts with acetylene derivatives or with olefins are stabilized by loss of carbon dioxide, yielding pyrrole[1] or 2-pyrroline derivatives, respectively[2]. Aldehydes, α-diketones, and α-keto carboxylic esters can also induce elimination of carbon dioxide from *(1)*, such reactions yielding the *N*-benzoylalkenylamines *(4)* to *(11)*.



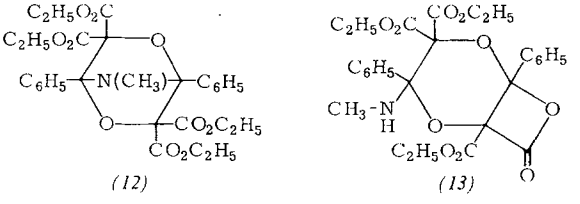
(1) *(2)* *(3)* *(4)–(11)*

	R	R′	Reaction temp. (°C)	CO_2 (%) from (1)	Yield (%)	M.p. (°C)
(4)	H	H	80	48	45	93–94
(5)	CH_3	H	[a]		32	139
(6)	C_6H_5	H	33	49	46	110.5–111.5
(7)	(4)-ClC_6H_4	H	37	59	52	140–141
(8)	(4)-$CH_3OC_6H_4$	H	36	66	45	149–150
(9)	CO–C_6H_5	C_6H_5	100	73	60	191
(10)	CH_3	CO_2CH_3	20	49	51	103–103.5
(11)	$CO_2C_2H_5$	$CO_2C_2H_5$	20	66	57	103–104.5

[a] From *(15)* at 120 °C.

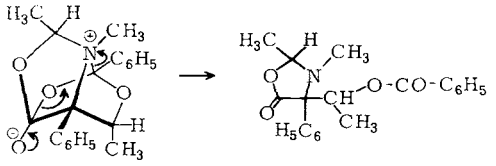
Proofs of structure: *(4)* was hydrogenated to a product identical with authentic *N*-methyl-*N*-(α-phenethyl)benzamide. *(5)* and an acid solution of 2,4-dinitrophenylhydrazine gave a 92% yield of the propiophenone derivative. Analogously *(6)* was converted into deoxybenzoin 2,4-dinitrophenylhydrazone in 81% yield. With 85% phosphoric acid the benzil adduct *(9)* afforded ω,ω′-dibenzoyltoluene in 65% yield; similar treatment of *(11)* yielded acetophenone, benzoic acid, methylamine, and CO_2. The amide I bands of *(4)* to *(11)* are at 1627–1655 cm^{-1}.

If the oxazolone *(1)* is stirred slowly into an ethereal solution of an excess of diethyl mesoxalate, addition of the dipolarophile to the intermediate *(3)*, which is a new cyclic azomethine ylide, competes with ring opening of this intermediate to give *(11)*. The product is the bicyclic diadduct *(12)* which on mild treatment with acid gives the β-lactone *(13)* (C=O at 1820, 1755, 1737 cm^{-1}) and on energetic hydrolysis in the presence of 2,4-dinitrophenylhydrazine gives phenylglyoxal osazone. *(12)* decomposes at 160 °C into mesoxalic ester and 80% of *(11)*.

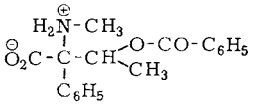


(12) *(13)*

Treating the oxazolone *(1)* with acetaldehyde at 0 °C afforded 73% of a bisadduct *(15)*, without loss of carbon dioxide. Presumably here the intermediate *(2)* is trapped by addition of the second molecule of acetaldehyde, which yields *(14)*. Ring opening thereof then explains the formation of the oxazolidone derivative *(15)* [NMR (in $CDCl_3$), 2 CH–CH_3 3.89 (q) and 8.44 (d) τ, as well as 5.48 (q) and 8.83 (d) τ; IR (KBr), ring C=O 1788, ester C=O 1715 cm^{-1}].



(14) (15)



(16)

2,4-Dinitrophenylhydrazine in acid solution converts *(15)* into the acetaldehyde derivative (90 %) and into the threonine derivative *(16)* (88 %), the latter being cleaved by alkali to *N*-methylphenylglycine, acetaldehyde, and benzoic acid. At 120 °C *(15)* yields 32 %, and at 170 °C *(16)* yields 49 %, of the *N*-benzoylalkenylamine *(5)*.

The reaction path *(1)* → *(4)* to *(11)* is thus proved by trapping of the intermediates *(2)* and *(3)*.

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[*] Prof. Dr. R. Huisgen and Dipl.-Chem. E. Funke
Institut für Organische Chemie der Universität
Karlstr. 23
8 München 2 (Germany)

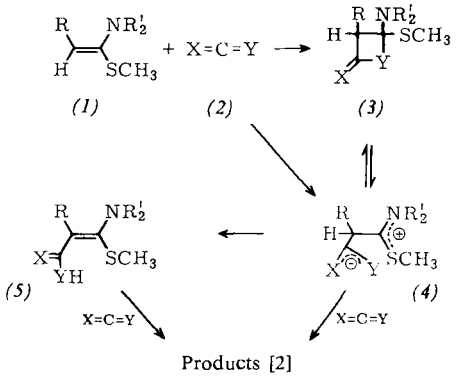
[1] *R. Huisgen, H. Gotthardt, H. O. Bayer,* and *F. C. Schaefer,* Angew. Chem. *76*, 185 (1964); Angew. Chem. internat. Edit. *3*, 135 (1964).

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Stable 1,4-Dipoles from Ketene Acetals and Carbon Disulfide and their Use for Synthesis of Heterocycles

By *R. Gompper* and *W. Elser* [*]

Reaction of simple ketene *S,N*-acetals *(1)* [1] with acylating agents *(2)* gives either acylated ketene *S,N*-acetals *(5)* or, by way of *(4)* and *(5)*, heterocycles such as pyrimidines [2].



(1) (2) (3)

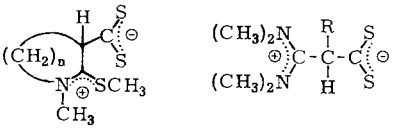
(5) (4)

Products [2]

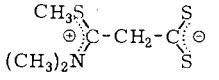
R = H, Alkyl, Aryl
X, Y = O, S, NR'', CR_2''

To test whether 1,4-dipoles *(4)* are intermediates and whether they arise directly from *(1)* and *(2)* or from the cycloaddition products *(3)*, we treated *(1)* and corresponding ketene aminals with carbon disulfide in acetonitrile at −40 °C. Orange to red crystalline compounds were obtained (in some cases isolated only on precipitation by ether), which are stable at −40 to −20 °C but decompose slowly at room temperature.

According to their elemental analyses they are 1:1 adducts. Their IR spectra (in Hostaflon oil) are characterized by intense bands at 1590–1620 cm^{-1}, such as are observed also in the spectra of quaternary salts of thioamides. We thus conclude that we are dealing with the 1,4-dipoles *(6)*, *(7)*, and *(8)*.

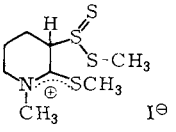


(6a), n = 2 *(7a)*, R = H
(6b), n = 3 *(7b)*, R = CH_3

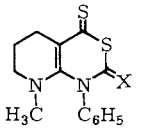


(8)

The NMR spectra (determined in liquid SO_2) are in agreement with this formulation. The temperature-dependence of the NMR spectrum of *(7)* is remarkable: at 0 to −10 °C the signal of the N–CH_3 protons appears as a singlett; however, at −50 °C a doublet (intensity ratio 1:1) appears in the spectrum of *(7a)*, and in that of *(7b)* there is also a doublet but with an intensity ratio of 3:1. The N–CH_3 signal in the spectrum of *(8)* is always a singlet. Compounds *(6)*, *(7)*, and *(8)* can be readily alkylated; for instance, the red compound *(6b)* reacts with methyl iodide to give the yellow salt *(9)*, m.p. 143–145 °C.

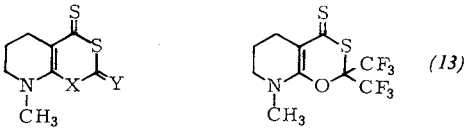


(9)



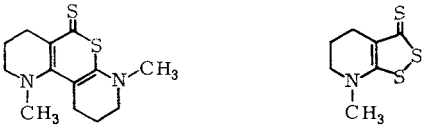
(10a), X = O
(10b), X = S
(10c), X = NC_6H_5

The 1,4-dipoles *(6)* undergo (4 + 2)-cycloadditions [when carried out at −20 to 0 °C in acetonitrile; only *(14)* was prepared at 40 °C]. Thus, with *(6b)*, phenyl isocyanate yields *(10a)*, m.p. 197–199 °C, phenyl isothiocyanate yields *(10b)*, m.p. 194 °C, diphenylcarbodiimide yields *(10c)*, m.p. 191–193 °C, diphenylketene yields *(11)*, m.p. 210 to 211 °C, cyanomethoxycarbonylthioketene [3] yields *(12)*, m.p. 223 °C, hexafluoroacetone yields *(13)*, m.p. 133 °C, 1,4,5,6-tetrahydro-1-methyl-2-methylthiopyridine [1] yields *(14)*, m.p. 182–183 °C, and sulfur yields *(15)*, m.p. 143–144 °C. Elemental analyses and IR and NMR spectra correspond to the structures indicated. On treatment of *(6a)* with diphenylketene the product *(16)*, m.p. 202–203 °C, is accompanied by the isomer *(17)*, m.p. 262–265 °C.

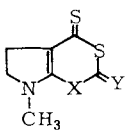


(13)

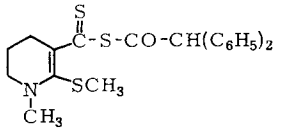
(11) X = O, Y = $C(C_6H_5)_2$
(12) X = S, Y = $C(CN)CO_2CH_3$



(14) *(15)*



(16), X = O, Y = $C(C_6H_5)_2$
(17), X = $C(C_6H_5)_2$, Y = O



(18)

When compound *(18)* (red needles, decomp. at 88 °C), obtained from *(6b)* and diphenylacetyl chloride, is kept in solution in acetonitrile, it affords compound *(11)*. It is thus shown that cycloadditions to *(6)*, *(7)*, and *(8)* can occur in two stages; nevertheless a synchronous process is not excluded.

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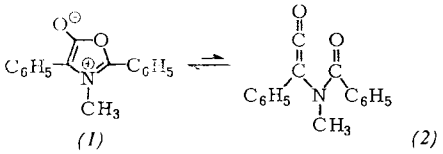
[*] Prof. Dr. R. Gompper and Dr. W. Elser
Institut für Organische Chemie der Universität
Karlstr. 23
8 München 2 (Germany)

[1] *R. Gompper* and *W. Elser*, Tetrahedron Letters *1964*, 1971.
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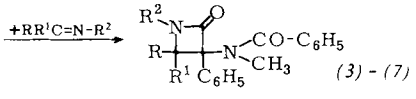
Possible Valence Tautomerism of a Mesoionic Oxazol-5-one with an Acylaminoketene

By *R. Huisgen*, *E. Funke*, *F. C. Schaefer*, and *R. Knorr* [*]

Anhydro-5-hydroxy-3-methyl-2,4-diphenyloxazolium hydroxide *(1)* reacts as a 1,3-dipole with olefins, acetylenes, nitriles, as well as with carbonyl and thiocarbonyl compounds [1] in accord with the cycloaddition scheme 3 + 2 → 5. In reaction with C=N double bonds a new mode of reaction appears, namely cycloaddition 2 + 2 → 4: on reaction of compound *(1)* with azomethines at 80 to 100 °C we obtained the α-acylamino-β-lactams *(3)* to *(7)* (the penicillins also belong to this class of compounds). The azetidinones *(3)* to *(7)* show the lactam carbonyl band at 1730 to 1755 cm^{-1} as well as the amide I band at 1630 to 1656 cm^{-1}.



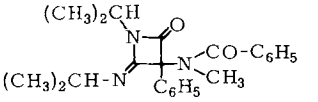
(1) *(2)*



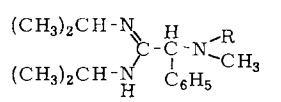
(3) - *(7)*

	R	R^1	R^2	Yield (%)	M.p. (°C)
(3)	H	C_6H_5	CH_3	62	158–159
(4)	H	C_6H_5	CH_2–C_6H_5	47	156–157
(5)	H	C_6H_5	C_6H_5	33	162.5–163
(6)	C_6H_5	C_6H_5	C_6H_5	25	170.5–171
(7)	Fluorenylidene		C_6H_5	56	208.5–209

Compound *(1)* reacts with diisopropylcarbodiimide at 137 °C to give the azetidinedione imine *(8)* (yield 63 %; m.p. 159–160 °C), whose IR spectrum (KBr) shows bands at 1808 (lactam C=O), 1687 (C=N), and 1637 cm^{-1} (amide I). Dilute hydrochloric acid converts this product into the *N,N'*-diisopropylamidine *(9)* of α-(*N*-benzoylmethylamino)phenylacetic acid, whereas concentrated hydrochloric acid yields *(10)* in 87 % yield.



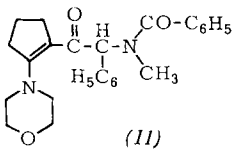
(8)



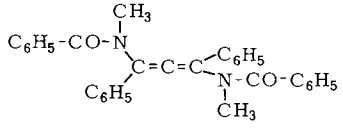
(9), R = CO-C_6H_5
(10), R = H

The simplest explanation of these reactions rests on valence tautomerism of the mesoion *(1)* with (*N*-benzoylmethylamino)phenylketene *(2)*. Formation of β-lactams from ketenes and azomethines has been known for 60 years [2], and cycloaddition to carbodiimides has also been described [3].

We have been able to confirm the hypothesis that enamines (the most active "ketenophiles" [4]) react with the ketene form *(2)*. We obtained compound *(11)* (yield 45 %) from *(1)* and 4-(1-cyclopentenyl)morpholine. Ring opening of the initially formed cyclobutanone derivative to yield the β-acylalkenylamine *(11)* follows a known pattern [5].

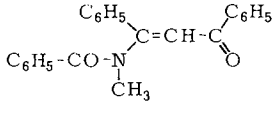


(11)

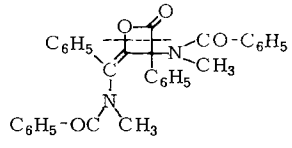


(12)

The presence of the ketene tautomer has not yet been demonstrated spectroscopically; the equilibrium concentration must be very small. Thermolysis of *(1)* in boiling xylene can be simply explained by way of *(2)*: loss of 1 mole of CO_2 from 2 moles of *(1)* yields the tetrasubstituted allene *(12)*, decomp. 186–187 °C (yield 86 %). The IR spectrum of *(12)* shows the typical allene band at 1920 cm^{-1}. The two N–CH_3 groups are equivalent (NMR in $CDCl_3$, s 6.98 τ). In the presence of HCl one equivalent of water in dioxane at room temperature causes partial hydrolysis to *(13)*, whereas on reaction with 3N HCl double enamine hydrolysis leads to dibenzoylmethane.



(13)



(14)

Dimerization of the ketene tautomer to the β-lactone could be the initial step, which is followed by loss of carbon dioxide with formation of *(12)*. Analogous formation of the allene from the β-lactone dimer of dimethylketene [6] or bis(trifluoromethyl)ketene [7] occurs only at 450 °C or 600 °C, respectively. Apparently the acylamino groups in *(14)* promote cleavage of the molecule.

Loss of CO_2 from a solution of *(1)* in benzonitrile at 115, 120, and 140 °C is a second-order reaction with $\Delta H^{\neq} = 19.1$ kcal/mole and $\Delta S^{\neq} = -17$ cal deg^{-1} $mole^{-1}$.

The evidence for the tautomerism *(1)* ⇌ *(2)* is thus only chemical at present; there is as yet no physical evidence to support this hypothesis.

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[*] Prof. Dr. R. Huisgen, Dipl.-Chem. E. Funke, and Dr. R. Knorr
Institut für Organische Chemie der Universität
Karlstr. 23
8 München 2 (Germany)
Dr. F. C. Schaefer
American Cyanamid Co., Research Laboratories
Stamford, Conn. (U.S.A.)

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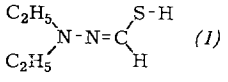
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Isomerism of *N'*,*N'*-Diethylthioformohydrazide with Its Betaine

By *W. Walter* and *K.-J. Reubke* [*]

On the basis of spectroscopic results, structure *(1)* has been assigned to *N'*,*N'*-diethylthioformohydrazide, which was recently synthesized by *Bredereck et al.* [1].



(1)

On thioformylation of asymmetric diethylhydrazine with thioformic ester [2] we obtained a product *(2)* which differs in melting point (77–78 °C) and IR spectrum, as well as in behavior on thin-layer chromatography, from the compound prepared by *Bredereck*'s method (m.p. 102–104 °C; lit. [1] 101–105 °C), although in agreement with the latter in molecular weight and composition, We ascribe the thioformohydrazide structure to the isomer *(2)*, and a betaine structure *(3)* with mainly intramolecular hydrogen bridges to the isomer formulated as *(1)* by *Bredereck et al.*, Structures *(1)* and *(3)* are both in accord with the IR spectrum.

The two substances are interconvertible. When *(2)* is dissolved in boiling ethyl formate, *(3)* separates on cooling. If *(3)* is boiled in chloroform for 20 min and the solution is poured into an ice-cooled vessel, then *(2)* can be detected by thin-layer chromatography and by its IR spectrum in the equilibrium mixture that is precipitated.

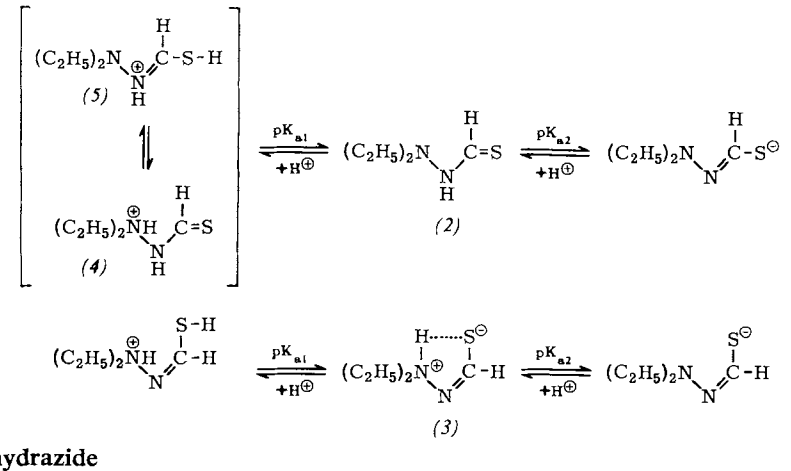
The ^{1}H–NMR spectrum of *(3)* contains, not only the signals of the ethyl protons (triplet at τ = 8.72, quadruplet at 6.77) and a sharp signal at τ = 0.97 (thioformyl proton), but also a broad strong signal that we attribute to a hydrogen bridge between sulfur and nitrogen (a sharp signal would be expected for a S–H proton).

The ^{1}H–NMR spectrum of *(2)* contains the ethyl signals at higher field (triplet at τ = 8.97, quadruplet at τ = 7.23). At τ = 0.90 and 0.73 there are two sharp signals, and at τ = 1.30 and 1.13 two broad signals of unequal intensity; these four signals together correspond to two protons. The spectrum can be interpreted as that of the thioformohydrazide structure if hindered rotation around the C–N bond is assumed. The IR spectrum of *(2)* contains all the bands that are characteristic of thioacylhydrazines [3].

We ascribe the three bands between 2700 and 2780 cm^{-1} in the IR spectrum of *(3)* to a $^+$NHR$_2$ group; dimethylhydrazine hydrochloride also shows a split band in this region. We ascribe the strong band at 1460 cm^{-1} to a C–N double bond.

The betaine structure *(3)* is favored by the pK_a values that were determined photometrically for the two isomers: *(2)*, pK_{a1} = 2.8, pK_{a2} = 10.4; *(3)*, pK_{a1} = 3.4, pK_{a2} = 11.7. The value pK_{a2} = 10.4 for *(2)* was confirmed by potentiometric titration.

We interpret these findings by means of the following equilibria.



Comparison of the pK_a values for *(2)* with those of other thioacylhydrazines [4] shows agreement for pK_{a2} (9.2 to 11.1), but pK_{a1} for *(2)* is smaller than for other thioacylhydrazines (4.2 to 6.2). Since the pK_{a2} for *(3)* is greater than that for *(2)*, the former compound cannot be a thiol since then the pK_a would be smaller – or at least not higherthan that for compounds in which the form *(1)* can be considered toccur by inclusion of the N–N–C(=S) group in a ring that is capable of mesomerism. *Sandström* [5] recently found pK_a values between 5.01 and 8.19 for such compounds.

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[*] Prof. Dr. W. Walter and K.-J. Reubke
Chemisches Staatsinstitut, Institut für Organische Chemie
Papendamm 6
2 Hamburg 13 (Germany)

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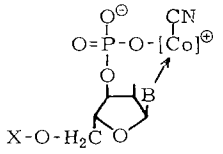
Isolation of Cyanocobalamine 5'-Phosphate [1]

By *P. Renz* [*]

When a crude extract of *Propionibacterium shermanii* is incubated with cobinamide and 5,6-dimethylbenzimidazole in the presence of tris/HCl buffer (pH = 7.5) for 10 h at 37 °C, subsequent product recovery in the presence of KCN gives cyanocobalamine 5'-phosphate *(2)* (*ca.* 15 %) along with cyanocobinamide (*ca.* 70 %) and cyanocobalamine (*ca.* 15 %) *(1)*.

The phosphate was identified as follows: On electrophoresis it moves rapidly to the anode in 0.5 N acetic acid. It contains two atoms of phosphorus per corrinoid molecule. Its UV spectrum is the same as that of vitamin B_{12} *(1)*. It behaves

like synthetic cyanocobalamine 5′-phosphate[3] on paper chromatography in four solvents[2] and on paper electrophoresis at pH 2.5, 7.5, or 11.0. Like the synthetic product, it is degraded to vitamin B_{12} *(1)* by acid phosphatase at pH = 4.8.



[Co] = Cobinamide residue
B = 5,6-Dimethylbenzimidazole
(1), X = H (Cyanocobalamine)
(2), X = PO_3H^- (Cyanocobalamine 5′-phosphate)

Evidence for location of the second phosphate group of *(2)* at the 5′-position of ribose is the color reaction with carbazole in sulfuric acid that is characteristic of ribose 5-phosphates[4]. The spectrum, which was recorded with the product of the carbazole reaction of *(2)* in the sample cell and the product from *(1)* in the comparison cell, shows an absorption maximum at 585 nm; the product of the carbazole reaction of adenosine 5′-phosphate also has a maximum at this position. Since incubating *(2)* with crude extracts of *P. shermanii* in the presence of 2-mercaptoethanol affords vitamin B_{12} *(1)*, it is possible that *(2)* is a biosynthetic precursor of *(1)*.

Formation of *(2)* can be explained as follows: *P. shermanii* extracts give α-ribazole 5′-phosphate from 5,6-dimethylbenzimidazole[5]. On the other hand, under mildly aerobic conditions *in vivo*[6], *P. shermanii* yields much *P*(1)-cobinamide *P*(2)-guanosine 5′-pyrophosphate *(3)*, along with *(1)*, from cobinamide[7]. It is thus possible that *(2)* arises directly by transfer of the cobinamide phosphate part of *(3)* to the 3′-position of α-ribazole 5′-phosphate.

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[*] Dr. P. Renz
Institut für Biochemie und Biotechnologie der
Technischen Hochschule
Azenbergstr. 14
7 Stuttgart N (Germany)

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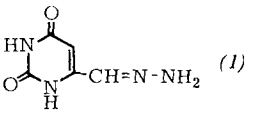
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4-Uracilcarbaldehyde Hydrazone[1]

By *R. Brossmer* and *D. Ziegler*[*]

Whereas 5-uracilcarbaldehyde and hydrazine give only a stable azine, the isomeric 4-carbaldehyde gives also a hydrazone *(1)* [yield 82% (without product recovery from the mother liquor); m.p. 260 °C (decomp.)], that is difficultly soluble in water and has λ_{max} = 311 nm ($\varepsilon = 15.8\times10^3$) 1 and λ_{min} = 250 nm($\varepsilon = 3.4\times10^3$).

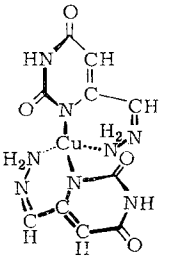


(1)

The hydrazone *(1)* reacts with aliphatic, aromatic, and heterocyclic aldehydes in hot aqueous or aqueous-alcoholic solution, giving mixed azines. The pale yellow to orange-yellow products usually crystallize out directly and are pure

Mixed azine of *(1)* with	Yield [2] (%)	M.p. (°C)
Crotonaldehyde	75	212–213
Salicylaldehyde	83 [3]	> 300
Terephthaldehyde[4]	82	> 300
1-Naphthaldehyde	64	274 (decomp.)
3-Pyridinecarbaldehyde	96	278–280 (decomp.)
5-Uracilcarbaldehyde	90	> 300

without recrystallization. Dialdehydes, *e.g.* terephthalaldehyde, react with *(1)* in the molar ratio 1:2, yielding bisazines. An aqueous solution of *(1)* with Cu(II) salts gives quantitatively the well crystalline, olive-green, and very insoluble paramagnetic complex *(2)*.



(2)

As a molecular model shows, this complex must be tetrahedral. It is the first inner orbital complex, of this kind, of copper with a pyrimidine derivative. It is decomposed by mineral acids to Cu(II) salt and yellow crystals which, according to the composition and the IR spectrum, are 4-uracilcarbaldehyde azine.

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[*] Priv.-Doz. Dr. R. Brossmer and Dipl.-Chem. D. Ziegler
Max-Planck-Institut für Medizinische Forschung
Institut für Chemie
Jahnstr. 29
69 Heidelberg (Germany)

[1] Part IV of Studies of Pyrimidines. -- Part III: *R. Brossmer* and *D. Ziegler*, Tetrahedron Letters *1966*, 5253.

[2] Without product recovery from the mother liquor.

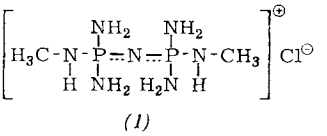
[3] Recrystallized from dimethylformamide.

[4] Molar ratio (1): terephthalaldehyde = 1:1.

The Structure of $[P_2N_7H_{10}(CH_3)_2]I$

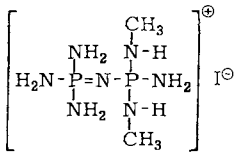
By *M. Ziegler*[*]

Gutmann et al.[1] obtained the compound $P_2N_7C_2H_{16}Cl$ by the ammonolysis of $(Cl_3PNCH_3)_2$; they suggested the symmetrical structure *(1)*.



(1)

On the other hand, X-ray structure analysis of the iodide[2] showed that both the N–CH_3 groups are bound to the same phosphorus atom *(2)*.



(2)

The iodide crystallizes as monoclinic crystals with C_{2h}^5-$P2_1/n$ space grouping. The lattice constants are a = 6.03 Å, b = 23.87 Å, c = 8.27 Å, β = 97°46′. There are four structural units in the unit cell. The structure is established by three-dimensional Patterson- and Fourier-syntheses.

Provisional parameters are:

	x	y	z		x	y	z
I	0.9892	0.1271	0.0824	N_4	0.6198	0.9939	0.7557
P_1	0.4136	0.0379	0.7332	N_5	0.8107	0.1010	0.5105
P_2	0.5744	0.1259	0.5528	N_6	0.4424	0.1620	0.4066
N_1	0.4283	0.0756	0.5781	N_7	0.6633	0.1694	0.6976
N_2	0.4571	0.0665	0.9102	C_1	0.5400	0.2085	0.3330
N_3	0.1706	0.0087	0.7094	C_2	0.4696	0.2032	0.7495

The iodine is ionically bound and the angle at the nitrogen bridge atom is approximately 130°. The distance of the two phosphorus atoms from this nitrogen bridge are different and less than the other P–N distances; the latter are similar and average 1.61 Å. The provisional residual value amounts to 0.13.

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[*] Dr. M. Ziegler
Anorganisch-Chemisches Institut der Universität
Tiergartenstr.
69 Heidelberg (Germany)

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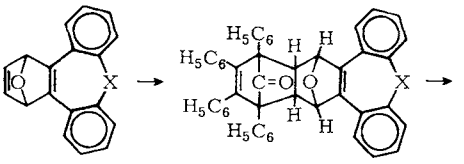
[2] *M. Becke* and *B. Scharf,* unpublished.

Synthesis of an Optically Active Tribenzothiepin *S,S*-Dioxide[1]

By *W. Tochtermann* and *C. Franke*[*]

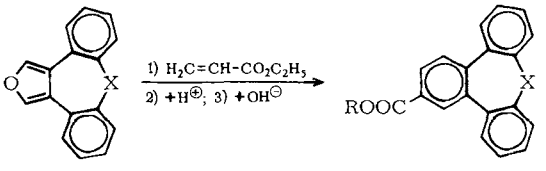
Tribenzocyclohepten-9-ylideneacetic acid[1a] and methylenedibenzocycloheptenes[2] can be resolved into optical antipodes. In order to determine whether optical antipodes can also be obtained when the seven-membered ring contains a heteroatom we synthesized tribenzothiepin-2-carboxylic acid *S,S*-dioxide *(5b)*. As the formulae show, the same process can be used for synthesis of 9-oxotribenzocycloheptene-2-carboxylic acid *(5a)*, and we have thus a generally available route to chiral benzologous seven-membered ring systems.

The Diels-Alder adducts *(2)* from the epoxides *(1)*[3] and tetraphenylcyclopentadienone decompose in boiling xylene, yielding carbon monoxide, 1,2,3,4-tetraphenylbenzene, and the furan derivatives *(3)*; the last products undergo a further Diels-Alder addition with ethyl acrylate[4]. The epoxide *(1)* and tetraphenylcyclopentadienone (molar ratio 1.1:1) are heated in boiling xylene under nitrogen until the characteristic color of the ketone has disappeared, then an excess of ethyl acrylate is added and the whole is boiled for a further 16 h. The 1,2,3,4-tetraphenylbenzene is then separated (yield 80 to 90%) from the acrylic ester adduct [yield 50% from *(1a)*, 25% from *(1b)*] by chromatography on Al_2O_3 (eluent CCl_4 and $CHCl_3$). In each case, this procedure yields two stereoisomeric adducts [(from *(1a)*, m.p. 173–175 °C and m.p. 153–154 °C)], which can be dehydrated by acetic anhydride (10 min at 140 °C; a little concentrated H_2SO_4 is added) to *(4)* [*(4a)*, m.p. 132–133 °C, yield 75 %; *(4b)*, m.p. 197–199 °C, yield 50 %)]. Hydrolysis of *(4)* yields the carboxylic acids *(5a)*, m.p. 280–281 °C, and *(5b)*, m.p. 335–337 °C, the structure of which was confirmed by elemental analysis and IR and UV spectra.



(1)(a), X = CO
(b), X = SO_2

(2)



(3)

(4), R = C_2H_5
(5), R = H

Tribenzothiepin-2-carboxylic acid *S,S*-dioxide *(5b)* can be resolved by brucine into the enantiomers, since the brucine salt of the levorotatory acid crystallizes preferentially from acetone/ethanol (1:1, v/v). The specific rotations for *(5b)* are $[\alpha]_{436}^{24} = -250°$ and $[\alpha]_{436}^{24} = +200°$ (c = 0.01 g/ml in diglyme). Racemization occurs when the solutions are heated. At 92 °C $t_{1/2}$ is *ca.* 5 h, whence it follows that for *(5b)* ring inversion of the boat-form of the seven-membered ring requires an energy of about 29 kcal/mole.

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[*] Priv.-Doz. Dr. W. Tochtermann and cand. chem. C. Franke
Organisch-Chemisches Institut der Universität
Tiergartenstr.
69 Heidelberg (Germany)

[1] This research has been supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

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[4] *(3)* can be isolated if dienophiles are absent [*(3a)*: m.p. 102 to 103 °C; *(3b)*: m.p. 203–204 °C].

Difluoro(trifluoromethylsulfenylimino)sulfur $CF_3SN{=}SF_2$ and Bis(trifluoromethylsulfenylimino)sulfur $CF_3SN{=}S{=}NSCF_3$

By *A. Haas* and *P. Schott*[*]

When a mixture of trifluoromethylsulfenylamine $CF_3S{-}NH_2$ and SF_4 (molar ratio 1:1.3) is heated in the presence of CsF (as HF-absorber) in an autoclave at 20–60° (2–5 atm), a mixture of $CF_3SN{=}SF_2$ *(1)* and $CF_3SN{=}S{=}NSCF_3$ *(2)* is formed. Compund *(1)* distils at −20 °C/0.1 mm into a cold trap cooled in liquid air. Repeated fractional condensation in a Stock vacuum apparatus yields pure *(1)* as a pale yellow liquid that decomposes in glass at 20 °C (yield 30 %). The residue is purified by distillation at reduced pressure, compound *(2)* distilling over as a pale red liquid, whose dilute solution in benzene is yellow (yield 40 %). Both substances were characterized by elemental analysis, determination of molecular weight, and IR, ^{19}F-NMR, and mass spectra.

The IR spectrum of *(1)*, measured in the NaCl and KBr regions, shows strong bands at 1287 (νS=N), 1189 (ν_{as}C–F), 1135 (ν_sC–F) 736 (ν_{as}S–F), and 665 cm^{-1} (ν_sS–F). The ^{19}F–NMR spectrum contains two signals, at −59.8 ppm (SF_2) and 51.9 ppm (CF_3S), referred to CCl_3F as external standard. The mass spectrum shows, besides the molecule ion at *m/e* = 185, typical fragments $CF_3SN{=}SF$ (*m/e* 166), CF_3SN (115), SNS (78), and SN (46) as well as other peaks.

Product *(1)* is also formed, along with other products, on reaction of CF_3SNCO with SF_4 in a 300 ml steel autoclave at 100 °C and 15 atm.

Compound *(2)* boils at 77 °C/80 mm and melts at −58 °C. Its IR spectrum contains two very intense bands at 1171 and 1105 cm^{-1}. Absorptions of medium intensity occur at 940, 753, 650, 503, and 464 cm^{-1}. The chemical shift of the ^{19}F signal is at 52.39 ppm (Cl_3CF as external standard). Typical fragments CF_3SNSNS (*m/e* 193), CF_3SNS (147), SNS (78), CF_3 (69), SN (46), and S (32) appear in the mass spectrum along with the molecular ion at *m/e* = 262.

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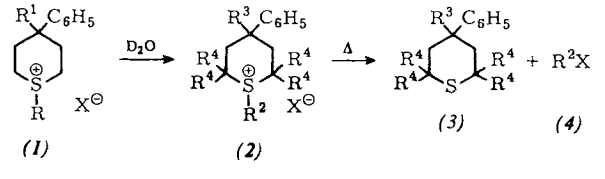
[*] Doz. Dr. A. Haas and Dipl.-Chem. P. Schott
Anorganisch-Chemisches Institut der Universität
Hospitalstr. 8–9
34 Göttingen (Germany)

Synthesis of 1-Deuterioalkyl Halides from Cyclic *S*-Alkylsulfonium Salts and Heavy Water

By *H. Dorn* [*]

Dedicated to Professor A. Rieche on his 65th birthday

Alkyl halides deuterated on the 1-carbon atom were previously accessible only from 1-deuterated alcohols, which are obtained from carbonyl compounds by means of $LiAlD_4$ [1]. We have now found a simple synthesis of 1-deuterioalkyl halides, *i.e.* deuteration of cyclic *S*-alkylsulfonium salts *(1)* and subsequent thermal fission of the deuterated products to sulfides and alkyl halides.



(1) *(2)* *(3)* *(4)*

	X	R	R¹		R²	R³	R⁴
(a)	Cl	CH_3	H	D_2O	CD_3	H	H
(b)	Cl	CH_3	OH	⟶	CD_3	OD	H
(c)	Br	C_2H_5	OH		CD_2CH_3	OD	D

In D_2O containing 0.04 mole of NaOD per mole of sulfonium salt, the salts *(1a)* and *(1b)* exchange all three protons of the CH_3 in 56 h at 35 °C and 120 h at 36 °C, respectively. If there is a longer alkyl chain on the sulfur atom more energetic conditions must be used, with the result that not only the protons of the 1-methylene group of the alkyl chain but also the protons at positions 2 and 6 of the ring are exchanged for deuterium. Thus, when the salt *(1c)* is heated (150 min at 100 °C) with D_2O containing 5 mole-% of NaOD, the compound *(2c)* is obtained.

The sulfonium salts *(2)* are isolated in crystalline form with yields of over 90 % and give the 1-deuterated alkyl halides *(4)* on dry heating at 160–170 °C *(2a)*, 170 °C *((2b)*, or 125–150 °C *(2c)*. Yields of deuterated alkyl halide amount to 100 %.

The sulfides *(3)* can be alkylated again in yields of 90–98 %. The sulfonium bromides can be prepared directly from the sulfide and alkyl bromide; the sulfonium chlorides, quantitatively, from ethereal HCl and an acetone solution of the picrates which are quantitatively precipitated from solutions of, *e.g.*, the iodides or bromides by 25 % lithium picrate solution. 4-Phenylthiacyclohexane *(3a)*, m.p. 55 °C, is formed on catalytic hydrogenation of 4-phenylthiacyclohex-3-ene [2] in ethanol in the presence of Adams catalyst at 45 °C and 6 atm. Sulfides with R^1 = OH are less suitable for preparative purposes since traces of acid or overheating cause partial loss of HDO which interferes with re-use of the sulfides. It is unnecessary to separate the diastereoisomers of *(1)* for the synthesis described above.

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[*] Dr. H. Dorn
Institut für organische Chemie, Deutsche Akademie der Wissenschaften zu Berlin
1199 Berlin-Adlershof (Germany)
Work carried out at:
University of East Anglia, School of Chemical Sciences
Norwich (England)

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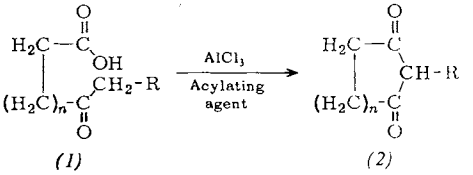
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Preparation of 2-Alkyl-1,3-cycloalkanediones by Cyclization of γ- and δ-Keto Carboxylic Acids

By *H. Schick, G. Lehmann*, and *G. Hilgetag* [*]

Dedicated to Professor A. Rieche on his 65th birthday

2-Alkyl-1,3-cyclopentanediones hold a key position in the total synthesis of steroids. We have found that γ-keto carboxylic acids *(1)*, $n = 1$ [1], can be cyclized to 2-alkyl-1,3-cyclopentanediones *(2)*, $n = 1$, under the conditions of the Friedel-Crafts reaction in the presence of an acylating agent such as propionyl chloride, acetyl chloride, or acetic anhydride. δ-Keto carboxylic acids *(1)*, $n = 2$ [2], give 2-alkyl-1,3-cyclohexanediones *(2)*, $n = 2$, analogously.



(1) *(2)*

Yields are higher than from any other known process [3], particularly for the higher alkyl derivatives.

R	*n*	Acylating agent (mole)		$AlCl_3$ (mole)	Solvent	Yield (%) [a]	M.p. (°C)
CH_3	2	Propionyl chloride	0.1	0.12	Nitromethane	35	204–206
CH_3	1	Propionyl chloride	0.1	0.24	Nitrobenzene	70	214–216
	1	Acetyl chloride	0.1	0.12	Nitromethane	45	
C_2H_5	1	Acetic anhydride	0.1	0.24	Nitromethane	50	175–177
n-C_3H_7	1	Propionyl chloride	0.1	0.24	Nitromethane	50	180–182
n-C_5H_{11}	1	Propionyl chloride	0.1	0.12	Nitrobenzene	65	149–151

[a] In each case from 0.05 mole of keto acid.

2-Methyl-1,3-cyclopentanedione

4-Oxohexanoic acid (6.5 g, 0.05 mole), sublimed aluminum chloride (32 g, 0.24 mole), and propionyl chloride (9.3 g, 0.1 mole) are heated in nitrobenzene (30 ml) for 3 h at 80 °C with exclusion of moisture. The mixture is cooled to 10 °C, then poured onto ice (50 g), the whole is cooled to 0 °C, and the crude 2-methyl-1,3-cyclopentanedione that separates is filtered off, washed with cold water, and recrystallized from water with addition of active charcoal. A further fraction can be obtained by boiling the aqueous phase of the filtrate with active charcoal, filtering, and continuously extracting the filtrate with ether. Total yield, 3.9 g (70 %).

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[*] Dr. H. Schick, Dr. G. Lehmann, and Prof. Dr. G. Hilgetag
Institut für Organische Chemie der Deutschen Akademie der Wissenschaften zu Berlin
Rudower Chaussee 5
X 1199 Berlin-Adlershof (Germany)

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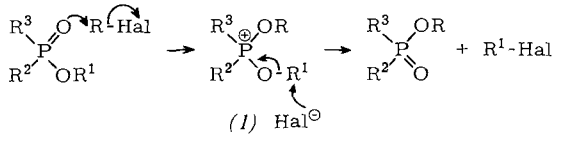
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Preparation of Alkoxyphosphonium Salts by Alkylation of Phosphoryl Compounds

By *H. Teichmann, M. Jatkowski,* and *G. Hilgetag* [*]

Dedicated to Professor A. Rieche on his 65th Birthday

Phosphinic [1], phosphonic [2], and phosphoric esters [2,3] undergo exchange reactions with alkyl halides. The first step is clearly nucleophilic substitution by the phosphoryl oxygen:



R^2 and R^3 = alkyl or alkoxyl

Whereas the intermediate corresponding to *(1)* in the alkylation of thiophosphoric esters can be isolated [4], isolation of the alkoxyphosphonium salts *(1)* has hitherto not been accomplished. The only reports published recently concern the alkylation of triphenylphosphine oxide to stable alkoxytriphenylphosphonium salts [5] and the preparation of tetramethoxyphosphonium hexachloroantimonate *(1g)* from trimethyl phosphite, methyl hypochlorite, and antimony(v) chloride [6].

On alkylation of phosphinic, phosphonic, and phosphoric esters by trialkyloxonium salts in methylene chloride we obtained high yields of the alkoxyphosphonium hexachloroantimonates as unexpectedly stable, well crystalline substances. Analytical values and IR and ^{1}H–NMR spectra agree with the structure assumed.

	R	R^1	R^2	R^3	M.p. (°C)
(1a)	C_2H_5	CH_3	CH_3	CH_3	182
(1b)	C_2H_5	C_2H_5	CH_3	CH_3	179
(1c)	C_2H_5	CH_3	C_2H_5	C_2H_5	178
(1d)	C_2H_5	C_2H_5	C_2H_5	C_2H_5	174
(1e)	C_2H_5	i-C_4H_9	C_2H_5	C_2H_5	48
(1f)	C_2H_5	C_2H_5	C_2H_5	OC_2H_5	144–145
(1g)	CH_3	CH_3	OCH_3	OCH_3	135
(1h)	C_2H_5	C_2H_5	OC_2H_5	OC_2H_5	125

The ^{31}P resonance lines of the dialkylphosphinic esters are shifted by *ca.* 40 ppm to lower field on alkylation to *(1a)* to *(1e)*. However, the ^{31}P values for the tetraalkoxyphosphonium salts [–5 and –3 (±3) ppm for *(1g)* and *(1h)*, respectively] are very close to those for the trialkyl phosphates; the recorded value [6] for the tetramethoxy compound *(1g)* could not be reproduced. IR and ^{1}H–NMR spectra of *(1g)* agree well with published data [6].

Alkoxyphosphonium salts are strong alkylating agents. The alkylating power of the tetraalkoxy compounds *(1g)* and *(1h)* is particularly marked and they react analogously to trialkyloxonium salts, *e.g.* with phosphinic esters:

$$(CH_3)_2P(O)OCH_3 + (1h) \rightarrow (1a) + (C_2H_5O)_3PO$$

Tetraethoxyphosphonium Hexachloroantimonate (1h):

A solution of triethyl phosphate (4.5 g, 24.7 mmoles) in methylene chloride (10 ml) is added dropwise to a solution of triethyloxonium hexachloroantimonate (7.5 g, 17.2 mmoles) in methylene chloride (saturated at room temperature) at –78 °C, with stirring and exclusion of moisture. Warming to room temperature then gives a clear solution which is treated an hour later with anhydrous ether to incipient turbidity and cooled in a CO_2/acetone bath. Filtration of the precipitate gives 7.2 g (77.5 %) of the product *(1h)* as fine leaflets, m.p. 118–120 °C (125 °C after one recrystallization from n-butyl chloride).

In the preparation of *(1a)–(1f)* the ester need not be used in excess; the product can be recovered immediately after warming to room temperature; yields [except for *(1e)* which is precipitated as an oil and is difficult to crystallize] amount to 80–90 %.

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[*] Dr. H. Teichmann, Dipl.-Chem. M. Jatkowski, and Prof. Dr. G. Hilgetag
Institut für organische Chemie der Deutschen Akademie der Wissenschaften
Rudower Chaussee
X 1199 Berlin-Adlershof (Germany)

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Adsorption and Partition

The Analytical Chemistry Group of the *Chemische Gesellschaft in der DDR* held a lecture meeting on "Adsorption and Partition" at Leipzig on October 31st and November 1st, 1966.

From the lectures:

Partition of Triphenyl-lead Derivatives between Aqueous and Organic Phases

By *R. Bock* and *H. Deister*[*]

On treatment of chloroform solutions of triphenyl-lead chloride or bromide with aqueous alkali, triphenyl-lead hydroxide is formed. It remains in the organic phase with extensive condensation to hexaphenyldilead oxide. With this reagent, many organic and inorganic anions can be extracted from aqueous solutions (*e.g.* $Cl^{\ominus}$, $Br^{\ominus}$, $I^{\ominus}$, $CO_3^{2\ominus}$, $AsO_4^{3\ominus}$).

The anions can be re-extracted from the organic phase with aqueous alkali, with regeneration of the reagent. In this way anion separations are possible, *e.g.* selenite-tellurite, chloride-sulfate, organic hydroxy acids – amino acids.

Determination of Benzoic and Phthalic Acids in Terephthalic Acid by Partition Chromatography

By *W. Czerwiński* and *J. Guberska*[**]

Differences in the adsorption of benzoic and phthalic acids on strongly acidic cation exchangers in the hydrogen form were used for the chromatographic separation and determination of small quantities of these acids in terephthalic acid. It is possible to determine from 0.05 to 2 % of benzoic acid and 0.1 to 2 % of phthalic acid.

The sample (about 0.4 g) is dissolved in pyridine, and most of the terephthalic acid is precipitated as the pyridinium salt with benzene. To determine the phthalic acid in the filtrate, this is evaporated to dryness under reduced pressure, and the residue is dissolved in a little pyridine and introduced into the cation-exchange column.

Since the chromatographic band of benzoic acid can be partly masked by the terephthalic acid still present, further terephthalic acid must be extracted from the benzene solution with dilute sulfuric acid before the benzoic acid can be determined. The solution is made alkaline with aqueous sodium hydroxide before the benzene is evaporated.

The separation is carried out in a column (inside diameter 0.4 cm, length 80 cm) containing Dowex 50 W-X4 cation exchanger (200–400 mesh). The separated acids are eluted with water/ethanol, the ethanol concentration being continuously increased (gradient elution). The eluate is automatically titrated to constant pH with sodium hydroxide solution.

[*] R. Bock
H. Deister
Institut für Anorganische Chemie und Kernchemie
der Universität
65 Mainz (Germany)

[**] Dr. Witold Czerwiński and J. Guberska
Institute of General Chemistry
Rydygiera 8
Warszawa 86 (Poland)

Chromatographic Separation of Metal Ions with Anomalous Exchange Properties on Chelating Ion-Exchange Resins

By *R. Hering* and *D. Haupt*[*]

Ion-exchange resins with chelating groups such as those of sarcosine, iminodiacetic acid, or β-carboxymethylamino-propionic acid ("chelon resins") react with metal ions in the same way as the corresponding monomers to form complexes of different stability. The exchange behavior is influenced by the shift of redox potential associated with complex formation.

Metal ions with normal exchange properties are quantitatively complexed, transcomplexed, or decomplexed even at room temperature without kinetic inhibition. This group includes most bivalent metal ions (arranged in order of decreasing complex stability): Cu^{2+}, (UO_2^{2+}), Pb^{2+}, Ni^{2+}, Cd^{2+}, Zn^{2+}, Co^{2+}, Be^{2+}, Mn^{2+}, Ca^{2+}, Mg^{2+}, Sr^{2+}, Ba^{2+}. However, there are also a number of metal ions having anomalous exchange properties. The anomalies are due to kinetically inhibited complexing and transcomplexing reactions (inert complexes, *e.g.* with Pd^{2+}, Hg^{2+}, Fe^{3+}, Cr^{3+}, or VO^{2+}), displacement of the redox potentials (*e.g.* with Au^{3+}, Hg_2^{2+}, Co^{3+}, V^{2+}, VO_4^{3-}, Fe^{2+}), or the deposition of hydrated oxides in the pores of the resin (*e.g.* with Sn^{2+}, ZrO^{2+}, Th^{4+}, MoO_4^{2-}, WO_4^{2-}). The anomalous exchange properties revert to normal behavior so that the metal ions in question can then be dealt with by metal-specific filtration on chelon resins by:

1. Raising temperature to 90 °C,
2. Increasing concentration of elution acid to 5 N.

The anomalies can be utilized for special separations, *e.g.* Au^{3+}/Cu^{2+}, Mg^{2+}, Ca^{2+}; $Au^{3+}/Pd^{2+}/Pt^{4+}$; Cr^{3+}/Al^{3+} and others.

Ion Flotation as a Separation Process in Toxicology

By *M. Hofman*[**]

The idea of concentration by foaming, *i.e.* using the gas/liquid phase boundary, is not new. Apart from the purely phenomenological observations by *Wo. Ostwald* in 1928, there are a whole series of methods for the solution of this problem. For example, *F. Schütz* observed in 1946 that surface-active substances can be successively separated by foaming in order of decreasing surface activity; the deciding influence is the substance-specific lowering of the surface tension.

However, this is not the case in *Sebba*'s ion flotation process [1]. In contrast to "classical" flotation, the principal role in this new technique is played by the attractive forces between the ions in the solution and those of the detergent. Surface-active ions of opposite charge are added to the aqueous solution of the ion to be concentrated, and fine gas bubbles are produced

[*] Dieter Haupt
Pädagogisches Institut
26 Güstrow (Germany)
Goldberger Straße 12

[**] Dr. M. Hofman
Praha 6 (ČSSR)
Dejvice, Tylišovská 7

[1] *F. Sebba*: Ion Flotation. Elsevier Monograph, Engng. Sect., Amsterdam 1962.

near the surface of the liquid. After a certain time, the resulting dynamic foam containing the complex of the ion sought with the detergent is broken down, and the liquid is analysed. The substances that are most important in toxicology, such as barbiturates, analgesics, alkaloids, and basic drugs, can be concentrated from the biological material and determined *e.g.* by means of the relatively simple apparatus described by *Karger* and *Rogers* (1961)[2].

The separation involves the following steps: 1. preparation of the sample, with deproteination of the blood or of the organ homogenate, 2. production of the liquified foam, 3. treatment of the latter, including elimination of the detergent, and 4. paper-chromatographic analysis.

Properties and Application of an Amphoteric Ion-Exchange Resin Based on Aminopropionic Acid

By *E. Hoyer* and *G. Kühn*[*]

A uniform, chemically stable ion-exchange resin is obtained by the reaction of cross-linked polychloromethylstyrene with ethyl *N*-methyl-β-aminopropionate followed by hydrolysis. Owing to the low stability of the aliphatic six-membered chelate ring and the inductive effect of the methyl group, the ampholytic action predominates and the complex formation is very weak. Of the metal ions studied, Cu^{2+}, UO_2^{2+}, Cr^{3+}, Bi^{3+}, Fe^{3+}, $[PtCl_6]^{2-}$, $[PdCl_4]^{2-}$, $[AuCl_4]^-$, and VO_3^- are bound, but not Ni^{2+}, Co^{2+}, Zn^{2+}, Cd^{2+}, Pb^{2+}, Mn^{2+}, NH_4^+, Tl^+, alkaline earth metal, alkali metal, or rare earth ions. This offers the following analytical possibilities: Copper(II) ions can be separated quantitatively from the ions of the second group above by simple filtration. UO_2^{2+}, and at about 85 °C Cr^{3+}, can be quantitatively separated from weakly acidic aqueous solutions. The resin is selective for bismuth at pH = 1 – 2. Fe^{3+} ions are quantitatively adsorbed in the presence of sodium sulfate. By use of the amphoteric properties it is possible to resolve a $Cu^{2+}/Mn^{2+}/VO_3^-$ mixture from weakly acidic to neutral solution, the vanadate being bound as the anion.

The resin has a high affinity for noble-metal ions, and can be used to concentrate such ions from extremely dilute solutions. The resin behaves towards acids as a medium-strong basic anion exchanger. It is suitable for the separation of glutamic acid/aspartic acid with 1 % acetic acid as the eluent.

Separation of Selenium with the Aid of Saturated Aliphatic and Aromatic Monoketones

N. Jordanov and *L. Futekov*[**]

In strong hydrochloric acid solution (> 4 N HCl), Se(IV) exists as a chloride complex, which reacts at room temperature with many saturated aliphatic (acetone, methyl ethyl ketone, diethyl ketone, *etc.*) and some aromatic ketones (*e.g.* acetophenone) to form organic selenium compounds. These are either white crystalline substances or yellow oils; they are soluble in chloroform. The solutions remain practically unchanged over long periods (about 7 days at about 25 °C). The ratio of selenium to ketone is 1:1 for the aliphatic ketones and 1:2 for acetophenone. The IR stretching vibrations show that the selenium is not bound *via* the carbonyl group, but *via* the methyl or methylene group of the ketone. The compounds decompose when heated with nitric acid.

This specific method was used for the separation of selenium from other elements such as: Te, Au, Fe, Cu.

Small quantities (0.05 to 0.2 ml) of ketone were added to a strong hydrochloric acid solution. The solution was allowed to stand for 20–30 min, and the organic selenium compound was then extracted with chloroform. After addition of water, the chloroform was evaporated on a water-bath, and the selenium compound remaining in the residue was decomposed with nitric acid. The selenium in the resulting solution can be determined by the tin chloride method in the presence of bismuth nitrate or with 3,3′-diaminobenzidine.

Multilayer Chromatography in Difficult Separations

R. Liebmann[*]

The adsorbents used in thin-layer chromatography are generally single substances. Thus variations in the experimental parameters are restricted to the eluent, the thickness of the layer, the development method, *etc.*

Attempts have been made to find a method permitting the utilization of the properties of different materials on a single plate for the resolution of mixtures, by direct and continuous transition between various adsorption layers. This "multilayer" was prepared with a modified version of *Stahl*'s coating apparatus. If strips (of variable number and thickness) of different materials, which are uniform in the flow direction, are arranged side by side (lane process), it is possible to test these materials simultaneously and under identical conditions for a given separation. However, if the adsorbents are arranged in succession across the flow direction (multilayer process), and if *e.g.* the activities of the adsorbents decrease in the flow direction, sample components that differ only slightly in their adsorption behavior are more effectively separated. On the other hand, if the activity increases in the flow direction, the distance between the spots of substances that differ greatly in their adsorption behavior will be reduced. The layers can also be arranged in any desired manner in order to match the adsorbent to the problem.

The possibilities are further widened by the use of multilayer chromatography in conjunction with the two-dimensional technique. In this way two basic operations (depending on whether the initial flow direction is along or across the layers) offer great versatility. The methods have been tested on combination pesticides and on mixtures of dyes.

Distribution Chromatography for the Analysis of Terephthalic Acid

By *J. Młodecka* and *B. Sekowska*[**]

The analysis of impurities (benzoic, isophthalic, and phthalic acids) in terephthalic acid prepared by disproportionation of potassium benzoate is carried out by multistage paper chromatography and by column chromatography.

In the first stage (flow distance: 1/3 of the length of the paper), a mixture of s-butyl alcohol, formic acid, and water (8:1:1) is used, and in the second stage (to the end of the paper) a mixture of chloroform, methyl alcohol, formic acid, and water (250:25:1:24); the detection limit is 0.3 %.

[2] *B. L. Karger* and *L. B. Rogers*, Analytic. Chem. *33*, 1165 (1961).

[*] Dr. Günther Kühn
Institut für anorganische Chemie der Universität
Leipzig C 1 (Germany)

[**] Dr. Nikolaj Jordanov
Institute for General and Inorganic Chemistry of the
Bulgarian Academy of Sciences
Sofia 13 (Bulgaria)

[*] Dipl.-Chem. Reiner Liebmann
VEB Fahlberg-List
X 3011 Magdeburg (Germany)
Alt Salbke 60–63

[**] Mgr. Jadwiga Młodecka
Instititute of General Chemistry
Rydygiera 8
Warszawa 86 (Poland)

Two methods are available for the quantitative determination of benzoic acid. The first is based on the removal of dicarboxylic acids on a silica-gel column. For benzoic acid contents lower than 2 %, sublimation at 250 °C must first be carried out. A solution of the crude product in pyridine or of the sublimate in chloroform is introduced into the column. The benzoic acid in the eluate is determined volumetrically (0.02 N alcoholic potassium hydroxide solution, thymol blue) for contents greater than 0.2 %, and spectrophotometrically for contents between 0.02 and 0.2 %.

The second method is based on the separation of benzoic acid with benzene as the eluent on Whatman paper purified with acetic acid, followed by spectrophotometric determination. Phthalic acid is best determined fluorimetrically without chromatographic separation. The small quantity of isophthalic acid in the end product does not interfere. [VB 36 IE]

German version: Angew. Chem. 79, 323 (1967)

Boundary-Layer Catalysis [1]

By *G.-M. Schwab* [*]

Most of the mixed catalysts of interest in industry are systems of at least two phases on which the reaction concerned has a lower activation energy than on a single component.

In "normal" mixed catalysts the carrier is a semiconductor and the catalyst is a metal. For typical examples – nickel as catalyst and aluminum oxide or zinc oxide as carrier – it can be shown that the activation energy of a reaction taking place on the catalyst can be changed by doping of the semiconducting carrier (with *e.g.* Li_2O, BeO, Ga_2O_3, or TiO_2). Thus dehydrogenations and hydrogenations are better catalysed by nickel the less n-conducting or the more p-conducting is the carrier. The band model explains this behavior qualitatively, since the Fermi level of the metal is necessarily displaced by a shift of that of the carrier, and thus entry or exit of electrons at the metal/gas boundary is facilitated or inhibited ("chemical rectifier").

Because of the high electron density of the metal it is to be expected that doping of "inverse" mixed catalysts (metal as carrier, oxide as the active component) will have a greater effect. It should be possible to influence strongly the activation energies of reactions on a semiconducting catalyst if the metallic carrier is doped to achieve a lower or higher Fermi energy. Moreover, a change in the thickness of the layer of semiconducting carrier (from *ca.* 50 Å to *ca.* 1000 Å) should affect the catalytic properties. Both expectations have been confirmed. The rate of combustion of carbon monoxide on nickel oxide deposited on silver has a maximum with layer thicknesses of the order of one boundary layer [1], and the activation energy and thus the rate of reaction in the synthesis of SO_3 on ferric oxide is lowered or raised by doping a silver carrier with mercury or palladium, respectively. The theoretical explanation is as follows: After doping, silver emits more or fewer electrons into the semiconductor; thus, in the boundary layer – and only there – the bands are curved downwards and the Fermi boundary shifts into the neighborhood of the conduction band; this has the same effect as n-doping of the semiconductor. [VB 39 IE]

Lecture at Zürich, December 14th, 1966, and at Basel, December 15th, 1966

German version: Angew. Chem. 79, 325 (1967)

[*] Prof. Dr. G. M. Schwab
Physikalisch-Chem. Institut der Universität
Sophienstr. 11
8 München 2 (Germany)

[1] The boundary layer is the surface layer of a semiconductor to the maximum depth (*ca.* 10^{-4} cm) at which the energy of the valence and conduction electrons is still dependent on their position (band curvature).

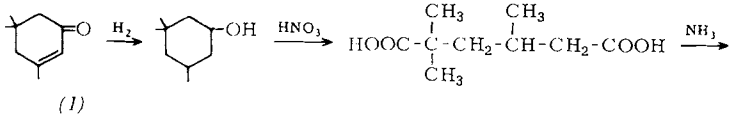
Chemistry of Acetone

By *K. Schmitt* [*]

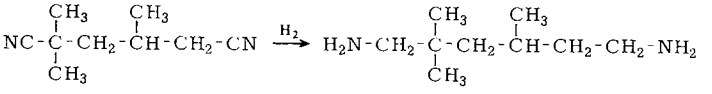
Besides the linear condensation of acetone, which leads in its first stage to diacetone alcohol and thence to important solvents such as mesityl oxide, isobutyl methyl ketone, 4-methyl-2-pentanol, hexylene glycol, and 2-methoxy-2-methyl-4-pentanone, the alkaline condensation of acetone to isophorone *(1)* is of special interest. Conditions for this reaction are: 200 °C; 30 atm gauge pressure; 0.03 % NaOH.

Owing to its energetically favored structure isophorone can be obtained in *ca.* 90 % yield; a particularly economical commercial process is that developed by Scholven-Chemie AG., in which the key step is a pressure-distillation reactor permitting successive condensation, fractionation, and hydrolysis; yields and quality are considerably improved in comparison with customary procedures. Whereas, up till recently, isophorone was used only as solvent, it has now achieved importance as raw material for chemical syntheses: Selective hydrogenation of the olefinic double bond leads to 3,3,5-trimethylcyclohexanone. This compound can be prepared by an elegant process of distillative hydrogenation in which reaction and distillation take place in one unit. (Conditions: 1 atm; 160 °C; palladium).

Under more specific conditions (100 atm of H_2, 200 °C, nickel catalyst) 3,3,5-trimethylcyclohexanol is obtained almost quantitatively. Hydrogenation in the presence of ammonia gives 3,3,5-trimethylcyclohexylamine, which is used as an anticorrosion agent and as an antiicer.

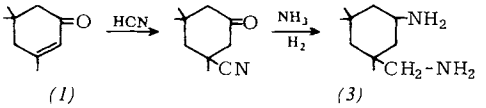


(1)



(2)

2,2,4-(2,4,4)-Trimethylhexamethylenediamine *(2)* is obtained from isophorone *(1)* by the following steps: (1) hydrogenation of isophorone to trimethylcyclohexanol; (2) oxidation to trimethyladipic acid; (3) conversion into the dinitrile; and (4) hydrogenation to trimethylhexamethylenediamine.



(1) *(3)*

A different diamine, 3-aminomethyl-3,5,5-trimethylcyclohexylamine *(3)*, is obtained as a mixture of two stereoisomers by addition of hydrogen cyanide to the carbon-carbon

double bond of isophorone (1 atm; 0.1 % alkali; 150 °C) and subsequent aminating hydrogenation of the ketonitrile.

The diamines *(2)* and *(3)* are used as, for example, hardeners for epoxy resins and as starting materials for the synthesis of diisocyanates. In spite of their structural differences, *(2)* and *(3)* behave similarly as amine components of polyamides, but they differ from hexamethylenediamine in respect of the crystalline form of the products. Owing to the unsymmetrical nature of the molecules, their reactions with dicarboxylic acids such as adipic acid and terephthalic acid yield completely transparent, amorphous polycondensates, even in admixture with conventional components.

[VB 41 IE]

Lecture at Aachen on November 8th, 1966
German version: Angew. Chem. *79*, 384 (1967)

[*] Dr. K. Schmitt
Hiberniastr. 43
468 Wanne-Eickel (Germany)

Inorganic Components of the Hard Tissues of Bones and Teeth

By *H. Newesely* [*]

The homogeneity range of hydroxyapatite $Ca_5(PO_4)_3OH$ (as end product of continued hydrolysis of calcium phosphate in aqueous solution) and of tetracalcium hydrogen trisphosphate ("octocalcium phosphate") $Ca_4H(PO_4)_3 \cdot 2\,H_2O$ (prepared by controlled partial hydrolysis) has been determined for variations of the parameters temperature, pH, and concentration [1,2]. The apatitic structure has also been confirmed for the inorganic components of the hard tissue of teeth by X-ray and electron diffraction, as well as by electron microscopy [3]. However, it must be noted that the presence of other ions accelerates, or is indispensable for the formation of the apatite-like crystals by a reaction mechanism outlined below. Under physiological conditions, equilibrium is not attained in the dissolution and crystallization of hydroxyapatite and less crystalline precipitates are formed in weakly alkaline solution, particularly in the presence of pyrophosphate or carbonate [4].

Tetracalcium hydrogen trisphosphate would be stable in purely aqueous systems in neutral or weakly acidic conditions at temperatures up to 40 °C. The real structure of "octocalcium phosphate" crystals is of interest for characterization of biological mineralizations that lead to apatite: there is more or less complete conversion of pre-formed apatite-like lattice regions in the {100} direction of octocalcium phosphate by hydrolysis [2,4]. The composition of these phases varies within the limits Ca:P = 1.33 ("octocalcium phosphate") and 1.67 (hydroxyapatite).

This change is greatly favored by traces of fluoride, as well as by alkali:

$$Ca_4H(PO_4)_3 \cdot 2\,H_2O \xrightarrow{H_2O,\,(F^-)} Ca_5[(OH, F)(PO_4)_3]$$

Formation of the apatitic structure in this way is a more efficient effect in the fluoridization of teeth than are, say, the solubility differences between hydroxyapatite and fluoridated hydroxyapatite [5].

Further, for the paracrystalline "octocalcium phosphate"/hydroxyapatite system, the carbonate content of tooth and bone substance can be clearly explained: partial replacement of the HPO_4 group of "octocalcium phosphate" gives a product that approaches the apatite type in basicity, namely, $Ca_4(PO_4)_2(HPO_4)_{0.4}(CO_3)_{0.6}$. The morphological properties of this compound correspond to those of the inorganic crystalline components of bones and dentine [6]. Magnesium, as secondary constituent, is able to stabilize a tricalcium phosphate structure (as whitlockite) [7].

[VB 42 IE]

Lecture at Berlin-Dahlem on November 7th, 1966
German version: Angew. Chem. *79*, 384 (1967)

[*] Priv.-Doz. Dr. H. Newesely
Forschungsgruppe für Mikromorphologie
Fritz-Haber-Institut
1 Berlin 33 (Germany)

[1] *E. Hayek, H. Newesely, W. Hassenteufel,* and *B. Krismer,* Mh. Chem. *91*, 249, 1020 (1960).

[2] *W. E. Brown, J. P. Smith, J. R. Lehr,* and *A. W. Frazier,* Nature (London) *196*, 1048 (1962); Proceed. Int. Symposium on Tooth Enamel, London 1964, edited by *M. V. Stack* and *R. W. Fearnhead.* J. Wright and Sons, Bristol 1965.

[3] *J. G. Helmcke,* Dtsch. zahnärztl. Z. *10*, 1461 (1955); Studium Generale *18*, 50 (1965).

[4] *H. Newesely,* Mh. Chem. *95*, 94 (1964); Fortschr. chem. Forsch. *5*, 688 (1966).

[5] *H. Newesely,* Proceed. ORCA 8, Suppl. Archs. oral Biol. *5*, 174 (1961).

[6] *E. Hayek, H. Konetschny,* and *E. Schnell,* Angew. Chem. *78*, 679 (1966); Angew. Chem. internat. Edit. *5*, 669 (1966).

[7] *E. Hayek* and *H. Newesely,* Mh. Chem. *89*, 88 (1958).

Gas-Chromatographic Separation of Metal Chlorides

By *E. Stumpp* [*]

Gas chromatography has hitherto been little used for separation of inorganic substances. We have studied the possibility of its application to the separation of elements that are chemically very similar, such as zirconium and hafnium, or niobium and tantalum, by means of their volatile derivatives.

Many metal chlorides can be volatilized unchanged and, further, are easy to prepare, so that they seem particularly suitable for gas-chromatographic separations. However, some metal chlorides have rather high boiling points, or are chlorinating agents, and, since they are strong Lewis acids, prevent the use, in general, of liquid phases of gas-liquid chromatography. In connection with investigations on metal chloride-graphite compounds, we have now found that graphite is a suitable stationary phase for separating metal chlorides: metal chlorides are strongly adsorbed on graphite, reversibly and differentially, and they can be separated by the technique of solid-gas chromatography.

For the experimental separations an all-Pyrex construction was used to avoid attack on the apparatus by the chlorides. Initially the detector was of the heat-conductivity type with platinum heating wires, but later was of the gas-density type. A novel construction permitted injection of the solid metal chlorides. Helium, or, with the gas-density detector, argon, was used as carrier gas.

The following mixtures, *inter alia*, were separated on a 2.5 m column filled with synthetic, highly purified graphite (grain size 0.5–0.6 mm): $AlCl_3/GaCl_3$ at 210 °C; $AlCl_3/ZrCl_4$ at 300 °C; $TaCl_5/NbCl_5$ at 270 °C; $NbCl_5/NbOCl_3$ at 450 °C; $HfCl_4/ZrCl_4$ at 295 °C; $AlCl_3/HfCl_4/ZrCl_4$ at 290 °C. Small amounts of zirconium-free hafnium chloride could be thus obtained preparatively.

[VB 43 IE]

Lecture at Tübingen on December 2nd, 1966
German version: Angew. Chem. *79*, 385 (1967)

[*] Dr. E. Stumpp
Laboratorium für anorganische und analytische Chemie der Universität
Tübingen (Germany)

Nucleophilic Enzymatic Reactions of Acetyl-CoA

By *H. Eggerer* [*]

Since acetyl-CoA does not form a carbanion [**][1,2] it was difficult to determine the mechanism of enzymatic carboxymethylations of oxo acids by acetyl-CoA. An aldol-like mechanism has now been demonstrated for two enzymes. Three formal steps are necessary :

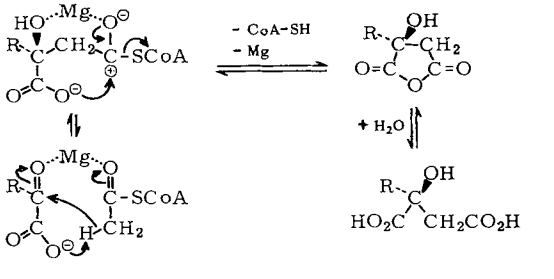
1) enolization of the acetyl-CoA, 2) addition of the enol to the carbonyl group, giving the 2-hydroxyacyl-CoA, and 3) hydrolysis of this intermediate.

Citrate synthase catalyses the synthesis of citrate from acetyl-CoA and oxaloacetate. Steps 2) and 3) could be demonstrated by simultaneous aldol fission and hydrolysis by citryl-CoA, and the isolated step 3) by (*S*)-malyl-CoA. Step 1) provides the key to understanding of the enzymatic catalysis: step 1) requires the carboxylate anion of the reactant oxaloacetate as basic co-factor [2]. Its proof was obtained with (*S*)-malate, which is bound by the enzyme in place of oxaloacetate but cannot add to the enol. (*S*)-Malate thus induces enol formation and leads to isotopic exchange between the methyl hydrogen atom of the acetyl group and tritiated water [3]. Citrate that is synthesized in tritiated water in the absence of (*S*)-malate is free from tritium; acetyl-CoA is unlabeled after partial reaction with oxaloacetate, *i. e.* enolic acetyl-CoA obtained in the slowest step of the synthesis reacts at once with the keto group, yielding (*S*)-citryl-CoA. Since its "chemical hydrolysis" in neutral aqueous solution occurs by way of 2-(carboxymethyl)-2-hydroxysuccinic anhydride [4,5], its enzymatic hydrolysis presumably begins with the same step.

Malate synthase catalyses the synthesis of malate from acetyl-CoA and glyoxylate and is dependent on Mg^{2+} ions as co-factors for this reaction [6]. The enzyme enolises acetyl-CoA (step 1); for this step it is dependent on the Mg^{2+} ions [7], whose action is considered as acid-catalysis. The thioester carbonyl group is polarized by linkage to the Lewis acid, the methyl hydrogen atom becoming acidic.

Since the enolization is slow it seemed probable that for each enzyme there are base- and acid-catalysis mechanisms that act cooperatively with both enzyme systems. A chemical model is *Swain* and *Brown*'s bifunctional catalyst [8]. Accordingly α-oxo acids induce enolization of acetyl-CoA by malate-synthase; the efficiency of this induction increases with decrease of their chain lenght *i.e.* with increasing similarity to glyoxylic acid. Pyruvate inhibits the synthesis of malate competitively ($K_i = 10^{-3}$ M) and has measurable affinity for the enzyme ($K_M = 10^{-3}$ M). The rate of enolization in the "bifunctional enzyme system" and the rate of synthesis of malate are almost identical. Carboxylate anions and Lewis acids act cooperatively: the enzymatic enolization ceases if Mg^{2+} ions or pyruvate are removed. Since enolic acetyl-CoA is formed in the slowest step of the synthesis (proof as for citrate-synthase), it reacts at once with the carbonyl group of the glyoxylate, giving (*S*)-malyl-CoA. If used as a substrate, (*S*)-malyl-CoA is hydrolysed by malate synthase (step 3).

The following reaction scheme is in accord with the experimental observations:



Citrate synthase: R = CH_2CO_2H Malate synthase: R = H

The reactants are bound to the enzyme in such a way that their intramolecular conversion into the products follows naturally. In the related enzyme catalyses and with citrate synthase Mg^{2+} ions can be replaced by Lewis acids that form part of the protein structure and can be arranged in steric opposition to the group R of the α-oxo acid. [VB 46 IE]

Lecture at Marburg (Germany) on November 18th, 1966
German version: Angew. Chem. 79, 383 (1967)

[*] Dr. H. Eggerer
Institut für Biochemie der Universität
8 München 2 (Germany)

[**] The acetyl-CoA carbanion and enol are not differentiated in the text.

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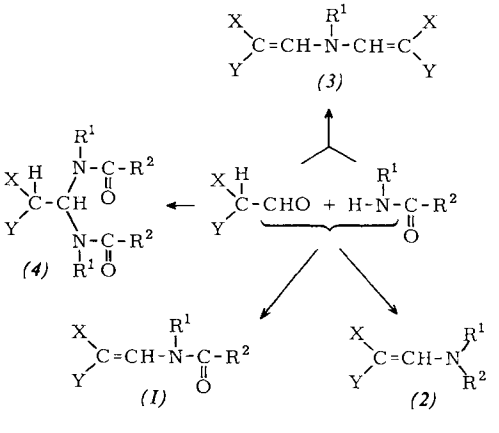
[7] *H. Eggerer* and *A. Klette*, Europ. J. Biochem., in press.

[8] *C. G. Swain* and *F. J. Brown*, J. Amer. chem. Soc. *74*, 2538 (1952).

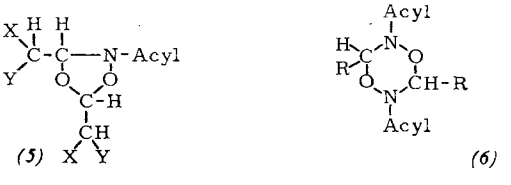
Preparation and Reactions of Enamides

By *F. Eiden* [*]

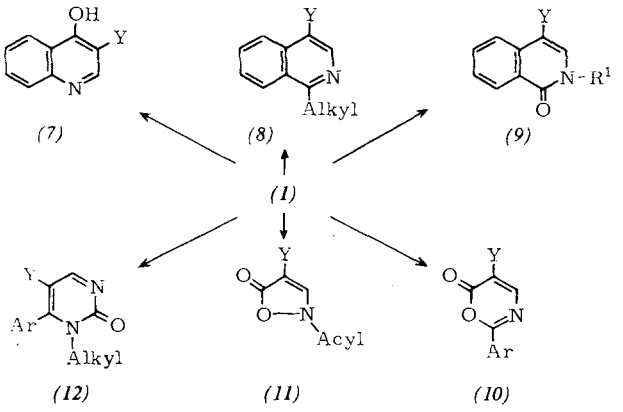
According to the conditions, reaction of substituted acetaldehydes with carboxamides, sulfonamides, or phosphoramides in the presence of acid catalysts yields enamides *(1)*, enamines *(2)*, divinylamines *(3)*, or diacylaminals *(4)*. If hydroxamic acids are used in place of acid amides, then, *inter alia*, *N*-hydroxyenamides [*(1)*, R^1 = OH], *N*-hydroxydivinylamines [*(3)*, R^1 = OH], or, again, enamides are obtained; and use of hydrazides gives, *inter alia*, enehydrazides [*(1)*, R^1 = NHR].



N-Hydroxyaminoalcohols, which can be formulated as intermediates in the reactions of hydroxamic acids, can be trapped in some cases as dihydro-1,4,2-dioxazoles *(5)* or tetrahydro-1,4,2,5-dioxadiazines *(6)*.



The enamides *(1)* are often obtainable in good yield and are useful for synthesis of heterocyclic compounds. For instance; 4-hydroxyquinolines *(7)* result if in *(2)* X = CO–OAlkyl, R^1 = H, and R^2 = Aryl; isoquinolines *(8)* if X = Aryl, R^1 =



H, and R^2 = CO–R; isocarbostyrils *(9)* if X = Aryl, R^1 = H, and R^2 = CO–OAlkyl; oxazin-(6*H*)-6-ones *(10)* if X = CO–OAlkyl, R^1 = H, and R^2 = Acyl, isoxazolones *(11)* if X = CO–OAlkyl, R^1 = OH, and R^2 = Acyl, and 2-pyrimidinones *(12)* if X = benzoyl, R^1 = CO–NH-Alkyl, and R^2 = H.

The structures put forward have been proved by chemical methods as well as by means of UV, IR, and NMR spectra.

[VB 47 IE]

Lecture at Karlsruhe (Germany), on November 17th, 1966
German version: Angew. Chem. *79*, 385 (1967)

[*] Prof. Dr. F. Eiden, Dr. B. S. Nagar, and Dr. W. Seemann
Pharmazeutisches Institut der Freien Universität Berlin
Königin-Luise-Str. 2/4
1 Berlin-Dahlem (Germany)

SELECTED ABSTRACTS

The formation and interception of the 2,2,2-triphenylethyl radical *(1)* has been reported by *L. Kaplan*. Reduction of 1-chloro-2,2,2-triphenylethane with triphenyltin hydrazide yields 1,1,1-triphenylethane *(2)*, the reaction being assumed to proceed as follows:

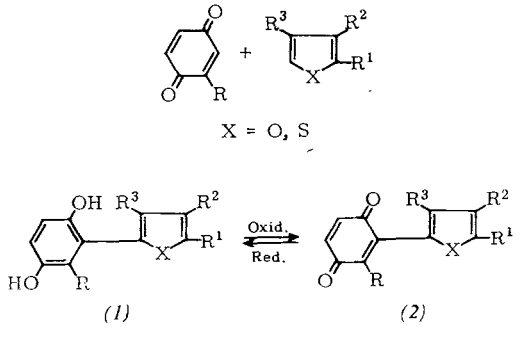
$$(C_6H_5)_3\cdot + (C_6H_5)_3C{-}CH_2Cl \longrightarrow (C_6H_5)_3SnCl + (C_6H_5)_3C{-}CH_2\cdot \quad (1)$$

$$(C_6H_5)_3C{-}CH_2\cdot + (C_6H_5)_3SnH \longrightarrow (C_6H_5)_3C{-}CH_3 + (C_6H_5)_3Sn\cdot, \text{ etc.} \quad (1) \quad (2)$$

The reaction is carried out in benzene at about 70–130 °C, and *(2)* is formed in yields of 27– > 90%. The free radical *(1)* has a strong tendency to rearrange, so that all previous attempts to isolate it have led to derivatives of the 1,1,2-triphenylethyl radical. 1,1,2-Triphenylethane is isolated as a by-product. / J. Amer. chem. Soc. *88*, 4531 (1966) / –Ma.

[Rd 609 IE]

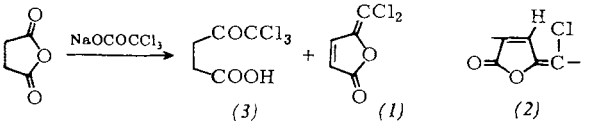
Furyl- and thienylbenzoquinones *(1)*, a group of new dyes, were obtained by *N. Baumann, S. Fumagalli, G. Weisgerber*, and *C. H. Eugster* by the acid-catalysed addition of furan,



thiophene, and their alkyl homologues to negatively substituted quinones (*e.g.* acetyl-*p*-benzoquinone, methoxycarbonyl-*p*-benzoquinone, cyano-*p*-benzoquinone), alkylbenzoquinones, and benzoquinone. The initially formed hydroquinone derivatives *(2)* are readily oxidized to *(1)*. The new compounds have intense long-wave absorption bands in the visible region. / Helv. chim. Acta *49*, 1794 (1966) / –Ma.

[Rd 610 IE]

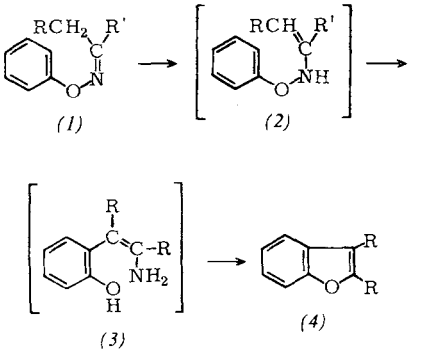
Yellow to red copolymers have been obtained by *A. Winston* and *G. T. C. Li* by polymerization of the now readily obtainable dichloroprotoanemonin (5,5-dichloro-4-hydroxy-2,4-pentadienolactone) *(1)* with methyl acrylate, methyl methacrylate, vinyl acetate, and vinylidene chloride. The polymerization proceeds as a 1,4-addition with subsequent elimination of HCl to form the highly conjugated structural



unit *(2)*. *(1)* is obtained together with 5,5,5-trichlorolevulinic acid *(3)* by reaction of sodium trichloroacetate with succinic anhydride; *(3)* also gives *(1)* on treatment with concentrated H_2SO_4. / 152nd Meeting Amer. chem. Soc. *1966*, W 30, p. 160 / –Ma.

[Rd 615 IE]

The use of Fischer's indole synthesis for the preparation of benzofurans has been described by *T. Sheradsky*. *O*-phenyloximes *(1)*, which can be obtained from carbonyl compounds and *O*-phenylhydroxylamine in boiling ethanol with a trace of HCl, are converted into benzofurans *(4)* at 100 °C with



boron trifluoride ether adduct as the catalyst. The reaction probably proceeds analogously to the indole synthesis, *via* *(2)* and *(3)*. Examples: 2-methylbenzofuran, yield 71% (based on the starting ketone); 2-phenylbenzofuran, 92%; 1,2,3,4-tetrahydro-9-oxafluorene, 74%. / Tetrahedron Letters *1966*, 5225 / –Ma.

[Rd 616 IE]

Polyfluorocyclohexenes can be prepared in good yields by fluorination of perfluorinated or partly fluorinated aromatic hydrocarbons with CoF_3 in the gas phase. Under these conditions, unfluorinated aromatic compounds give mainly saturated polyfluorohydrocarbons. For example, at 80 °C, perfluorotoluene gave 82% of perfluoro(1-methylcyclohexene), 15% of perfluoro(1-methyl-1,4-cyclohexadiene) (λ_{max} = 210 mμ; ε = 288), and 2% of perfluoro(1- or 2-methyl-1,3-cyclohexadiene) (λ_{max} = 255 mμ; ε = 4280) (gas-chromatographic product analysis). / *J. Riera* and *R. Stephens*, Tetrahedron *22*, 2555 (1966) / –Bu. [Rd 621 IE]

The isomer distribution in electrophilic aromatic substitutions on neopentylbenzene has been studied by *D. F. Gurka* and *W. M. Schubert*. The *o/p* ratios obtained were considerably higher than in the case of t-butylbenzene, as is shown by a comparison with values given by *H. C. Brown*:

Reaction	Toluene	t-Butyl-benzene	Neopentyl-benzene
Nitration in H_2SO_4, 25 °C	*o* 58.5	15.8	44.9
	m 4.4	11.5	3.2
	p 37.2	72.7	51.8
Chlorination in glacial acetic acid, 25 °C	*o* 59.8	21.5	25.5
	m 0.5	2.3	0
	p 39.7	76.2	74.5
Bromination in 85 % acetic acid, 25 °C	*o* 32.9	1.2	8.5
	m 0.3	1.5	0
	p 67.1	97.3	91.5

The product ratio was determined by gas chromatography. The substitution site of the various isomers separated by preparative gas chromatography was determined by comparison of the NMR, IR, and UV spectra. / J. org. Chemistry *31*, 3418 (1966) / –Bu. [Rd 623 IE]

A new method for the preparation of disulfones has been developed by *G. C. Denzer, P. Allen, P. Conway*, and *J. M. van der Veen*. These authors obtained relatively good yields in the oxidation of sulfinic acids in 10 N H_2SO_4 at about 5 °C with cobalt(III) sulfate. Known methods give disulfones in maximum yields of 16%, and it is difficult to separate the disulfones from other reaction products. Examples: n-$C_8H_{17}SO_2H$ gave 43% of $C_8H_{17}-SO_2-SO_2-C_8H_{17}$, *m*- or *p*-HOOC–$C_6H_4SO_2H$ gave 65% of (*m*-or *p*-HOOC–$C_6H_4-SO_2)_2$ (m.p. 190 and 265 °C respectively). / J. org. Chemistry *31*, 3418 (1966) / –Bu. [Rd 625 IE]

The low-pressure hydrogenation of benzenepolycarboxylic acids to cyclohexanecarboxylic acids, according to *M. Freifelder, D. A. Dunnigan* and *E. J. Baker*, can be carried out with rhodium catalysts in aqueous media at 60–70 °C and 2.7 atm. Hydrogenation is complete after about 90 min. Examples: phthalic acid gave 91% of cyclohexane-1,2-dicarboxylic acid (*cis*:*trans* = 86:13); isophthalic acid gave 96% of cyclohexane-1,3-dicarboxylic acid (*cis*:*trans* = 60:40); terephthalic acid gave 90% of cyclohexane-1,4-dicarboxylic acid (*cis*:*trans* = 80:20). / J. org. Chemistry *31*, 3438 (1966) / –Bu. [Rd 626 IE]

A cyclic N_3 species having D_{3h} symmetry has been detected by *J. I. Bryant* during the UV photolysis of alkali metal azides at 77 °K. In the infrared spectrum of the irradiated azides (single crystals and KBr disks), which were also used with isotopic labeling ($K^{14}N_3$, $K^{14}N^{15}N^{14}N$, $K^{14}N^{14}N^{15}N$, $K^{15}N_3$), one new band appears in the case of the salts that contained only one isotope of nitrogen; the azides containing two different isotopes give the spectrum of the unlabeled compound with the addition of three new bands, as is to be expected for C_{2v} symmetry (isosceles triangle). The frequency shifts between the bands of the azides containing different isotopes also correspond to the values calculated for the triangular structure. At higher temperatures the IR spectrum becomes more complex, and has not yet been fully interpreted. / Spectrochim. Acta *22*, 1475 (1966) / –Hz. [Rd 628 IE]

The isotopic composition of lead in archaeological objects and lead ores was studied by *N. Grögler, J. Geiss, M. Grünenfelder*, and *F. G. Houtermans*. These authors compared the mass ratios $^{207}Pb/^{206}Pb$ and $^{208}Pb/^{206}Pb$ in ten Roman lead pipes and lead ingots found on the European mainland (Portugal, Italy, Switzerland, Carinthia) with the isotope content of European lead ores (England, Germany, Spain, Italy, Greece, Yugoslavia, Austria). The difference in the isotope ratios for samples from various sources can be more than 2%, with a maximum error of 0.3%. Thus new information about the origin of, and trading in, ancient lead objects can be obtained in extreme cases of isotope distribution in the object and in the ore. When no certain conclusion can be reached, the uncertainty can be reduced by additional determination of trace elements. / Z. Naturforsch. *21a*, 1167 (1966) / –Hz. [Rd 629 IE]

Metallic conductivity in supercritical mercury has been discovered by *E. U. Franck* and *F. Hensel*. The vapor pressure curve was obtained from the discontinuities in the temperature-conductivity curves at constant pressure (T_c = 1490 ± 15 °C; p_c = 1510 ± 30 bar). At temperatures below 1200 °C, the conductivity depends only slightly on pressure, but above this temperature it increases rapidly with pressure. At 1520 °C, compression from 1580 to 2100 bar leads to an increase in conductivity from $10^{-2}\ \Omega^{-1}\ cm^{-1}$ to $5 \times 10^{2}\ \Omega^{-1}\ cm^{-1}$. At higher supercritical temperatures, the pressure-dependence of the conductivity again decreases. As is characteristic of metals, the conductivity of supercritical mercury decreases with rising temperature. / Physical Rev. *147*, 109 (1966) / –Hz. [Rd 630 IE]

BOOK REVIEWS

Anwendungen der Schwingungsspektroskopie in der Anorganischen Chemie (Applications of vibrational spectroscopy in inorganic chemistry). By *H. Siebert*. Vol. VIII of the series "Anorganische und Allgemeine Chemie in Einzeldarstellungen" (Inorganic and general chemistry in monographs). Springer-Verlag, Berlin-Heidelberg-New York 1966. 1st Edit., 209 pp., 28 figures, cloth DM 39.60.

This book is a review of the applications of vibrational spectroscopy in inorganic chemistry and of the results obtained. It begins with an introductory chapter on the theory of molecular vibrations, their classification according to symmetry, and their quantum-mechanical treatment. However, this survey of the theory in only 37 pages will probably be insufficient for the reader approaching this subject for the first time; he would need to refer to the standard texts by *G. Herzberg* and *Wilson-Decius-Cross*.

The next three chapters present a summary of the frequencies of the normal vibrations and the force constants determined from these. Chapter II deals with molecules of the type X_mY_n, Chapter III with the other non-complex inorganic

compounds, and Chapter IV with coordination compounds. The book closes with a list of over 1000 references, as well as a substance index and a subject index.

This book should be useful to anyone interested in the application of IR spectroscopy to inorganic problems; it is particularly suitable for use as a reference work.

W. A. Bingel [NB 566 IE]

Chemistry and Cytochemistry of Nucleic Acids and Nuclear Proteins. By *G. Scholtissek et al.* Vol. V/3 of "Protoplasmatologia". Edited by *M. Alfert et al.* Springer-Verlag, Vienna-New York 1966. 1st Edit., iv, 236 pp., 67 figures, paper DM 81.–; subscr. DM 65.–.

The book contains four independent articles: – *C. Scholtissek*: "The Chemistry and Biological Role of Nucleic Acids" (47 pp.), *B. M. Richards*: "Cytochemistry of Nucleic Acids" (34 pp.), *R.* and *C. Vendrely*: "Biochemistry of Histones and Protamines" (76 pp.), and *D. P. Bloch*: "Cytochemistry of Histones" (51 pp.). These are good neviews with numerous references. The first article presents the textbook knowledge of the chemistry and functions of nucleic acids, and goes as far beyond this scope as is possible in 47 pages.

The other three artieles are more specialized; they are intended for those who wish to familiarize themselves with these fields or who are looking for specific data and references.

However, one must ask who will look for articles of this type in a "Handbook of Protoplasm Research", which is otherwise concerned with spherosomes, flagellae, vitamins, frost resistance, *etc.* In raising this question, it is not intended to cast doubt on the quality of any article, but only on the organization of the classical handbook system. However, the volume can be bought separately, and it should not be absent from the libraries of institutes concerned with these fields.

H. G. Zachau [NB 576 IE]

Organisch-chemische Experimentierkunst (Experimental organic chemistry) by *C. Weygand* and *G. Hilgetag*, in collaboration with *A. Martini*. Johann Ambrosius Barth Verlag, Leiozig 1964. 3rd revised Edit., xxiv, 11442 pp., 213 figures, DM 65.20.

This book, which first appeared more than 25 years ago, is now available in a completely revised edition. The former textbook has now become a reference work, the various chapters of which have been written by specialists. The arrangement of the contents have remained unchanged, the characteristic division into "Materials and Operations", "Reactions", and "Chemical and Physical Characterization" being retained. It was evidently again intended to provide a comprehensive work, from which the user could learn all he needed to prepare and characterize a product, in the order corresponding to the course of an organic-chemical operation. The aims of the book have remained those of a textbook. It suffers from the fact that the transition from a textbook to a handbook has not been consistent.

The first part (113 pp.) contains useful information about the most important chemical operations, particularly purification and separation processes. However, the treatment is not sufficiently detailed for a handbook, and hardly goes beyond that found in any good textbook of practical organic chemistry. It is essential that the next edition deal with ion-exchange chromatography and zone melting. The section on "Purification, Drying, and Testing of solvents" should include tetrahydrofuran and refer to the use of molecular sieves. The section on working with small quantities of substances is well written. The survey of equipment and apparatus is far from complete, and is also out of date in places. No mention is made of equipment that has long been regarded as indispensable. Users with access to other handbooks, such as Houben-Weyl-Müller, will hardly look up Weygand-Hilgetag on this topic.

The third part of the book (85 pp.) is of practically no value. One might ask why, in a book intended for preparative organic chemists, 44 pages are devoted to quantitative analysis. Among other things, *Unterzaucher*'s apparatus for the determination of oxygen is described in detail. Quantitative analysis, apart from the determination of a few functional groups, has long been a matter for the analytical specialist, who will scarcely seek advice in this book. The contents of the section on "Physical Characterization" are out of date. By far the most important physical methods for the characterization of organic compounds, *i.e.* the spectroscopic methods, are dismissed in three pages. IR spectroscopy is covered in 20 lines, and the 2 pages on UV spectroscopy are of little interest to preparative organic chemists. NMR spectroscopy, ESR spectroscopy, and mass spectroscopy are not even mentioned.

The main part of the book (896 pp.) deals with synthetic methods. Seventeen experts present a first-class survey of old and new reactions. A concise and informative chapter on organometallic compounds has been added. The reviewer has profited from a study of this part of the book; he knows of no single-volume work on preparative organic chemistry that provides a comparable wealth of information. The fact that a few methods have been omitted cannot detract from the positive overall impression. However, the following reactions should be included in the next edition: the Hansley-Prelog and Stoll acyloin condensation, Cope elimination, Haller-Bauer cleavage, Baeyer-Villiger oxidation, alkylation with Meerwein salts, the Bamford-Stevens reaction, the Forster reaction, and the formation of cyclobutadiene rings by cycloaddition. The value of the book is enhanced, and the practical experience of the authors demonstrated, by numerous references to advantages and disadvantages of the various processes and by many hints, *e.g.* on how to improve the yields or how notoriously stubborn reactions can be made to "go". The same is true of the more than 1200 "recipes", which are skilfully selected for their relevance as examples. Some 6000 carefully cited references enable the reader to consult the original publicatrons when necessary. This part of the book unquestionably contains numerous highlights. Unfortunately, many of these are not easy to find. The reviewer doubts whether the arrangement according to formation and cleavage of certain bonds is so well conceived as is asserted in the preface. The full value of the book will be enjoyed only by the few readers who work through it systematically like a textbook and then know where to find any given piece of information. Anyone whose theoretical knowledge is so immense as to enable him to plan his synthesis step by step on paper will also find the book excellent, since it will offer examples for each step. However, this will be true only if he is perfectly familiar with the Weygand key, and so knows what reactions to look for in chapters with headings such as "Formation of the C–O Bond by Exchange with Formation of further C–O Bonds". On the other hand, someone with no clear idea of the synthetic rule to follow and the starting materials to use will probably soon lay Weygand-Hilgetag aside and turn to a handbook arranged according to the class of substance.

U. Schöllkopf [NB 565 IE]

Handbuch der Kolorimetrie. Band III: Kolorimetrie in der Biologie, Biochemie und Medizin. 1. Organischer Teil. (Manual of colorimetry, Vol. III: Colorimetry in biology, biochemistry, and medicine, 1. Organic section.) By *B. Kakáč* and *Z. J. Vejdělek*. Translated by *E. Hachová*. Gustav-Fischer-Verlag, Jena 1966, 1st Edit., xiii, 857 pp., 77 figures. DM 74.–.

Volume I of this work[1] dealt with methods for the determination of substances of plant origin used in pharmacy by light absorption in the visible region. Similar methods for synthetics and substances of animal origin were discussed in Volume II[2]. Volume III now deals with methods for the determination of biochemically important substances. Long

chapters are devoted to amino acids, peptides and proteins, carbohydrates and their derivatives, sterines, and steroids. There follows a discussion of metabolic products, the determination of which is important in the study of biochemical processes or for diagnostic purposes, *e.g.* for the testing of organ functions or for the determination of pathological changes in function.

The majority of such problems involve the determination of compounds in organic materials of plant or animal origin. Consequently, if the isolation and purification operations are not to be too expensive, the specificity of the method plays an importance role. The critical notes in this connection, which also deal with sensitivity, reproducitivty, and possible errors of each individual method, therefore will be particularly valuable to the user. Furthermore, as in the previous volumes, an attempt is again made together in the course of the color reactions on which a determination is based. The literature is systematically covered up to the end of 1962, and "a number of important studies published in 1963 are also taken into account".

This volume of the manual again gives an impression of having been carefully compiled. The volume will be very welcome in all laboratories in which such investigations are carried out, since, by obviating the need for laborious literature searches, it greatly facilitates the choice of a method. *H. Böhme* [NB 554 IE]

[1] Cf. Angew. Chem. *75*, 390 (1963).

[2] Cf. Angew. Chem. *76*, 700 (1964).

Fortschritte der Arzneimittelforschung. Progress in Drug Research. Progrès des recherches pharmaceutiques, Vol. 9. Edited by *E. Jucker*. Birkhäuser Verlag, Basel-Stuttgart 1966. 1st Edit., 414 pp., numerous figures and tables, cloth DM 88.–.

The 9th volume of the series[*] again presents detailed reviews of important topics. *H. J. Melching* and *C. Streffer* report (118 pp.) on work on "The influence of drugs on the sensitivity of mammals to radiation". After a short introductory passage on the biochemistry of radiation damage, the various groups of active substances are critically discussed and a brief description of their action mechanism closes the section. A discussion of "Structural considerations on psychopharmaceutics: attempted correlation of chemical constitution and clinical effect" is presented by *K. Stach* and *W. Pöldinger* (61 pp.). The pharmacology and clinical use of the drugs, with particular reference to the tricyclic diphenylamine and diphenylmethane derivatives, and the relationships between chemical constitution and activity are discussed. Special mention is made of the difference between planar (chlorpromazine type) and twisted (imipramine type) ring systems. The article also contains sections on *Rauwolfia* alkaloids, benzoquinolizines, and butyrophenone and hydrazine derivatives. A report by *R. Hawking* on the "Chemotherapy of Filariasis" covers 27 pages. A concise description of the types of *Filaria* that are important in clinical research and of *in vitro* and *in vivo* evaluation methods precedes a discussion of the chemotherapeutic agents of proven activity in this field: diethyl-carbamazine, antimony, arsenic and cyanine compounds, suramin, and bisquinolinium compounds. A very comprehensive article on "3,4-Dihydroxyphenylalanine and related compounds" is presented by *A. R. Patel* and *A. Burger* (56 pp.). Comprehensive tables first give the physical and chemical properties of the intermediates and the yields in the synthesis of 3,4-dopa, its positional isomers, and a number of derivatives. This is followed by analytical and pharmacological data on dopa. Finally, the dopa decarboxylase inhibitors, particularly α-methyldopa are discussed and a brief section on 3,4-dihydroxyphenylserine concludes the article.

R. L. Smith contributes 54 pages on "The biliary excretion and enterohepatic circulation of drugs and other organic compounds." After a discussion of the mechanisms involved in biliary excretion, the fate of the excreted products in the intestines and their possible role as carcinogens are examined. The author goes on to give a survey of the classes of substances that are predominantly excreted with the bile and the constitutional factors involved. The article by *K. Wiesner* and *H. Fink* on "Activity and side effects of metronidazol in the treatment of trichomoniasis" presents a critical evaluation of all the existing literature. For the reader's guidance, the numerical data from the various publications are reproduced in tables (24 pp.).

The value of this work for orientation in the field of drug research is enhanced by an excellent subject index for the present volume and an author and article index for the nine volumes published so far. The presentation of the book is once again excellent. *O. Schaumann* [NB 557 IE]

[*] Cf. Angew. Chem. *78*, 831 (1966); Angew. Chem. internat. Edit. *5*, 854 (1966).

Compilation of Mass Spectral Data. By *A. Cornu* and *R. Massot*. Published jointly by Heyden & Sons Ltd., London, and Presses Universitaire de France, Paris 1966. 1st Edit., xv, 617 pp., cloth £ 14.

Mass spectra, like IR spectra, are well suited to the characterization of organic compounds. Although many reference spectra have been compiled in recent years, these exist mainly in company collections and are not generally accessible.

In the present book, *Cornu* and *Massot* have compiled tables of the data required for the mass-spectroscopic identification of compounds (the intensity values of the ten highest peaks) from a total of some 5000 spectra taken from such collections and from the literature. It is easy to find a compound quickly, since the tables are arranged according to the empirical formula, the molecular weight, the strongest peaks, and the source of the spectra.

Unfortunately, no line representations of spectra have been taken into account in the compilation of the tables, though this is the type of representation almost exclusively used by organic chemists nowadays. Thus the collection does not contain a single spectrum from the hundred or so fundamental studies by *Djerassi*. On the other hand, the spectra published several times in the API catalogue of mass spectra also appear several times in the book for example, on pages 11B and 12B there are five spectra of cyclohexene, distinguished only by a slight difference in the intensity values. These differences are due to variations in equipment and experimental conditions and are of no great experimental importance. It was therefore unnecessary to give the intensity values to an accuracy of tenths of a percent, since such an accuracy cannot be achieved in comparative work with different instruments.

To summarize, it can be said that this collection of spectra is very useful for the identification of thermally stable compounds (*e.g.* hydrocarbons, esters, and aromatic compounds), the spectra of which could be recorded before 1960 by the methods usual at that time; however, the reader will search in vain for spectra of such compounds as have been analysed by mass spectrometry during the past five years. These spectra already form a large part of the available data. This defect could be overcome by the publication of a supplementary volume. *G. Spiteller* [NB 553 IE]

Light: Physical and Biological Action. Edited by *H. H. Seliger* and *W. D. McElroy*. Academic Press, New York-London 1965. 1st Edit., xi, 417 pp., several figures. $ 12.–.

The book is intended to give the beginner a general picture of the problems and the state of photobiology. The first part (Chapters 1 to 3) deals with the physical principles, and the second part (Chapters 4 and 5) with the biological phenomena.

In Chapter 1, an introduction on the nature of light is followed by a discussion of the measurement of light, the characteristics of various light sources, and the production of monochromatic light. This is followed, in Chapter 2, by a description of primary photophysical processes, starting with energy level diagrams and electronic states, then fluorescence and energy transport, and finally reactions in gases and in solution. The chapter ends with a discussion of the photographic process and examples of photochroism and photoisomeric reactions. Chapter 3 deals with chemiluminescence in gases and liquids, and Chapter 4 with luminescence in biological systems. After a description of biological structures, Chapter 5 discusses photosynthesis. This is followed by descriptions of the phenomenon of vision, photoperiodism, phototaxis, and the action of UV light on biological cells.

The book ends with seven appendices containing a number of data and descriptions of instruments including the laser.

In view of the range of material covered, the choice of examples is necessarily limited However, the selection of subject matter is often not very suitable. For example, it is superfluous to describe photographic processes and their sensitization or lasers in this context, when protolytic reactions, redox processes, and flash photolysis are not dealt with. On the other hand, a preparatory treatment of the problems of energy transport is presented in the first part although this phenomenon in photosynthesis is not even mentioned in the second part. A better correlation of the physical and biological parts is to be hoped for in the second edition.

The treatment of biological structures deals with ideas that were current in 1959, but not with the more recent results. The chapter on photosynthesis is too brief, and inaccurate in places. On p. 86, the energies of the emission bands are given incorrectly.

H. T. Witt [NB 551 IE]

Ligand Substitution Processes. By *C. H. Langford* and *H. B. Gray*. From the series "Frontiers in Chemistry". W. A. Benjamin, Inc., New York-Amsterdam 1965. 1st Edit., viii, 111 pp., numerous figures, $9.35.

At a time of rapid progress in the study of ligand exchange processes the appearance of this monograph, presenting a modern interpretation of "classical" results, is to be welcomed. An introductory chapter lays down a new principle for the classification of ligand exchange reactions in which both the mechanism established from kinetic studies and the molecular processes involved are taken into consideration. The applicability of this classification, as applied to the most thoroughly studied complexes of Pt(II) and of Co(III), is demonstrated in the two following chapters. More recent investigations on other metals are also briefly mentioned, but the methods of investigation are not discussed. Each chapter ends with a summary and a list of original publications (up to 1965)

In view of the small size of the book, some knowledge of coordination chemistry and reaction kinetics is presupposed by the authors. Nevertheless, the book is very clearly written and excellently illustrated, and can be recommended even as an introduction to this special field.

Th. Kruck [NB 569 IE]

Advanced Physical Chemistry. Molecules, Structure and Spectra, by *J. C. Davis jr.* The Ronald Press Company, New York 1965. 1st Edit., x, 632 pp., numerous figures, cloth $ 12.00.

Physical chemistry is not only an independent scientific discipline, but also serves as a link between physics and chemistry. One of the tasks of a textbook of physical chemistry is therefore to introduce the chemist to the physical methods that are important to him, including those of theoretical physics. A few decades ago, thermodynamics was undisputedly the most important field of theoretical physics as far as chemists were concerned; nowadays, however, a knowledge of molecular dynamics, quantum theory, statistical mechanics, and the theory of magnetism is becoming increasingly important in chemical research. Accordingly, at least half of the present textbook is a sort of "Theoretical Physics for Chemists". The adjective "advanced" in the title means only that the subject matter goes beyond the usual training in physical chemistry. No previous knowledge is required, apart from some experimental physics and as much mathematics as the average American reader might be expected to possess.

The principles of classical mechanics and of quantum mechanics are introduced in a rigorous form and are clearly interpreted. The reader should be able to gain an understanding of operator calculus from this textbook. One chapter is devoted to the fundamentals of statistical mechanics and its relation to thermodynamics. Further chapters deal with the theory of angular momentum, spin, and magnetic moments, the approximation methods of quantum mechanics, and the theory of the absorption and emission of light. Special attention is given to molecular rotation (also with respect to applications of microwave spectroscopy), the theory of molecular vibrations (but stopping before normal coordinate analysis), and the fundamentals of nuclear magnetic resonance spectroscopy. The treatment of the relationship between electronic structure and UV spectra is somewhat short, and the theory of chemical bonding us really only touched upon.

The book is well compiled from the didactic standpoint, logically arranged, and as lucid as possible in its reasoning. The main emphasis is always placed on the fundamental relationships. Special applications are presented for illustration rather than as ends in themselves. A wealth of interesting exercises (unfortunately the solutions are not given) enables the reader to check how much he has understood.

In many places the reader may notice a lack of absolute rigor or failure to mention details that are not unimportant. The transition from the Lagrange function to the Hamiltonian function should (like the transition from internal energy to enthalpy in thermodynamics) be substantiated. An important point in the derivation of the Planck radiation formula is that Bose statistics for light quanta are used. The derivation given for the Boltzmann velocity distribution is not quite rigorous. In Chapter 7, the term "hydrogen-like functions" is used in a very unconventional sense. The Dirac δ function is incorrectly defined on p. 504. The statement (p. 454) that VB functions are known as bond orbitals is also incorrect. On the other hand, one finds many critical comments on the concepts introduced. The author generally avoids oversimplified "proofs".

Anyone concerned with or interested in molecular spectroscopy or questions of molecular structure in general will find what theoretical principles he requires in this book.

W. Kutzelnigg [NB 561 IE]

Conformational Analysis. By *E. L. Eliel, N. L. Allinger, S. J. Angyal,* and *G. A. Morrison.* John Wiley & Sons, Inc., New York-London 1965. 2nd ed., xiii, 524 pp., numerous illustrations, paper $ 15.00.

The object of stereochemistry is to correlate the spatial arrangement of the atoms in molecules with the physical and chemical properties of the latter. This undertaking formerly met with only limited success, since the internal mobility of the molecules, which seemed excessively complicated, was disregarded. It is now accepted that it is unnecessary to consider all steric arrangements (*e.g.* conformations) of mobile molecules. Many "pure" substances simply consist of a few molecular species (mostly conformers), which (at present) cannot be separated owing to their rapid interconversion.

Conformational analysis consists in the determination of the composition of these mixtures by physical methods, and so

permits the correlation of the steric arrangement of the component molecules with their physical properties (*e.g.* energy). The intramolecular strains deduced from these properties are then used for the analysis of specifically arranged transition states, so that a direct relationship is found between molecular structure and chemical properties.

This work testifies to the fruitfulness and the wide applicability of this young discipline of organic chemistry.

The book deals with theoretical aspects of thermodynamics, kinetics, ultraviolet, infrared, microwave, and NMR spectroscopy, rotatory dispersion, and molecular refraction. It contains tables of rates, strain energies, equilibria, and rotation barriers. The different interests of the authors ensure a many-sided balance of subject matter, as is shown by the following randomly-chosen key phrases: conformational energy, kinetic determination of equilibria, isomerization of hydrocarbons (with methods), 2-, 3-, an 4-alkyl ketone effect, *gem*-dimethyl effect, 1,2-diaxial rearrangement, syn-axial interaction, medium and large rings, reflex effects, synthesis of cortisone from cholic acid, Δ^2-effect, anomeric effect in pyranosides, deformation of the cyclohexane chair, flexible form, entropy in equilibria, specific reactions of sugars, terpenoids, and steroids. The authors offer interesting rationalizations of a number of "rules", such as the von Auwers rule, the octant rule, the Brewster rule, and the phenylosotriazole rule.

A very large part of the book is concerned with the chemistry of cyclohexane and its derivatives, in which conformational analysis first took root, and in which it still finds its most successful applications. The reason for this is the small number of conformers involved and the depths of their energy minima.

It is regrettable that the designation of partial conformations by "*syn*-clinal (sc)", "*anti*-periplanar (ap)" *etc.* was not used consistently by the authors, since this together with the sequence rule (which is not mentioned) permits a simple and comprehensive description of any conformation.

Unfortunately, the four reactions given on pages 28–30 do not illustrate the Curtin-Hammett principle in a convincing manner. The first example is open to another interpretation (see footnotes on pp. 29 and 30), while the other three are really different cases of "steric" control of a reaction in which two "stereoelectronic" routes are possible. The 2:1 excess of the *erythro* product described on p. 34 scarcely can have resulted from the reaction of methylmagnesium bromide with 3-phenyl-2-butanone.

In spite of a few such minor shortcomings, the book by these four authors from the U.S.A., Australia, and England is an outstanding contribution to stereochemistry. The book is really absorbing in many places, and should not be missed by any diligent student or research worker. It gives a review, both panoramic and detailed, of the field of conformational analysis. The book also shows that the originally qualitative, and hence simple method has now entered a much complicated, but quantitative phase.

A. S. Dreiding [NB 514 IE]

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Benzene Oxide-Oxepin Valence Tautomerism

BY E. VOGEL AND H. GÜNTHER [*]

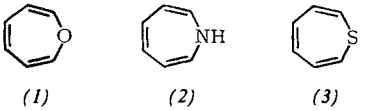
Dedicated to Prof. R. Criegee on the occasion of his 65th birthday

Benzene oxide and the potential 8π-electron system oxepin exist in valence-tautomeric equilibrium with each other, to which both components contribute to approximately the same extent. NMR spectroscopic measurements show that the equilibrium is rapidly established (activation energies of the forward and reverse reactions 9.1 and 7.2 kcal mole^{-1}, respectively). The present knowledge of the properties of oxepin justifies its classification as a "heterotropilidene". Benzene oxide-oxepin represents a system having fluctuating bonds, the equilibrium of which can be displaced from one extreme to the other by means of suitable substituents. The oxide component determines the reactions of the system with most agents.

With 1,6-oxido[10]annulene, which is formally a 2,7-bridged oxepin, the oxepin character is completely suppressed by the formation of a delocalized 10π-electron system extending over the C_{10} perimeter. The existence and aromatic character of 1,6-oxido[10]-annulene give rise to the conception of a homologous series of oxygen bridged annulenes (1,6;8,13-bisoxido[14]annulene, 1,6;8,17;10,15-trisoxido[18]annulene etc.), which, like the parent acenes, possess a (4n + 2)π-electron system. Molecular models demonstrate that a considerable flattening of the C_{4n+2} perimeter is achievable in the case of a syn or all-syn arrangement of the oxygen bridges, and that the requirement for aromaticity is thus satisfied. This is confirmed in a striking manner by the synthesis and properties of syn-1,6; 8,13-bisoxido[14]annulene.

I. Introduction

The discovery of the tropolones and the tropylium ion [1] resulted in the rapid development of the chemistry of carbocyclic aromatic seven-membered ring systems and an increased interest in the as yet unknown heterotropilidenes oxepin *(1)*, azepine *(2)*, and thiepin *(3)*, which are formally homologues of furan, pyrrole, and thiophene. *(1)*, *(2)*, and *(3)* are potential 8 π-electron systems, isoelectronic with the unstable cycloheptatrienyl anion [2] and cyclooctatetraene; thus they do not satisfy the Hückel rule, and therefore should not exhibit an electronic stability comparable with that of the tropylium compounds. Consequently, heterotropilidenes may provide an interesting test of the modern theories regarding the nature of aromaticity [3]. A knowledge of the heterotropilidenes above all promises valuable information on similarities and



(1) *(2)* *(3)*

[*] Prof. Dr. E. Vogel and Dr. H. Günther
Institut für Organische Chemie der Universität
Zülpicher Str. 47
5 Köln (Germany)

[1] *T. Nozoe* in *D. Ginsburg*: Non-Benzenoid Aromatic Compounds. Interscience, New York 1959, p. 339; *W. v. E. Doering*: Theoretical Organic Chemistry. Butterworths, London 1959, p. 35; *D. M. G. Lloyd*: Carbocyclic Non-Benzenoid Aromatic Compounds. Elsevier, Amsterdam 1966.

[2] *H. J. Dauben jr.* and *M. R. Rifi*, J. Amer. chem. Soc. *85*, 3041 (1963); *W. v. E. Doering* and *P. P. Gaspar*, *ibid. 85*, 3043 (1963); *R. Breslow* and *H. W. Chang*, *ibid. 84*, 1484 (1962).

[3] *E. Hückel*, Z. Physik *70*, 204 (1931); Grundzüge der Theorie ungesättigter und aromatischer Verbindungen. Verlag Chemie, Berlin 1938; *A. Streitwieser*: Molecular Orbital Theory for Organic Chemists. J. Wiley, New York 1961, p. 256.

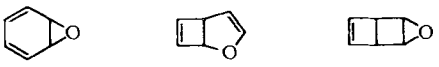
differences in the properties of $4n$- and $(4n+2)$-π-electron systems.

Despite their simple structure, all attempts to synthesize oxepin and thiepin have so far been unsuccessful [4]; however, *N*-alkoxycarbonylazepines [5] and *N*-cyanoazepines [6] have become readily accessible by thermolysis of azidoformates and cyanazide in benzene and its derivatives. No detailed information is yet available concerning the parent compound 1*H*-azepine *(2)*, which, it is claimed, results from the alkaline hydrolysis of *N*-ethoxycarbonylazepine. It is evidently a very reactive substance, which rearranges rapidly into the tautomeric 3*H*-azepine [7,8]. *N*-Methylazepine, which is prepared from *N*-ethoxycarbonylazepine [7,9], and whose spectral properties should be very close to those of *(2)*, is also rather unstable; on standing for a short time it changes into a dimer [9].

The successful preparation of the *N*-methylated azepine suggested that, of the heterotropilidenes *(1)* to *(3)*, at least oxepin should be isolable. Like its analogues, this compound would be able to isomerize into the benzenoid system (formation of phenol); however, there is no possibility of tautomerization (such as exists with *(2)*) or of spontaneous elimination of the hetero atom (as is conceivable for *(3)*, *via* benzene sulfide).

Most of the earlier attempts to synthesize oxepin were patterned on *Willstätter*'s cycloheptatriene synthesis, *i.e.* attempts were made to introduce the missing double bonds into tetrahydro- or dihydrooxepins [10]. Critical examination of the results of these efforts suggests that no oxepin was formed in most cases. However, if the desired product had been formed in one of these reactions, it could have had little chance of survival because of the drastic conditions used.

In view of the difficulty of obtaining oxepin *via* partially hydrogenated derivatives, an attractive alternative method of preparation would seem to be the thermal rearrangement of strained valence isomers of oxepin [11]. The obvious choice of isomer is the hypothetical benzene oxide *(4)*, which was assumed, more intuitively than from thermodynamic considerations, to be less stable than oxepin. On the basis of this estimated stability relationship a ready benzene



(4) *(5)* *(6)*

oxide → oxepin isomerization could be envisaged, particularly since the disrotatory course of the reaction [12] and the geometry of the valence-isomeric system are matched to each other. In the case of the four-membered ring valence isomer 2-oxabicyclo-[3.2.0]hepta-3,6-diene *(5)*, on the other hand, the result of thermolysis is more difficult to predict. The cleavage of the cyclobutene ring in *(5)* does not conform stereochemically (conrotatory process) with the rearrangement to the oxepin [12,13], so that the isomerization temperatures required would almost certainly prove too high for the product. In the final case to be considered, *i.e.* the oxide of Dewar-benzene *(6)*, the conversion into oxepin would again appear promising, since the extremely high ring strain should allow homolytic cleavage of the bond common to the two four-membered rings, even at low temperatures. The sterically unfavorable synchronous isomerization of the cyclobutene ring would thus be bypassed.

II. Thermolysis of Epoxide C–C Bonds

The dehydrohalogenation of 1,2-epoxy-4,5-dibromocyclohexane *(17)* [14] provides a simple scheme for the synthesis of benzene oxide. However, according to investigations by *Meinwald* and *Nozaki* [15], only phenol can be isolated when *(17)* is heated with γ-collidine or sodium glycolate in an excess of ethylene glycol. Dehydrohalogenation experiments on *(17)* carried out simultaneously by our own research group [16] with a series of nitrogen bases were also unsuccessful.

The fact that dehydrohalogenation of *(17)* to benzene oxide under very mild conditions, as well as the benzene oxide-oxepin isomerization (which involved cleavage of an epoxide C–C bond), had to be regarded as unusual reactions at that time, may explain the reluctance to pursue further the above route to oxepin. However, following recent reports of the cleavage of the C–C bond in epoxides, it became almost certain that at least the second reaction step was feasible.

Braun's study [17] of the LiCl-catalysed pyrolysis of 1,2-divinylethylene carbonate *(7)* (mixture of *cis* and

[4] 3-Benzoxepin has become known through investigations by *K. Dimroth* [*K. Dimroth, G. Pohl,* and *H. Follmann,* Chem. Ber. *99*, 634 (1966); *K. Dimroth* and *G. Pohl,* Angew. Chem. *73*, 436 (1961)]; earlier papers deal with derivatives of 3-benzoxepin and its N and S analogues.

[5] *K. Hafner* and *C. König,* Angew. Chem. *75*, 89 (1963); *K. Hafner, D. Zinser,* and *K.-L. Moritz,* Tetrahedron Letters *26*, 1733 (1964); *R. J. Cotter* and *W. F. Beach,* J. org. Chemistry *29*, 751 (1964); *W. Lwowski, T. J. Maricich,* and *T. W. Mattingly jr.,* J. Amer. chem. Soc. *85*, 1200 (1963).

[6] *F. D. Marsh* and *H. E. Simmons,* J. Amer. chem. Soc. *87*, 3529 (1965).

[7] *K. Hafner,* Angew. Chem. *75*, 1041 (1963); Angew. Chem. internat. Edit. *3*, 165 (1964).

[8] A tricarbonyliron complex of 1*H*-azepine was recently obtained by *E. O. Fischer* and *H. Rühle,* Z. anorg. allg. Chem. *341*, 137 (1965).

[9] *K. Hafner* and *J. Mondt,* Angew. Chem. *78*, 822 (1966); Angew. Chem. internat. Edit. *5*, 839 (1966).

[10] *S. Olsen* and *R. Bredoch,* Chem. Ber. *91*, 1589 (1958); *E. E. Schweizer* and *W. E. Parham,* J. Amer. chem. Soc. *82*, 4085 (1960); *J. Meinwald, D. W. Dicker,* and *N. Danieli, ibid. 82*, 4087 (1960); *W. Kinzebach,* Diploma Thesis, Universität Marburg, 1962.

[11] Review on valence isomerizations in strained ring systems: *E. Vogel,* Angew. Chem. *74*, 829 (1962); see also *S. J. Rhoads* in *P. de Mayo*: Molecular Rearrangements. Wiley. New York 1963, p. 655.

[12] *R. B. Woodward* and *R. Hoffmann,* J. Amer. chem. Soc. *87*, 395 (1965).

[13] For the stereochemistry of the valence isomerization of cyclobutenes, see *R. Criegee, D. Seebach, R. E. Winter; B. Börretzen,* and *H.-A. Brune,* Chem. Ber. *98*, 2339 (1965).

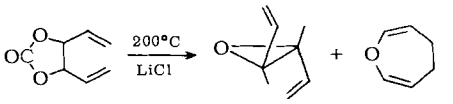
[14] *E. E. van Tamelen,* J. Amer. chem. Soc. *77*, 1704 (1955).

[15] *J. Meinwald* and *H. Nozaki,* J. Amer. chem. Soc. *80*, 3132 (1958).

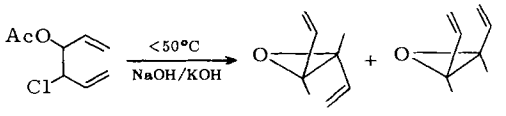
[16] *J. Ferry,* Diploma Thesis, Technische Hochschule Karlsruhe, 1959.

[17] *R. A. Braun,* J. org. Chemistry *28*, 1383 (1963).

trans isomers) is particularly relevant to the benzene oxide-oxepin problem. This reaction, which requires a temperature of 200 °C, gives not only *trans*-1,2-divinylethylene oxide *(8)*, but also 4,5-dihydrooxepin



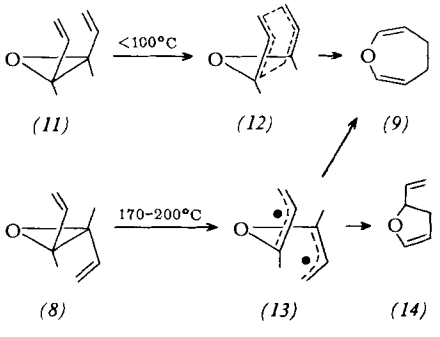
(7) *(8)* *(9)*



(10) *(8)* *(11)*

(9), the formation of which is probably due to a Cope rearrangement of initially formed *cis*-1,2-divinylethylene oxide *(11)*, facilitated by the strain in the epoxide ring. In order to avoid the pyrolysis of the carbonate, which is prohibitive to the isolation of *(11)*, *Stogryn, Gianni*, and *Passannante* [18] studied the action of alkali metal hydroxide on 3-chloro-4-acetoxy-1,5-hexadiene *(10)* (presumably a mixture of the two diastereoisomers). In this case, epoxide formation occurred at 40 to 50 °C, and it was possible to isolate *cis*-1,2-divinylethylene oxide. As expected, the *cis*-1,2-divinylethylene oxide undergoes the Cope rearrangement *(11)* → *(12)* below 100 °C, with quantitative formation of 4,5-dihydrooxepin *(9)*.

We investigated the thermal behavior of the relatively stable *trans*-1,2-divinylethylene oxide [19] and found that, at 170–200 °C, it also rearranged completely with cleavage of the epoxide C–C bond. As in the case of the *cis*-isomer, 4,5-dihydrooxepin was obtained; however, this was accompanied by a second product, which had escaped the earlier investigators, and which was identified as 2-vinyl-2,3-dihydrofuran *(14)*. Between 170 and 200 °C, the ratio of the quantities of seven-membered to five-membered ring ethers (30:70) is practically independent of the temperature and of the pyrolysis time. It is deduced from the relatively high isomerization temperatures and from the observed branching of the reaction that the rearrangement of *trans*-1,2-divinylethylene oxide *(8)* proceeds *via* the biradical intermediate *(13)*.



(11) *(12)* *(9)*

(8) *(13)* *(14)*

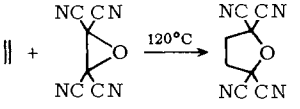
[18] *E. L. Stogryn, M. H. Gianni*, and *A. J. Passannante*, J. org. Chemistry *29*, 1275 (1964).

[19] *E. Vogel, R. Sundermann*, and *R. Schubart*, unpublished.

The mechanistic interpretation of the pyrolysis of *cis*- and *trans*-1,2-divinylethylene oxide, which is based largely on analogy with the thermal behavior of *cis,trans*-isomeric 1,2-divinylcycloalkanes containing strained rings [11, 20–24], was supported by a kinetic study. The isomerizations of the two compounds in the gas phase strictly obeyed the first-order rate law. The reaction of the *cis* oxide was not appreciably accelerated by an increase in surface area, whereas slight wall catalysis was observed in the case of the *trans* oxide. The activation parameters found for the rearrangement of the *cis* compound were $\Delta H^{\ddagger} = 24.6$ kcal mole^{-1} and $\Delta S^{\ddagger} = -11.3$ cal deg^{-1} mole^{-1}, while those for the *trans* compound were $\Delta H^{\ddagger} = 36.0$ kcal mole^{-1} and $\Delta S^{\ddagger} = -0.4$ cal deg^{-1} mole^{-1} [19].

Thus *cis*-1,2-divinylethylene oxide has a low activation energy and a highly negative activation entropy, whereas the *trans* compound has a relatively high activation energy and only a slightly negative activation entropy. If in addition one considers the nature of the rearrangement products, the essential criteria for a synchronous mechanism in the isomerization of the *cis* oxide and for a free-radical mechanism in the case of the *trans* oxide are satisfied. The difference of 11 kcal mole^{-1} in the activation energies for the concerted rearrangement of *(11)* and the free-radical cleavage of *(8)* is of the order of magnitude found for analogous cases [23–26].

Linn, Webster, and *Benson* [27] observed another example of the cleavage of an epoxide at the C–C bond, namely in tetracyanoethylene oxide *(15)*. This compound can undergo cycloadditions with olefins and acetylenes to form tetracyanotetrahydrofurans *(16)* and tetracyanodihydrofurans. Tetracyanoethylene oxide can add to aromatic systems with formation of tetracyanotetrahydroisobenzofurans.



(15) *(16)*

A kinetic investigation of the reaction of tetracyanoethylene oxide with styrene and *trans*-stilbenes [28] showed that the addition step is preceded by a thermal

[20] *E. Vogel, K.-H. Ott*, and *K. Gajek*, Liebigs Ann. Chem. *644*, 172 (1961).

[21] *W. v. E. Doering* and *W. R. Roth*, Angew. Chem. *75*, 27 (1963); Angew. Chem. internat. Edit. *2*, 115 (1963).

[22] *W. v. E. Doering* and *W. R. Roth*, Tetrahedron *19*, 715 (1963).

[23] *G. S. Hammond* and *C. D. DeBoer*, J. Amer. chem. Soc. *86*, 899 (1964); *E. Schmidt*, Diploma Thesis, Universität Köln, 1964.

[24] *W. R. Roth*, personal communication.

[25] According to *W. v. E. Doering* and *J. C. Gilbert*, Tetrahedron Suppl. No. 7, 397 (1966), footnotes 36 and 37, the synchronous process in the case of 1,5-hexadiene leads to a lowering of the activation energy by 11 kcal mole^{-1} [cleavage of 1,5-hexadiene into free allyl radicals: $\Delta H^{\ddagger} = 46.5$ kcal mole^{-1}; Cope rearrangement of 1,1-dideuterio-1,5-hexadiene: $\Delta H^{\ddagger} = 35.5$ kcal mole^{-1}].

[26] *R. Sundermann* found the following activation parameters for the isomerization of *trans*-1,2-divinylcyclopropane into 1,4-cycloheptadiene; $\Delta H^{\ddagger} = 32$ kcal mole^{-1} and $\Delta S^{\ddagger} = -3.6$ cal deg^{-1} mole^{-1} (cf. [21]).

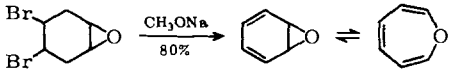
[27] *W. J. Linn, O. W. Webster*, and *R. E. Benson*, J. Amer. chem. Soc. *85*, 2032 (1963); *W. J. Linn* and *R. E. Benson*, *ibid. 87*, 3657 (1965).

[28] *W. J. Linn*, J. Amer. chem. Soc. *87*, 3665 (1965).

equilibrium between tetracyanoethylene oxide and an activated form thereof. When sufficiently reactive olefins, such as styrene, are used, the formation of excited tetracyanoethylene oxide becomes rate-determining. The addition taking place in the second step has the characteristics of a multi-center process.

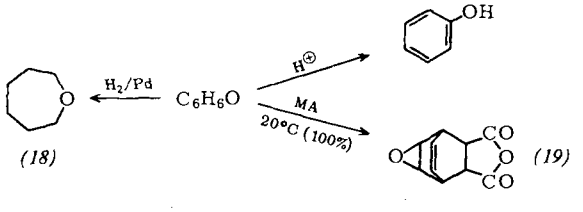
III. Benzene Oxide-Oxepin

The course of the thermolysis of *cis*- and *trans*-1,2-divinylethylene oxide gave new support to the concept of synthesizing oxepin *via* benzene oxide. The real problem was to find a suitable route to benzene oxide. Owing to the ready availability of the starting material, a reinvestigation of the dehydrohalogenation of 1,2-epoxy-4,5-dibromocyclohexane *(17)* [15,16] suggested itself. We found that the action of sodium methoxide on *(17)* in boiling ether gave an orange product C_6H_6O, (yield > 80 %) which was isomeric with phenol [29,30]. The question was whether this was benzene oxide, oxepin, or a valence-tautomeric mixture of benzene oxide and oxepin. As in the case of tropilidene [11], it turned out to be problematical to decide between these three possibilities by chemical means.



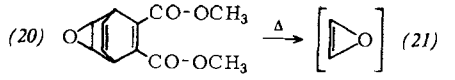
(17) *(4)* *(1)*

The substance C_6H_6O, which is stable at room temperature, readily isomerizes under the influence of Brönsted (proton) and Lewis-acids to form phenol; aromatization takes place, though only slowly, even in neutral aqueous solution. Distillation at normal pressure also leads to more or less complete rearrangement to phenol. Hydrogenation with palladium-charcoal produces mainly oxepane *(18)* (about 70 %)

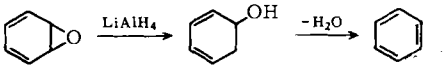


(18) *(19)*

together with cyclohexanol and unidentified products. Reaction with maleic anhydride, even at 20 °C, leads within a few minutes to an adduct *(19)*, which must, according to its NMR spectrum and the absence of a UV-maximum above 220 mμ, be derived from benzene oxide. Dimethyl acetylenedicarboxylate gives an adduct *(20)* of the same type after a few days (20 °C). Attempts to fragment *(20)* by the Alder-Rickert method into acetylene oxide *(21)* and dimethyl phthalate have not so far yielded conclusive results.

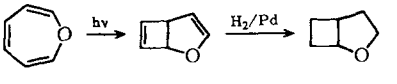


The dehydrohalogenation product C_6H_6O can be reduced with lithium aluminum hydride to form the vacuum-distillable cyclohexa-1,3-dien-5-ol *(22)* ("hydrated benzene"), which undergoes wall-catalysed decomposition into benzene and water on standing. Methyl-lithium gives a mixture of the relatively stable *cis*- and *trans*-1-methylcyclohexa-2,4-dien-6-ols in which the *cis*:*trans* ratio is higher than 90:10.



(4) *(22)*

While the result of hydrogenation is equally compatible with either the benzene oxide or the oxepin formula, the relatively easy diene synthesis, the isomerization into phenol, and the reduction with lithium aluminum hydride can best be explained by the benzene oxide formula. On the other hand, the recently observed, almost quantitative photochemical conversion of the product C_6H_6O into 2-oxabicyclo[3.2.0]hepta-3,6-diene *(5)* is indicative of the presence of oxepin [31]. It seems unlikely that oxepin is formed from benzene oxide on irradiation, since a photochemical benzene oxide-oxepin isomerization should be forbidden according to the Woodward-Hoffmann rule [12]. The photoisomer *(5)*, the structure of which is proved mainly by the formation of 2-oxabicyclo[3.2.0]heptane *(23)* on hydrogenation [32], exhibits the anticipated thermal stability. At the temperature required to isomerize *(5)* back into oxepin (150–160 °C) the latter is no longer stable, and thus only phenol is obtained as the pyrolysis product.



(1) *(5)* *(23)*

Though the above chemical reactions point very strongly to the existence of a valence-tautomeric mixture of benzene oxide and oxepin, they do not constitute conclusive proof, since a change in structure caused by the agent in question cannot be ruled out. Consequently, spectroscopic methods must be used in an attempt to clarify the benzene oxide-oxepin problem.

The UV spectrum of the product (Fig. 1) shows an unusually strong dependence on the solvent. The absorption curves show an isosbestic point, a sure indication of the presence of two compounds, benzene oxide and oxepin, in equilibrium with each other. In order to assign the maxima and to obtain some information regarding the ratio of the components,

[29] *E. Vogel, R. Schubart* and *W. A. Böll*, Angew. Chem. *76*, 535 (1964); Angew. Chem. internat. Edit. *3*, 510 (1964); Chem. Engng. News *42*, No. 40, 40 (1964).

[30] *E. Vogel, W. A. Böll*, and *H. Günther*, Tetrahedron Letters *1965*, 609.

[31] A similar photoisomerization was observed for 2,7-dimethyloxepin by *L. A. Paquette* and *J. H. Barrett*, J. Amer. chem. Soc. *88*, 1718 (1966).

[32] *L. A. Paquette, J. H. Barrett, R. P. Spitz*, and *R. Pitcher*, J. Amer. chem. Soc. *87*, 3417 (1965).

we tried to derive the UV spectra of benzene oxide and oxepin with the aid of suitable reference substances.

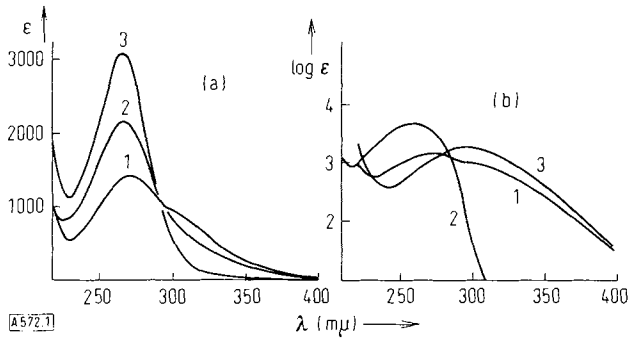
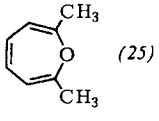


Fig. 1. (a) UV-Spectrum of benzene oxide-oxepin *(4)* ⇌ *(1)*.
1. in isooctane; 2. in methanol; 3. in water-methanol (85:15).
(b) UV-spectra in isooctane
1. benzene oxide-oxepin *(4)* ⇌ *(1)*; 2. 8,9-indan oxide *(24)*;
3. 2,7-dimethyloxepin *(25)*.

The model used for benzene oxide was 8,9-indan oxide *(24)*, in which the rearrangement into the oxepin isomer is blocked by the bracket effect of the trimethylene bridge (cf. Section IV. 5). The same principle had previously been used to fix the norcaradiene skeleton [33,34]. 8,9-Indan oxide *(24)* is colorless, and in isooctane possesses a UV spectrum of the cyclohexa-1,3-diene type with λ_{max} = 258 mμ (ε = 4900). A suitable reference substance for oxepin is its 2,7-dimethyl derivative *(25)*, in which the concentration of the oxide tautomer (if present) is below the detection limit of spectroscopic methods. The electronic spectrum of 2,7-dimethyloxepin contains a broad absorption band at λ_{max} (in isooctane) = 297 mμ (ε = 1800),

(24) 



(25)

which extends to about 430 mμ and gives the compound a yellow-orange color. Significantly, the UV spectra of both *(24)* and *(25)* are practically independent of the solvent.

These observations show that in the UV spectrum of the dehydrohalogenation product, the maximum at 271 mμ (ε = 1430) in isooctane is due to the benzene oxide component, whereas the shoulder at 305 mμ (ε = 900) corresponds to the oxepin maximum which must be located in this region. The position of the equilibrium cannot be accurately determined without knowledge of the extinction coefficients of the two valence tautomers, but it is estimated from comparison with the spectra of *(24)* and *(25)* that the benzene oxide concentration in isooctane is about 30 %, while that in water-methanol (85:15) is about 90 %. Concerning the solvent-dependence of the benzene oxide-oxepin equilibrium, which is presumably due to various factors, it is noteworthy that the proportion of benzene oxide increases with increasing dielectric constant of the solvent [30].

The existence of a benzene oxide-oxepin valence tautomerism with comparable concentrations of the components is clearly shown by NMR-spectroscopic investigations, which may also be used to deduce the thermodynamic and kinetic parameters of the equilibrium.

At room temperature, the ^{1}H–NMR spectrum of the product (Fig. 2) contains three groups of signals in the olefinic proton absorption region, the chemical shifts of which differ sufficiently to allow an assignment to the three pairs of protons of benzene oxide or oxepin purely on the basis of multiplicity. Thus the group of signals at τ = 4.8, which may be regarded to a first approximation as a doublet, must be assigned to the α-protons, while the multiplets at τ = 3.9 and τ = 4.4 can be assigned to the γ- and β-protons, respectively.

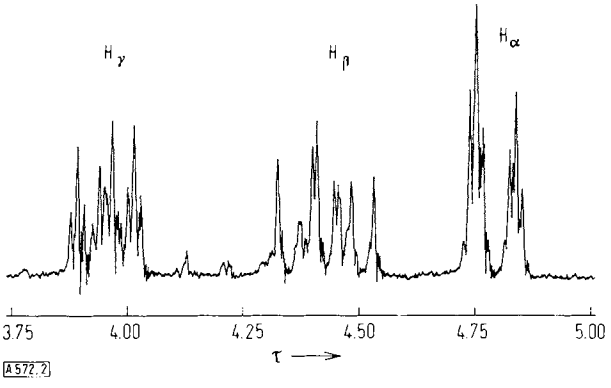


Fig. 2. ^{1}H–NMR spectrum of benzene oxide-oxepin at room temperature (in CS_2; 60 MHz; internal standard: tetramethylsilane).

The greatest difference in the spectra of benzene oxide and oxepin should be found for the position of the α-proton resonances. Taking cyclic enol ethers as a guide for oxepin, the α-protons of oxepin should absorb close to τ = 4.0. The resonance signals of the benzene oxide α-protons, on the other hand, would be expected to occur in the region of τ = 6.5 to 7.0, on the basis of experience with vinyl-substituted epoxides (Table 1).

Table 1. τ values of the α-protons of cyclic enol ethers and vinyl-substituted epoxides.

4,5-Dihydrofuran	3.77 [35]	*trans*-Divinylethylene oxide	6.9 [37]
5,6-Dihydro-γ-pyran	3.78 [35]	*cis*-Divinylethylene oxide	6.6 [37]
γ-Pyran	3.84 [36]	Cyclooctatetraene oxide	6.7 [37]
4,5-Dihydrooxepin	3.9 [37]	1,2-Epoxycycloocta-3,6-diene	6.5 [39]
2,3-Dihydrooxepin	3.69 [38]		
1-Benzoxepin	3.9 [37]		

[33] *E. Vogel, W. Wiedemann, H. Kiefer*, and *W. F. Harrison*, Tetrahedron Letters *1963*, 673.

[34] *J. Schreiber, W. Leimgruber, M. Pesaro, P. Schudel, T. Threlfall*, and *A. Eschenmoser*, Helv. chim. Acta *44*, 540 (1961); *R. Darms, T. Threlfall, M. Pesaro*, and *A. Eschenmoser*, *ibid. 46*, 2893 (1963).

[35] *L. M. Jackman*: Applications of NMR-Spectroscopy in Organic Chemistry. Pergamon Press, London 1959, p. 62.

[36] *S. Masamune* and *N. T. Castellucci*, J. Amer. chem. Soc. *84*, 2452 (1962).

[37] *E. Vogel, R. Schubart* and *H. Günther*, unpublished.

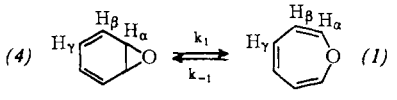
[38] *E. E. Schweizer* and *W. E. Parham*, J. Amer. chem. Soc. *82*, 4085 (1960).

[39] *P. Radlick* and *S. Winstein*, J. Amer. chem. Soc. *86*, 1866 (1964).

The observation that the α-proton resonance ν^{α} of the product lies between the expected values for benzene oxide and oxepin suggests a rapid valence tautomerism with comparable concentrations of the two forms, since for a rapid exchange ($k > 10^3$ sec^{-1}) of corresponding benzene oxide and oxepin protons, according to eq. (a), ν^{α} may be regarded as the average of the chemical shifts $\nu^{\alpha}_{(4)}$ and $\nu^{\alpha}_{(1)}$ ($p_{(4)}$, $p_{(1)}$ = mole fractions)[40]; the same is true of ν^{β} and ν^{γ}.

$$\nu^{\alpha} = p_{(4)}\,\nu^{\alpha}_{(4)} + p_{(1)}\,\nu^{\alpha}_{(1)} \qquad \text{(a)}$$

The assumption of an equilibrium of this type is confirmed by the temperature-dependence of the NMR spectrum[41] (Fig. 3).



The principal changes observed down to −80 °C are shifts of the resonance frequencies. The α-proton resonance undergoes a steady upfield shift, while the β-proton resonance is displaced in the opposite direction; the γ-proton resonance remains approximately constant. The same phenomena are observed in the room temperature spectra on changing the solvent from carbon tetrachloride to a polar medium such as methanol or dimethyl sulfoxide-water (cf. the solvent-dependence of the UV spectra, Fig. 1). The resonance shifts are therefore due to a displacement of the equilibrium. As can be deduced from the increasing shielding of the α-protons, the benzene oxide component is favored by a decrease in temperature, as well as by a change to a polar solvent.

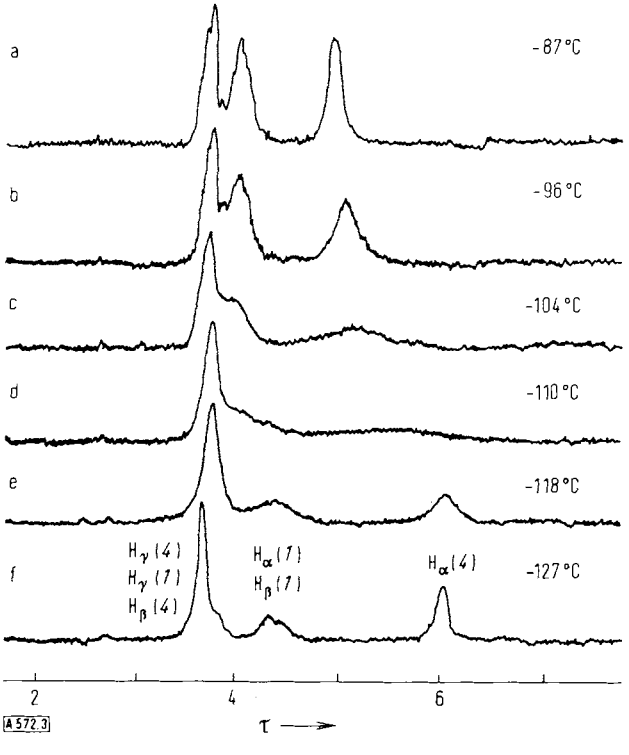


Fig. 3. ^{1}H—NMR spectra of benzene oxide-oxepin at various temperatures in CF_3Br/pentane (2:1) (60 MHz; internal standard: tetramethylsilane).

When the temperature is lowered below −80 °C, the exchange rate ultimately becomes so slow that the "average spectrum" is replaced by the individual spectra of the two equilibrium components (Fig. 3f). This process is shown particularly clearly by the α-proton signal, which reaches its maximum halfwidth at about −113 °C and then splits into two new absorptions which, as expected, are strongly separated, and which must be due to the α-protons in benzene oxide and oxepin.

In order to deduce the kinetics of the equilibrium *(4)* ⇌ *(1)* from the changes in the line shape of the spectrum, the assignment of the low temperature spectrum is essential. This can be made on the basis of the ratio of the signal areas and of the following considerations:

1. The resonance of the α-protons in benzene oxide must occur at the highest field strength[42].

2. The shift difference between the β- and γ-protons in benzene oxide must be small[43].

3. The shift difference between the β- and γ-protons in oxepin must be large[43].

The equilibrium constant K of the valence tautomerism *(4)* ⇌ *(1)* was determined below the coalescence temperature (−113 °C) from the ratio of the signal areas, and above this temperature from the resonance position of the α-proton signal. Its temperature-dependence gave a value of ΔH^0 ($=H^0_{(1)} - H^0_{(4)}$) = 1.7 ± 0.4 kcal mole^{-1} for the enthalpy of the isomerization *(4)* → *(1)*.

The lifetimes $\tau_{(4)}$ and $\tau_{(1)}$ of the valence tautomers, which must be known in order to find the activation parameters, are obtained from the halfwidths Δ' of the α-proton signal in the regions of slow and fast exchange (below −118 °C and above −110 °C respectively). Δ' was corrected for field inhomogeneity and coupling with the β-protons, whereas the long-range coupling with the γ-protons was not taken into account. For the limiting cases mentioned, the following relationships exist between the lifetime τ and the exchange broadening Δ_a of a resonance signal[40,44]:

$$\text{slow exchange: } 1/\tau_{(4)} = k_1 = \pi\Delta_a \qquad \text{(b)}$$

$$\text{fast exchange: } 1/\tau_{(4)} = k_1 = 4\pi p_{(4)}\, p^2_{(1)}\, (\delta\nu)^2/\Delta_a \qquad \text{(c)}$$

The rate constants k_1 ($=1/\tau_{(4)}$) and k_{-1} ($=1/\tau_{(1)}$) as found from equations (b) and (c) for ten different temperatures satisfy the Arrhenius equations:

$$k_1 = 10^{14.4 \pm 1.1} \exp\,[-(9100 \pm 800)/RT]\ (\text{sec}^{-1})$$

$$k_{-1} = 10^{12.1 \pm 1.4} \exp\,[-(7200 \pm 1000)/RT]\ (\text{sec}^{-1})$$

The ratio of the frequency factors gives the entropy difference ΔS^0 ($=S^0_{(1)} - S^0_{(4)}$) = 10.5 ± 8.3 cal deg^{-1} mole^{-1}. Using the equilibrium constant K for the calculation of ΔS^0 one obtains 11.0 ± 5.0 cal deg^{-1} mole^{-1}.

The favorable position of the equilibrium ($K < 20$) permits the observation and evaluation of the benzene oxide-oxepin valence tautomerism by NMR spectroscopy. According to these investigations the energy of benzene oxide is *ca.* 1.7 kcal mole^{-1} lower than that of oxepin. However, at room temperature the entropy gain associated with this rearrangement causes a considerable displacement of the equilibrium in favor of oxepin ($\Delta G \approx -1.3$ kcal mole^{-1}). Owing to the low activation energies of the forward and reverse reactions (9.1 and 7.2 kcal mole^{-1}, respectively), which

[40] *J. A. Pople, W. G. Schneider,* and *H. J. Bernstein*: High Resolution Nuclear Magnetic Resonance. McGraw-Hill Book Co., Inc., New York 1959, p. 218.

[41] *H. Günther*, Tetrahedron Letters *1965*, 4085.

[42] This follows from the data of Table 1.

[43] This condition follows from the changes in the resonance frequencies in the average spectrum with temperature.

[44] *L. H. Piette* and *W. A. Anderson*, J. chem. Physics *30*, 899 (1959).

permit the isomers to be isolated at best by crystallization, benzene oxide-oxepin may be regarded as a system with fluctuating bonds (at 0 °C the valence isomerization of the benzene oxide-oxepin system proceeds approximately 10^4 times faster than that of bullvalene) [45].

How are the stability relationships of the benzene oxide-oxepin system to be interpreted? An enthalpy of formation of 29 kcal $mole^{-1}$ has been calculated for oxepin (three *cis*-CH=CH groups and one O group) by the method of Franklin [46]. A corresponding calculation for benzene oxide (two *cis*-CH=CH, two CH, and one O group) gives values of 21 and 35 kcal $mole^{-1}$, respectively, depending upon whether the value of 13 [47] or 27 kcal $mole^{-1}$ [48] is taken for the epoxide ring strain. The difference between the enthalpies of formation of oxepin and benzene oxide is therefore calculated as 8 or −6 kcal $mole^{-1}$, whereas the experimentally determined value is 1.7 kcal $mole^{-1}$. The conclusion to be drawn [49] from these considerations is that the stabilization energy of oxepin (with an epoxide ring strain of 13 kcal $mole^{-1}$) is at most of the order of magnitude of that of tropilidene (7 kcal $mole^{-1}$) [50].

A clearer indication of the expected non-aromatic character of oxepin is given by spectroscopic investigation of 2,7-dimethyl- and 2,7-pentamethylene-oxepin (cf. Section IV.2). These investigations indicate that oxepin possesses a nonplanar ring skeleton, which should correspond closely to that of tropilidene. It is thus justified to speak of oxepin as a heterotropilidene.

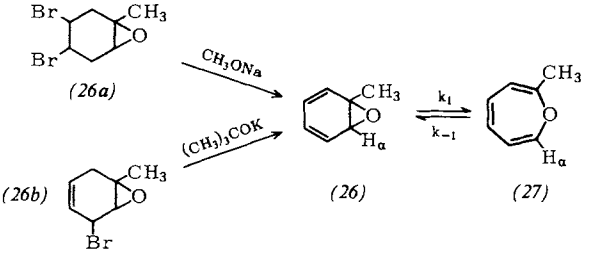
IV. Substituted Oxepins

The synthesis of oxepin described above is versatile, and has already been used for the preparation of a variety of substituted oxepins. The limiting factor of the method appears to be that the 1,4-cyclohexadienes used as starting materials are sometimes difficult to convert into 1,2-epoxy-4,5-dibromocyclohexanes, the immediate precursors of the arene oxide-oxepin systems. If the 1,4-cyclohexadienes are first converted into 1,2-epoxycyclohex-4-enes (instead of into dibromocyclohexenes), it can be advantageous to introduce the missing double bond by monohalogenation in the allyl position (with *N*-bromosuccinimide or t-butyl hypochlorite) followed by dehydrohalogenation, and not by bromination-dehydrobromination.

Owing to the sensitivity of the benzene oxide-oxepin equilibrium, it takes only small substituent effects to displace the position of the equilibrium from one extreme to the other. Substituents in the α-position would be expected, *a priori*, to favor the oxepin form electronically, and possibly sterically; the effects of substituents in the β- and γ-positions are more difficult to predict. A suitable model for the expected substituent-dependence of the equilibrium is the valence-tautomeric system bicyclo[4.2.0]octa-2,4-diene ⇌ cycloocta-1,3,5-triene [51], in which the components are also present in comparable quantities.

1. 2-Methyloxepin

2-Methyloxepin *(27)*, an orange liquid (b.p. 33.5 to 34 °C/11 mm Hg), has been obtained both from the dibromide *(26a)* and from the allyl bromide *(26b)* by dehydrobromination (with sodium methoxide and with potassium t-butoxide, respectively). It reacts with maleic anhydride to give a 1:1 adduct (m.p. 197 to 198 °C), the NMR spectrum of which indicates that it is derived from 1-methylbenzene oxide *(26)*.



According to NMR- and UV-spectroscopic studies, 2-methyloxepin, unlike 2,7-dimethyloxepin, still exists in "rapid" equilibrium with a considerable quantity of the corresponding arene oxide, *i.e.* 1-methylbenzene oxide [49].

The NMR spectrum, like that of oxepin, is temperature-dependent (Fig. 4). A decrease in temperature leads first to broadening and then to splitting of the signals (−113 °C); on further cooling (−119 °C), the individual spectra of *(26)* and *(27)* appear. The differences with respect to the spectrum at

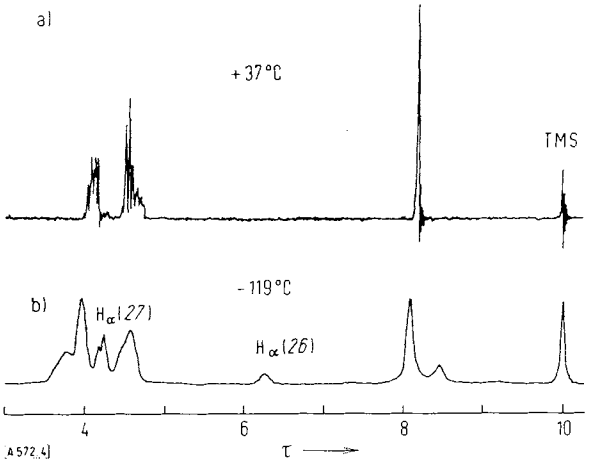


Fig. 4. ^1H—NMR spectrum of 2-methyloxepin (60 MHz; internal standard: tetramethylsilane) a) in CS_2 at +37 °C, b) in CF_3Br at −119 °C.

[45] *G. Schröder, J. F. M. Oth*, and *R. Merényi*, Angew. Chem. *77*, 774 (1965); Angew. Chem. internat. Edit. *4*, 752 (1965).

[46] *J. L. Franklin*, Ind. Engng. Chem. *41*, 1070 (1949).

[47] *R. A. Nelson* and *R. S. Jessup*, J. Res. nat. Bur. Standards *48*, 2307 (1952).

[48] *A. S. Pell* and *G. Pilcher*, Trans. Faraday Soc. *61*, 71 (1965).

[49] *H. Günther, R. Schubart*, and *E. Vogel*, Z. Naturforsch. *22b*, 25 (1967).

[50] *R. B. Turner, W. R. Meador*, and *R. E. Winkler*, J. Amer. chem. Soc. *79*, 4116 (1957); *R. B. Turner*: Theoretical Organic Chemistry. Butterworths, London 1959, p. 67.

[51] *A. C. Cope, A. C. Haven jr., F. L. Ramp*, and *E. R. Trumbull*, J. Amer. chem. Soc. *74*, 4867 (1952); *R. Huisgen*: Organic Reaction Mechanisms, Special Publ., Chem. Soc. (London) No. 19, 3 (1965).

37 °C are particularly noticeable in the case of the methyl proton absorption. In the low-temperature spectrum the doublet (J = 0.8 Hz) at τ = 8.20 initially observed for these protons is split into two signals (τ = 8.09 and 8.45), the positions of which correspond to those of the methyl protons in *(27)* and *(26)*. The intensities show that, under these conditions, the two compounds are present in a molar ratio of 7:3. The new signal at τ = 6.26 must be assigned to the α-proton in *(26)*, whereas the doublet at τ = 4.22 must be due to the corresponding proton in *(27)*. This is compatible with the coupling of about 5 Hz found for the latter proton. The intensity ratio of these protons again shows that the oxepin form predominates.

The equilibrium constant K of the valence tautomerism *(26)* ⇌ *(27)* below the coalescence temperature (−113 °C) was derived from the intensities of the methyl proton signals, and above this temperature from the chemical shift of the methyl protons. The reaction enthalpy ΔH^0 of the 1-methylbenzene oxide → 2-methyloxepin isomerization as calculated from the temperature-dependence of K is 0.4 ± 0.2 kcal mole^{-1}, *i.e.* 1.3 kcal mole^{-1} lower than that of the corresponding reaction in the parent system. ΔS^0 is calculated to be 5.0 cal deg^{-1} mole^{-1}.

The activation parameters for the equilibrium were deduced in this case from the changes in the methyl proton resonances with temperature. The evaluation was carried out with the aid of the complete equation of the absorption curve [40,52], the coupling of the methyl protons with the adjacent olefinic protons in the oxepin form also being taken into account. The theoretical spectra were calculated by means of a Fortran II program. Fitting calculated and experimental spectra by variation of the exchange rate permitted the determination of the lifetimes τ of the isomers. In the regions of slow and fast exchange, the approximations (b) and (c) could also be used for the determination of the τ values (lifetimes).

The Arrhenius equations obtained by these methods for the valence tautomerism *(26)* ⇌ *(27)* are:

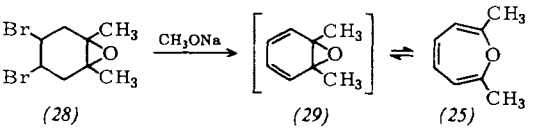
$$k_1 = 10^{14.2 \pm 0.9} \exp [-(9200 \pm 700)/RT] \text{ (sec}^{-1})$$

$$k_{-1} = 10^{13.1 \pm 0.9} \exp [-(8700 \pm 700)/RT] \text{ (sec}^{-1}).$$

In a comparison of the thermodynamic and kinetic quantities for the equilibrium *(26)* ⇌ *(27)* with those for the parent system, the decrease in the ΔH^0 value of the arene oxide-oxepin isomerization is particularly striking. Thus the introduction of the methyl group lowers the energy of the oxepin form in relation to that of the oxide form, either by hyperconjugation or by σ-bond stabilization [53]. The activation energy for the conversion of *(26)* into *(27)*, on the other hand, is practically the same as for the benzene oxide-oxepin rearrangement.

2. 2,7-Dimethyloxepin

In 2,7-dimethyloxepin *(25)* [29], which is obtained in high yield on dehydrobromination of 4,5-dibromo-1,2-epoxy-1,2-dimethylcyclohexane *(28)* with sodium methoxide, and which contains two α-methyl groups, the oxepin form is so strongly stabilized that the proportion of the oxide form in the equilibrium is below the spectroscopic detection limit (<5 %). However, 2,7-dimethyloxepin readily forms a maleic anhydride adduct derived from the oxide form. The strong displacement of the equilibrium to the oxepin side on α,α′-dimethyl substitution is undoubtedly not only the result of electronic interaction of the methyl groups with the double bond system in *(25)*, but is probably also due to the less favorable conformational situation in the oxide form (eclipsed *cis*-methyl groups).



(28) *(29)* *(25)*

The uniformity of 2,7-dimethyloxepin is shown in particular by the NMR spectrum (Fig. 5a). The positions of the methyl proton (τ = 8.19) and ring proton resonances ($H^{4,5}$: τ = 4.19, $H^{3,6}$: τ = 4.75) are in agreement with the triene structure *(25)*, as are the coupling parameters obtained by analysis of the AA′XX′-system of the ring protons. Practically the same couplings are found for the corresponding protons in 1,6-dimethylcycloheptatriene [54,55]. Comparison of the spectra of *(25)* and 1,6-dimethylcycloheptatriene (Fig. 5b) clearly shows the relationship between the two compounds. The NMR spectrum of *(25)* shows no sign of line broadening, even at −110 °C.

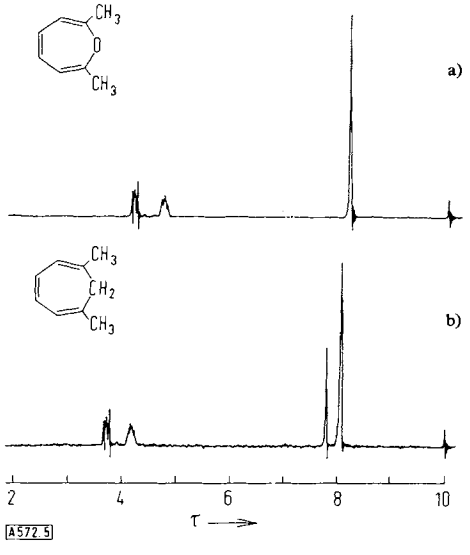


Fig. 5. ^{1}H—NMR spectra of a) 2,7-dimethyloxepin (in CS_2), b) 1,6-dimethylcycloheptatriene (in CCl_4) (60 MHz; internal standard: tetramethylsilane).

At the same time, the strong solvent-dependence of the UV spectrum observed for *(1)* and *(27)* is absent for *(25)*. Thus 2,7-dimethyloxepin appears to be best suited for physical studies on the oxepin system [56].

[52] *H. S. Gutowsky, D. W. McCall,* and *C. P. Slichter,* J. chem. Physics *21,* 279 (1953); *H. S. Gutowsky* and *C. H. Holm, ibid. 25,* 1228 (1956).

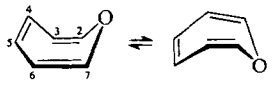
[53] *A. Streitwieser*: Molecular Orbital Theory for Organic Chemists. J. Wiley, New York 1961, p. 247.

[54] *H. D. Roth,* Dissertation, Universität Köln, 1965.

[55] *H. Günther* and *H.-H. Hinrichs,* Tetrahedron Letters *1966,* 787.

[56] The IR spectrum of 2,7-dimethyloxepin contains an enol ether band at 1155 cm^{-1} and intense C=C stretching bands at 1655 and 1584 cm^{-1}.

Oxepin should have a conformation *(30)* similar to that of cycloheptatriene, *i.e.* the molecule should be in a boat form, presumably in equilibrium with its mirror-image conformer.

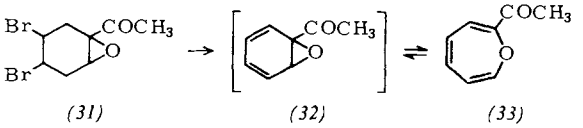


(30)

Evidence for such a nonplanar shape is provide by the coupling parameters of the olefinic protons of *(25)*, in conjunction with the UV spectrum of the 2,7-pentamethylene-bridged oxepin *(58)*. The coupling constant J_{34} (= J_{56}) should show a similar dependence on the dihedral angle to that observed for the analogous coupling in cycloheptatriene[57]. Thus it should be possible to deduce qualitatively the geometry of the triene part of *(25)* from the magnitude of J_{34}. The coupling constant J_{34} (5.5 Hz) is practically equal to the corresponding constants for cycloheptatriene and its 1,6-dimethyl derivative (5.5 and 5.4 Hz, respectively). It may therefore be taken as certain that the C_4–C_5 double bond does not lie in the plane of C-atoms 2,3,6, and 7. Owing to the good agreement between the UV spectra of *(25)* and of 2,7-pentamethyleneoxepin *(58)* (cf. Section IV.5), in which a deflection of the oxygen in relation to the triene part is forced by steric factors, it is likely that the oxygen atom also lies out of this plane.

3. 2-Acetyloxepin

An α-substituent that can enter into conjugation, *e.g.* an acetyl group, should be more effective than an α-methyl group in stabilizing the oxepin form. The red-brown 2-acetyloxepin *(33)* (b.p. 51 °C/0.4 mm)[59] obtained by dehydrobromination of 1-acetyl-1,2-epoxy-4,5-dibromocyclohexane *(31)* with 1,5-diazabicyclo[4.3.0]non-5-ene[58] (other bases always gave polymeric products) is uniform. This is shown by the NMR spectrum (complex multiplet for the olefinic protons between τ = 3.3 and 4.5, in which a doublet of triplets due to the proton H^7 is observed at τ = 4.06) and by the fact that the spectrum shows practically no change with temperature. The same conclusion can be drawn from the UV spectrum [λ_{max} (cyclohexane) = 222 mμ (ε = 10900), 315 mμ (2500), and 360 mμ (1200)] in conjunction with its weak solvent-dependence.



(31) *(32)* *(33)*

Though the oxide component *(32)* cannot be detected, it appears to determine the chemical reactivity, as in the case of 2,7-dimethyloxepin. 2-Acetyloxepin gives the adduct derived from the oxide form with maleic anhydride, and is aromatized by catalytic quantities of mineral acid, with formation of 2-hydroxyacetophenone.

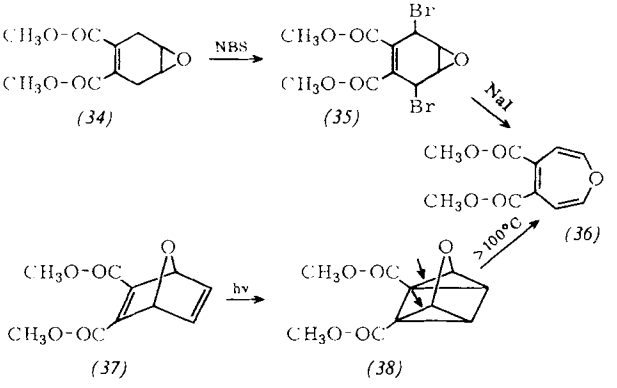
[57] *J. B. Lambert, L. J. Durham, P. Lepoutere,* and *J. D. Roberts,* J. Amer. chem. Soc. *87*, 3896 (1965); *H. Günther* and *R. Wenzl,* Z. Naturforsch. *22b*, 389 (1967).

[58] *H. Oediger, H.-J. Kabbe, F. Möller,* and *K. Eiter,* Chem. Ber. *99*, 2012 (1966). We are grateful to Dr. *K. Eiter,* Farbenfabriken Bayer, for supplying this base.

[59] *F.-G. Klärner,* Diploma Thesis, Universität Köln, 1965.

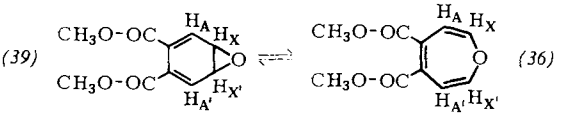
4. 4,5-Bis(methoxycarbonyl)oxepin

The γ,γ'-disubstituted oxepin *(36)* can be obtained from the oxide *(34)* of dimethyl 3,6-dihydrophthalate by allylic bromination with *N*-bromosuccinimide (NBS) and dehalogenation of the crude bromination product *(35)* with sodium iodide in acetone[60]. The same substance was very recently synthesized in an original manner by *Prinzbach, Arguëlles,* and *Druckrey*[61] from the Diels-Alder adduct *(37)* of furan and dimethyl acetylenedicarboxylate. Irradiation of the adduct yields the tetracyclic isomer *(38)*, which gives *(36)* on pyrolysis with cleavage of the indicated bonds in the three-membered rings.



(34) *(35)* *(36)* *(37)* *(38)*

The NMR spectrum of *(36)* consists of an AA'XX' system of the olefinic protons and a singlet due to the ester methyl protons. It is strongly temperature-dependent, so that a considerable proportion of the oxide tautomer *(39)* may be assumed to be present in the equilibrium. The changes in the τ- and *N*-values of the AA'XX' system when the temperature is lowered are shown in Table 2. The increasing shielding of



(39) *(36)*

Table 2. ^{1}H–NMR spectroscopic data for the system *(39)* ⇌ *(36)*.

	τA	τX	τCH$_3$	$N = J_{AX} + J_{AX'}$ (Hz)
+33 °C	3.44	5.10	6.21	4.7_2
−10 °C	3.26	5.25	6.18	4.5_4
−30 °C	3.16	5.33	6.17	4.4_0
−56 °C	3.04	5.41	6.16	4.3_5

the α-protons (H_X and $H_{X'}$) and the simultaneous deshielding of the β-protons (H_A and $H_{A'}$) (owing to the conjugation position of these protons in relation to the ester group in the arene oxide *(39)*, their resonance frequency should occur at lower field strengths than in *(36)*) show that the decrease in temperature results in a displacement of the equilibrium in favor of the oxide.

The same conclusion can be drawn from the changes in the parameter *N*, which represents the sum of the coupling constants J_{AX} and $J_{AX'}$. $J_{AX'}$ is negligibly small in both isomers, so that in the present case *N* depends essentially on the coupling constant J_{AX}. Since *(39)* undoubtedly has the lower coupling constant, a decrease in *N* must correspond to an increase in the oxide concentration.

The UV spectrum of *(36)* is strongly solvent-dependent, again indicating a valence tautomerism with comparable

[60] *R. Schubart,* Dissertation, Universität Köln, 1967.

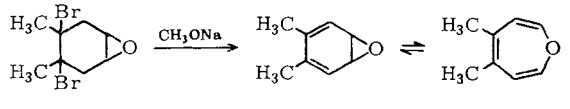
[61] *H. Prinzbach, M. Arguëlles,* and *E. Druckrey,* Angew. Chem. *78*, 1057 (1966); Angew. Chem. internat. Edit. *5*, 1039 (1966).

concentrations of the components. As in the parent system, a solvent change from cyclohexane to methanol causes a displacement of the equilibrium in favor of the arene oxide form.

An NMR spectrum similar to that of *(36)* (even in its temperature dependence) is found for 4,5-dimethyloxepin *(42)*, which can be prepared from 1,2-epoxy-4,5-dimethyl-4,5-dibromocyclohexane *(40)*, but which has so far been obtained only in solution [60].

The room-temperature spectrum of the compound *(42)* shows an AA'XX' system for the olefinic protons with τ_A = 4.2 and τ_X = 5.68 and a methyl proton signal at τ = 8.16. The difference $\tau_X - \tau_A$ increases noticeably with decreasing temperature, while the position of the methyl proton signal, as expected, changes only slightly. The chemical shifts at −65 °C are τ_A = 4.0 and τ_X = 6.2, showing that under these conditions the system consists almost entirely of the oxide form.

In both 4,5-disubstituted oxepins therefore, as in the parent system, the arene oxide is the low energy component.

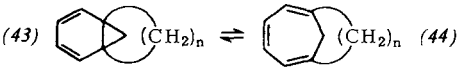


(40) *(41)* *(42)*

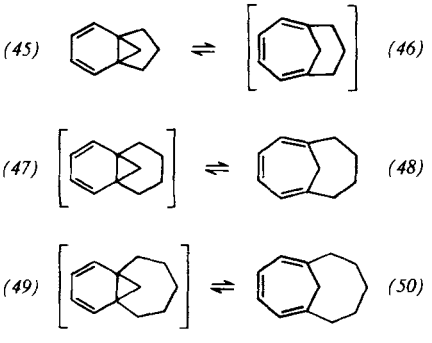
5. Fixed Arene Oxides

By bridging the oxepin in the 2,7-position with a methylene chain having a sufficiently small number of chain members *n*, it is possible, because of steric reasons, to achieve complete displacement of the arene oxide-oxepin equilibrium in favor of the arene oxide.

The influence of the number *n* of chain-CH_2 groups on the position of the equilibrium can be qualitatively estimated from the data for the corresponding bridged norcaradiene-cycloheptatriene systems *(43)* ⇌ *(44)* [33,54,62]. The strain imposed on the cycloheptatriene form *(46)* by a bridge having *n* = 3 is so great that the valence-tautomeric norcaradiene form *(45)* is frozen in. Surprisingly, however, a



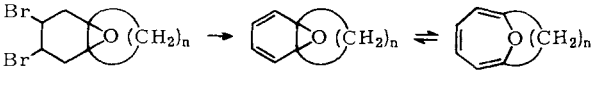
complete reversal of the equilibrium is observed when *n* is as low as 4. Though the cycloheptatriene form *(48)* is still appreciably strained, as is clearly shown by its spectral data and by its reactivity toward maleic anhydride, the norcaradiene isomer *(47)* can no longer be spectroscopically detected. A chain of five methylene groups gives a cycloheptatriene form *(50)* that is almost strain-free, though its conformation is fixed by the bridge. *(50)* is in fact uniform, and is very similar in its spectral properties to 1,6-dimethylcycloheptatriene [54].



[62] *E. Vogel* and *J. Eimer*, unpublished.

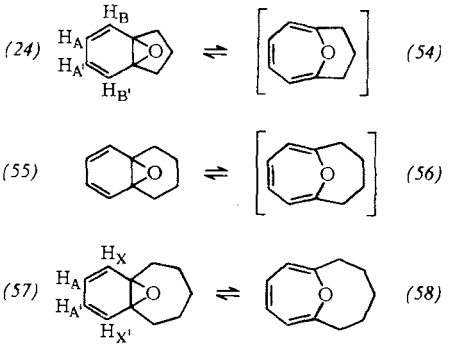
Taking into account the different equilibrium positions in the parent systems norcaradiene-cycloheptatriene and benzene oxide-oxepin, it is to be expected from the above findings that the bridged arene oxide-oxepin systems will still contain measurable concentrations of the tricyclic isomers in the equilibrium at *n* = 4, and possibly even at *n* = 5.

The bridged arene oxide-oxepin systems *(52)* ⇌ *(53)* were synthesized by dehydrohalogenation of the dibromides *(51)* with potassium t-butoxide in ether [63]. *(51)* with *n* = 3 gives the uniform, colorless arene oxide *(24)* (8,9-indan oxide). The structure of the



n = 3, 4, 5 *(51)* n = 3, 4, 5 *(52)* n = 3, 4, 5 *(53)*

compound is shown by the similarity of its NMR spectrum to that of *(45)*. The spectrum shows an AA'BB' system of the olefinic protons at τ = 3.4 to 4.1 ($J_{AA'}$ = 6.0, J_{AB} = 9.3, $J_{AB'}$ = 0.7 and $J_{BB'}$ = 1.2 Hz) [64] and a multiplet due to the methylene protons at τ = 7.5 to 8.8 (intensity ratio 4:6). The values of the coupling constants are compatible with the assumed diene structure, but not with the triene structure (concerning the UV spectra, cf. Section III).



The product obtained from *(51)* with *n* = 4 was also found to be uniform, but the NMR spectrum in this case does not permit a definite assignment, since the olefinic proton absorption consists simply of a sharp signal at τ = 3.85. A decision in favor of the arene oxide structure *(55)* (9,10-tetralin oxide) is possible from the UV spectrum, since the maximum at 259 mμ (ε = 3900) corresponds exactly in its position (though the extinction is lower) to that of 8,9-indan oxide *(24)*.

The reaction product obtained from *(51)* with *n* = 5 differs from *(24)* and *(55)* even in its external appearance, in that it has the characteristic orange color of oxepins. Its spectral properties indicate the presence of an arene oxide-oxepin mixture with comparable concentrations of the components. Both the UV spectrum and the NMR spectrum are strongly solvent-dependent.

In cyclohexane, two UV maxima are observed at 276 and 300 mμ, both with ε = 1400; corresponding bands are observed in methanol at 270 and 300 mμ, but in this case

[63] *M. Wiesel*, Dissertation, Universität Köln, 1966.

[64] *H. Günther* and *H.-H. Hinrichs*, Liebigs Ann. Chem., in press.

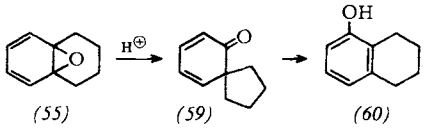
ε = 2100 and 1100. The oxide component, as in the parent system, is evidently favored in methanol. The changes in the NMR spectrum with the solvent are less pronounced, owing to the absence of α-protons, but point in the same direction. The olefinic protons absorb as an AA'XX' system, the N value ($J_{AX} + J_{AX'}$) of which is 7.2 Hz in cyclohexane and 8.1 Hz in methanol. Since a considerable amount of experimental evidence indicates that cyclic trienes have lower N values than the corresponding diene valence isomers [55], the increase in this quantity suggests an increase in the proportion of the oxide. The NMR spectrum shows no appreciable change when the temperature is lowered to −70 °C. This is not surprising, since the most pronounced changes are again associated with the presence of α-protons.

V. Chemistry of Arene Oxide-Oxepin Systems

Little investigation has been carried out on arene oxide-oxepin systems beyond the reactions mentioned in connection with the parent system. All the systems known are sensitive to Brönsted and Lewis acids, the action of which normally leads to aromatization. Unlike cycloheptatriene, these systems readily undergo Diels-Alder reactions, which yield the adduct derived from the arene oxide component. Another apparently general reaction is that with triphenylphosphine (at 120 to 150 °C), which leads to the hydrocarbon corresponding to the arene oxide. Removal of oxygen has also been observed under the action of carbonylchromium complexes [65], but in these cases the hydrocarbons were partly obtained as metal complexes. It is not yet known to what extent the addition of nucleophilic reagents can be achieved. Such additions are of interest, since as was shown by the formation of cyclohexa-1,3-dien-5-ol *(22)*, they would offer a possible route to 1,2-dihydrobenzene derivatives that are otherwise difficult to prepare.

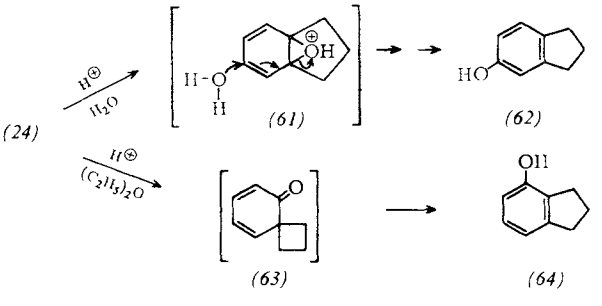
In the study of the chemistry of arene oxide-oxepin systems, the important question is: which reactions can be ascribed to arene oxides and which to oxepins? Now that the benzene oxide-oxepin equilibrium has been established, the Diels-Alder reaction can be definitely ascribed to the oxide component. If, as is likely, arene oxides are also the reacting species in acid-induced isomerizations, nucleophilic additions, and other reactions, the chemical behavior of arene oxide-oxepin equilibrium systems should be similar to that of fixed arene oxides. It therefore seemed advisable that the properties of arene oxides such as 9,10-tetralin oxide *(55)* and 8,9-indan oxide *(24)* should be investigated in greater detail [66].

At room temperature in the presence of catalytic quantities of a proton acid (aqueous-ethereal medium), 9,10-tetralin oxide *(55)* undergoes an almost quantitative carbonium ion rearrangement into spiro[5.4]-deca-7,9-dien-6-one *(59)* [67]. At higher acid concentrations and when Lewis acids are used, complete aromatization takes place with formation of 5-tetralol *(60)*; formation of 6-tetralol was not detected. Since the spiro ketone *(59)* undergoes the dienone-phenol rearrangement [68] into 5-tetralol under comparable conditions, it may be assumed to occur as an intermediate in the aromatization of *(55)*.



(55) *(59)* *(60)*

8,9-Indan oxide *(24)* behaves differently toward Brönsted and Lewis acids. Rearrangement into a spiro ketone, *i.e.* *(63)*, is associated in this case with an energetically unfavorable contraction of the five-membered ring to give a four-membered ring, so that side reactions that are not encountered with *(55)* can prevail. Thus the aromatization product obtained in aqueous media is found to be pure 5-indanol *(62)*, and not the 4-indanol *(64)* that would be expected if the reaction proceeded *via* the spiro ketone *(63)*. The possibility that *(64)* is in fact formed *via* *(63)*, but undergoes a phenol-phenol rearrangement [69] into *(62)*, can be ruled out on the basis of control experiments. The OH group of *(62)* appears instead to be derived from the solvent by the route *(24)* → *(61)*, since an attempted isomerization in methanol gave the 5-methoxyindan corresponding to *(62)*, again in a uniform reaction. It should be possible to determine definitely the source of the OH group in *(62)* by labeling with ^{18}O. In the absence of prototropic solvents, the reaction sequence carbonium ion rearrangement – dienone-phenol rearrangement [*(24)* → *(63)* → *(64)*] can also be observed with 8,9-indan oxide *(24)*. The dienone *(63)* can be isolated as a dimer when the oxide is treated with catalytic quantities of a proton acid in ether. The tendency of *(63)* to dimerize is evidently even stronger than that of *(59)*, a property that protects it against the dienone-phenol rearrangement into *(64)* and allows its detection.



(24) *(61)* *(62)* *(63)* *(64)*

On the other hand, when Lewis acids such as zinc chloride are used instead of proton acids, the catalyst becomes fully effective, so that both the carbonium ion rearrangement and the dienone-phenol rearrangement are observed as in the corresponding experiment with *(55)*.

[65] *W. Grimme* and *B. Haas*, unpublished.

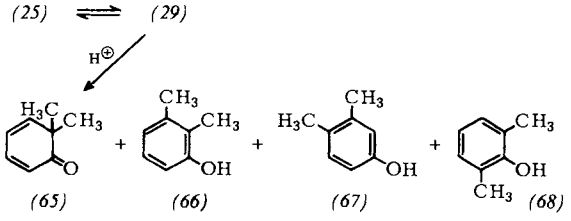
[66] Cf. the 9,10-phenanthrene oxide recently described by *M.S. Newman* and *S. Blum*, J. Amer. chem. Soc. *86*, 5598 (1964).

[67] *K. Alder, F. H. Flock*, and *H. Lessenich*, Chem. Ber. *90*, 1709 (1957).

[68] *E. N. Marvell* and *E. Magoon*, J. Amer. chem. Soc. *77*, 2542 (1955); *L. Fieser* and *M. Fieser*: Steroide. Verlag Chemie, Weinheim 1961, p. 360.

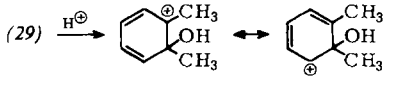
[69] *W. H. Hopff* and *A. S. Dreiding*, Angew. Chem. *77*, 717 (1965); Angew. Chem. internat. Edit. *4*, 690 (1965).

2,7-Dimethyloxepin *(25)*, which may be used for comparison purposes owing to its similarity of substitution, behaves toward dilute acids in much the same way as the two arene oxides *(55)* and *(24)*. The isomerization products obtained from *(25)* are 6,6-dimethylcyclohexadienone *(65)* and 2,3-, 3,4-, and 2,6-dimethylphenol [*(66)*, *(67)*, and *(68)*].



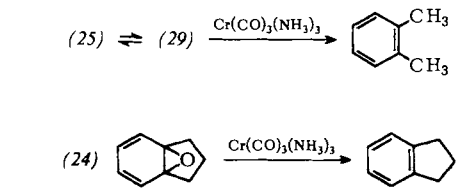
(65) *(66)* *(67)* *(68)*

6,6-Dimethylcyclohexadienone[68] is much more resistant to acids than the spiro ketones *(59)* and *(63)*. This explains why 2,3-dimethylphenol, which is related to this compound *via* the dienone-phenol rearrangement, is present only to a very small extent. The formation of 3,4-dimethylphenol corresponds to that of *(62)* from *(24)*, and as in that case, is best rationalized by assuming that the OH group is derived from the solvent. Finally, 2,6-dimethylphenol, which [like 6,6-dimethylcyclohexadienone *(65)*] is probably formed from the mesomeric carbonium ion *(69)* derived from *(29)* by cleavage of the epoxide ring, can have no analogues in the case of *(55)* and *(24)*, since this would involve *meta*-bridging of the aromatic nucleus by a chain of only 4 or 3 methylene groups.



(69)

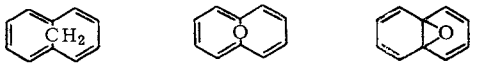
The similarity in the chemical properties of 2,7-dimethyloxepin *(25)* and of the above arene oxides also extends to the reactions with triphenylphosphine and $Cr(CO)_3(NH_3)_3$[65,70], in which both types of compounds lose oxygen and undergo aromatization. Finally, *(25)* resembles the arene oxides in that the oxygen can also be removed by catalytic hydrogenation (with platinum in ether at 0 °C)[71]; like the triphenylphosphine reaction, this hydrogenation leads to the corresponding aromatic hydrocarbons.



Though the comparative investigations of arene oxide-oxepin systems and fixed arene oxides have by no means been exhaustive, the results reported clearly indicate that the arene oxides are the more reactive components of the valence-tautomeric systems toward most reagents. The only chemical indication of the presence of the oxepins is the formation of 2-oxabicyclo[3.2.0]hepta-3,6-dienes[31,60] on photolysis.

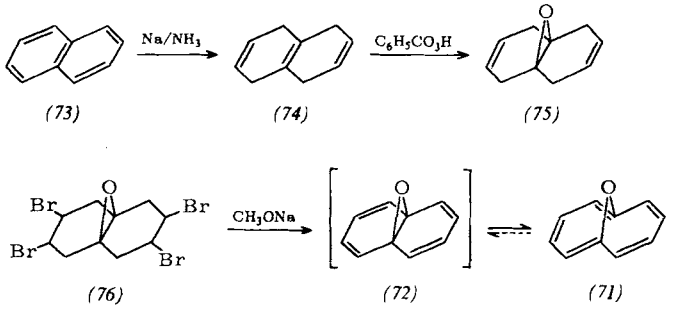
VI. 1,6-Oxido[10]annulene

The synthesis and the aromatic nature of the cyclic conjugated 10 π-electron system 1,6-methano[10]-annulene *(70)*[72] directed interest toward the analogous 1,6-oxido[10]annulene *(71)*, which can also be regarded as a 2,7-bridged oxepin. That *(71)* might be unstable in comparison with the valence-isomeric 9,10-naphthalene oxide *(72)* [cf. the position of the equilibrium *(55)* ⇌ *(56)*] seemed unlikely in view of the properties of *(70)*, which indicate that the 10 π-electron system possesses considerable resonance energy. *(71)*



(70) *(71)* *(72)*

was synthesized simultaneously by *Sondheimer*[73] and by *Vogel et al.*[74] by dehydrobromination of the tetrabromo epoxide *(76)* with sodium methoxide in ether, *(76)* being obtained from 1,4,5,8-tetrahydro-4a,8a-oxidonaphthalene *(75)*[75] which in turn is readily available from *(73)* *via* *(74)*. Though a total of four moles of hydrogen bromide had to be eliminated in this step, *(71)* was formed in yields of up to 90 %.



(73) *(74)* *(75)*

(76) *(72)* *(71)*

[70] For the preparation of $Cr(CO)_3(NH_3)_3$, see *W. Hieber*, *W. Abeck*, and *H. K. Platzer*, Z. anorg. allg. Chem. *280*, 252 (1955).

[71] With palladium-charcoal as the catalyst, on the other hand, *(25)* affords 2,7-dimethyloxepane.

[72] *E. Vogel* and *H. D. Roth*, Angew. Chem. *76*, 145 (1964); Angew. Chem. internat. Edit. *3*, 228 (1964); *E. Vogel* and *W. A. Böll*, Angew. Chem. *76*, 784 (1964); Angew. Chem. internat. Edit. *3*, 642 (1964); *E. Vogel*, Special Publ., Chem. Soc. (London), No. 21, in press.

[73] *F. Sondheimer* and *A. Shani*, J. Amer. chem. Soc. *86*, 3168 (1964).

[74] *E. Vogel*, *M. Biskup*, *W. Pretzer*, and *W. A. Böll*, Angew. Chem. *76*, 785 (1964); Angew. Chem. internat. Edit. *3*, 642 (1964); *M. Biskup*, Dissertation, Universität Köln, 1966.

[75] *W. Hückel* and *H. Schlee*, Chem. Ber. *88*, 346 (1955).

1,6-Oxido[10]annulene is a pale yellow crystalline substance (with an odor of naphthalene), which shows no tendency toward polymerization in air, despite the formal presence of five conjugated double bonds. The properties of the 10 π-electron system are evident from the spectra.

The ^{1}H–NMR spectrum (see Fig. 6) consists of an AA'BB' system with τ_A = 2.54 and τ_B = 2.74 and the coupling constants J_{AB} = 8.8, $J_{BB'}$ = 9.3, $J_{AB'}$ = 0.3, and $J_{AA'}$ = 1.1 Hz [76]. The absorption of the protons at relatively low field and the type of spectrum, according to which H^2 to H^5 and H^7 to H^{10} have identical NMR parameters, appear to be incompatible with a 1,6-oxido[10]annulene having localized double bonds. The NMR findings rather indicate that a ring current is present in the peripheral 10π-electron system, and hence that the compound has an aromatic structure [77]. Though the symmetry of the spectrum could likewise be explained by a molecule with rapidly fluctuating π-bonds, such a structure is not consistent with the position of the proton resonances.

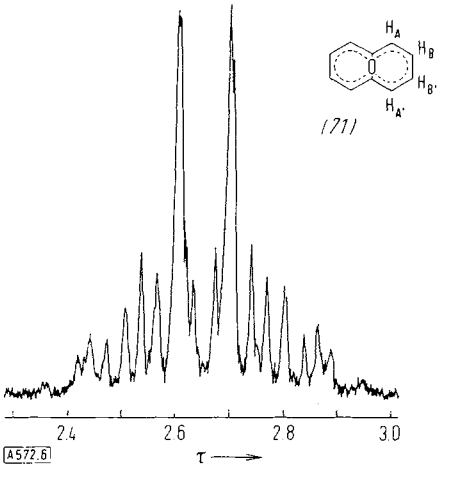


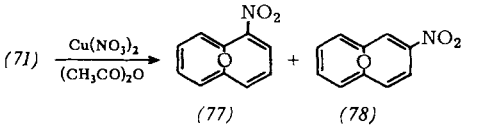
Fig. 6. ^{1}H–NMR spectrum of 1,6-oxido[10]annulene (in CCl_4; 60 MHz, internal standard: tetramethylsilane).

The coupling constants found for the AA'BB' system also fit into the above picture. This is particularly true of the vicinal couplings, which are almost identical, as is to be expected for a delocalized π-electron system in *(71)*. On the other hand, the vicinal coupling constants of olefinic protons in conjugated cycloolefins generally show considerable differences [57,64,78], which must be primarily due to the alternance of the bonds, if the double bond system is sufficiently planar [79]. It is interesting in this connection to note that the α-protons in *(71)* absorb at lower field strengths than the β-protons [80], *i.e.* the resonances occur in the opposite order to that found for the corresponding protons in oxepin and cycloheptatriene. In fact, the α-protons should be more strongly deshielded in *(71)* according to an estimate of the resonance positions using Pople's point-dipole model [81].

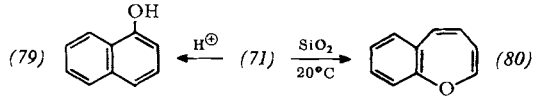
The electronic spectrum of 1,6-oxido[10]annulene contains three bands with maxima at 257 (ε = 74500), 302 (7100), and about 390 mμ (300), the last of these showing pronounced vibrational fine structure. 1,6-Methano[10]annulene gives a very similar spectrum. It may be concluded from this that there is no appreciable interaction between the free electron pairs on the bridge oxygen atom and the peripheral 10 π-electron system in the oxido compound. The habit of the spectra of *(71)* and *(70)* corresponds largely to that of the spectrum of benzene, and so points to a close relationship between the electronic structures of the π-systems in the 1,6-bridged [10]annulenes and in benzene [82].

In agreement with the symmetry shown by the NMR spectrum, the IR spectrum of 1,6-oxido[10]annulene contains relatively few bands. The C–C double-bond band at the unusually low frequency of 1538 cm^{-1}, which appears to be characteristic of the carbon skeleton, is reminiscent of C–C stretching vibrations of benzenoid compounds. This parallelism is also strongly suggested by the appearance of well-developed combination vibration bands in the range 1940 to 1580 cm^{-1}.

The aromatic nature of 1,6-oxido[10]annulene *(71)* is also apparent from its chemical behavior. The compound is not only relatively stable toward heat, oxygen, and light, but can also undergo substitution reactions with electrophilic reagents. Thus it can be nitrated with copper(II) nitrate in acetic anhydride, the nitro group being introduced into the 2- and 3-positions [*(77)* and *(78)*] [73,74].



However, the possibility of obtaining substituted products is considerably lower for 1,6-oxido[10]-annulene than for 1,6-methano[10]annulene, since the oxido compound and its derivatives, like the arene oxide-oxepin systems, are very sensitive toward proton and Lewis acids. 1,6-Oxido[10]annulene isomerizes to α-naphthol *(79)* under the action of proton acids in aqueous-ethereal media, while on silica gel in the presence of nonpolar solvents it rearranges almost uniformly into the intense yellow 1-benzoxepin *(80)* [74]. The formation of α-naphthol cannot involve *(80)* as an intermediate, since on treatment with acids *(80)* does not give α-naphthol, but products containing carbonyl groups; these indicate hydrolytic cleavage of the oxepin ring. The 1,6-oxido[10]annulene–1-benzoxepin rearrangement has also been observed with the 2-nitro



and 2-bromo derivatives of *(71)*. In the resulting nitro- and bromo-1-benzoxepins, the substituent is attached to the aromatic nucleus; its position has not yet been determined.

[76] *H. Günther*, Z. Naturforsch. *20b*, 948 (1965).

[77] *J. A. Elvidge* and *L. M. Jackman*, J. chem. Soc. (London) *1961*, 859; *L. M. Jackman, F. Sondheimer, Y. Amiel, D. A. Ben-Efraim, Y. Gaoni, R. Wolovsky*, and *A. A. Bothner-By*, J. Amer. chem. Soc. *84*, 4307 (1962).

[78] *C. Ganter* and *J. D. Roberts*, J. Amer. chem. Soc. *88*, 741 (1966).

[79] According to theoretical [*M. Karplus*, J. Amer. chem. Soc. *85*, 2870 (1963)] and experimental [*D. R. Eaton, A. D. Josey, W. D. Phillips*, and *R.E. Benson*, J. chem. Physics *39*, 3513 (1963)] findings, vicinal coupling constants depend on the bond length in the CH–CH segment in question.

[80] This assignment, which cannot be made purely on the basis of analysis, is established by specific deuteration in the α-position [*F. Gerson, E. Heilbronner, W. A. Böll*, and *E. Vogel*, Helv. chim. Acta *48*, 1494 (1965)].

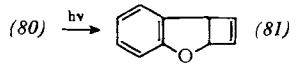
[81] *J. A. Pople*, J. chem. Physics *24*, 1111 (1956).

[82] *H.-R. Blattmann, W. A. Böll, E. Heilbronner, G. Hohlneicher, E. Vogel*, and *J.-P. Weber*, Helv. chim. Acta *49*, 2017 (1966).

Concerning the mechanism of the acid-catalysed isomerization of 1,6-oxido[10]annulene into α-naphthol, there is as yet no evidence (unlike in the oxepin-phenol rearrangement) that the reacting species is the corresponding arene oxide, *i.e.* 9,10-naphthalene oxide.

An alternative is that the proton attacks the α-carbon atom of *(71)* and so initiates the structural rearrangement (cf. the formation of an arene oxide on bromination). The same difficulty is encountered in the interpretation of the surface-catalysed rearrangement of 1,6-oxido[10]annulene into 1-benzoxepin on silica gel.

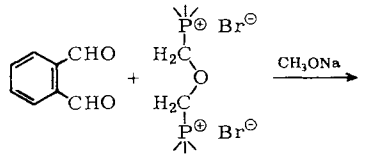
1-Benzoxepin is separated from its arene oxide valence isomer, 1,9-naphthalene oxide, by a relatively high energy barrier; consequently the oxepin character should be much more pronounced (though modified by the fused aromatic nucleus) than in the oxepin itself. As far as can be seen from the reactions studied so far,



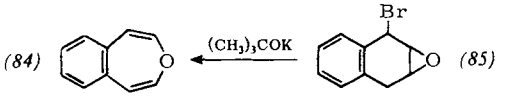
(80) *(81)*

the chemical behavior of *(80)* corresponds to that of an enol ether. Like oxepin, *(80)* can be photochemically isomerized into a cyclobutene derivative *(81)* [83].

We have confirmed that the 1-benzoxepin obtained from *(71)* is free from the isomeric 3-benzoxepin *(84)*, which is also yellow, and which was first synthesized by *Dimroth* and *Pohl*[4] by a Wittig reaction of dimethylether-α,α'-bis(triphenylphosphonium) dibromide *(83)* with phthalaldehyde *(82)*. 3-Benzoxepin has recently also been obtained by reaction of 1-bromo-2,3-epoxy-1,2,3,4-tetrahydronaphthalene *(85)* with potassium t-butoxide in ether [84].



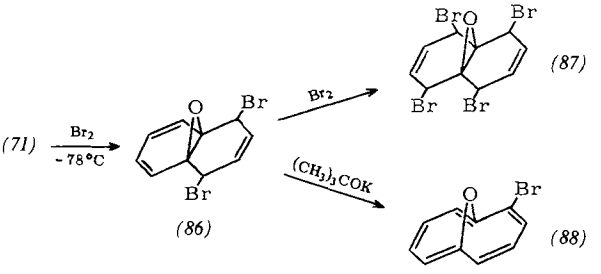
(82) *(83)*



(84) *(85)*

1,6-Oxido[10]annulene also resembles arene oxide oxepin systems in that the oxygen can be removed by triphenylphosphine (160 °C) or by $Cr(CO)_3(NH_3)_3$ (in boiling hexane) [65]; the reaction product is naphthalene. As a result of the resonance stabilization in 1,6-oxido[10]annulene, however, the reactivity towards dienophiles is drastically reduced.

A very close chemical relationship between 1,6-oxido-[10]annulene and arene oxides is established by addition-elimination reactions, a typical example of which is the bromination of the oxido compound [85]. Under the action of bromine in methylene chloride at −78 °C, 1,6-oxido[10]annulene gives a colorless dibromo adduct which can be isolated. This is identified spectroscopically as the benzene oxide derivative *(86)* with the bromine atoms *cis* to each other. Whereas symmetry of the NMR spectrum indicates that the position of the bromine atoms must be *cis*-2,5, but gives no further definite information (the protons of the double-bond system appear as a singlet), a conclusive decision between the benzene oxide and the oxepin structures is possible with the aid of the UV spectrum. As is to be expected for the benzene oxide structure *(86)*, the UV spectrum agrees closely with that of 8,9-indan oxide *(24)*, apart from

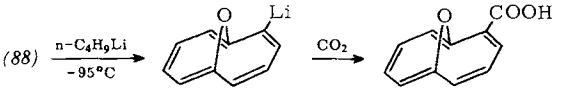


(71) *(86)* *(87)* *(88)*

the high end-absorption of the adduct due to the bromine atoms. An oxepin, on the other hand, should give an absorption extending into the visible region. It is not yet certain whether the bromine attacks the ring from above or below relative to the oxygen bridge.

On further bromination, the dibromo adduct is converted into a tetrabromo adduct which, according to the NMR spectrum, has the structure *(87)* with *cis* bromine atoms in both cyclohexene rings; thus another *cis*-1,4 addition has taken place. The pairs of bromine atoms probably have *syn* and *anti* configurations with respect to the epoxide ring. *(71)* can be regenerated quantitatively from both the dibromo and the tetrabromo adduct on treatment with sodium iodide in acetone.

Attempted thermal dehydrohalogenation of the dibromo adduct *(86)* [86] has so far led only to unidentifiable decomposition products. However, if the dehydrobromination is carried out with bases such as potassium t-butoxide (in ether), the reaction leads smoothly to 2-bromo-1,6-oxido[10]annulene *(88)*, the NMR and UV spectra of which correspond to those of 2-bromo-1,6-methano[10]annulene [72]. Treatment of *(88)* with butyl-lithium (ether, −95 °C) yields 2-lithio-1,6-oxido[10]annulene *(89)*, from which it is possible to obtain 1,6-oxido[10]annulene-2-carboxylic acid *(90)* and other 2-substituted 1,6-oxido[10]-annulenes.



(88) *(89)* *(90)*

The reaction of the tetrabromo adduct *(87)* with potassium t-butoxide led to a dibromo substitution product of *(71)*, which was found to be pure 2,7-di-

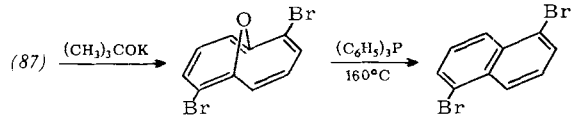
[83] A derivative of 1-benzoxepin was recently described by *H. Hofmann* [Angew. Chem. 77, 864 (1965); Angew. Chem. internat. Edit. 4, 872 (1965)]; see also *H. Hofmann* and *H. Westernacher*, *ibid.* 78, 980 (1966); Angew. Chem. internat. Edit. 5, 958 (1966).

[84] *E. Vogel*, *M. Biskup*, and *F.-G. Klärner*, unpublished.

[85] *E. Vogel*, *W. A. Böll*, and *M. Biskup*, Tetrahedron Letters *1966*, 1569.

[86] The dibromo adduct of 1,6-methano[10]annulene, which still has the same carbon skeleton as the hydrocarbon, loses hydrogen bromide even below 0 °C.

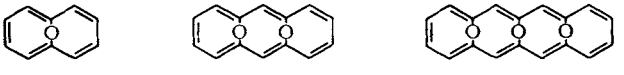
bromo-1,6-oxido[10]annulene *(91)*. This structure is based on a spectral comparison with 2,7-dibromo-1,6-methano[10]annulene[72], on the dipole moment[87], and on the formation of 1,5-dibromo-naphthalene *(92)* when *(91)* is heated with triphenylphosphine at 160 °C.



(91) *(92)*

VII. 1,6; 8,13-Bisoxido[14]annulene

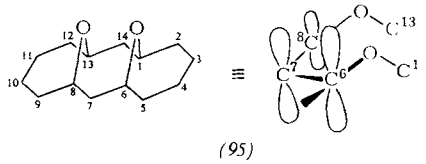
The fact that the spectral and, to a large extent, the chemical properties of 1,6-oxido[10]annulene *(71)* are dominated by the 10 π-electron system of the C_{10} perimeter and not by the "oxepin structural unit" suggested the idea of a homologous series of bridged annulenes *(71)*, *(93)*, *(94)*, *etc.*, which, like the linearly fused aromatic hydrocarbons (the acenes) on which they are based, contain $(4n+2)$ π-electrons. According to calculations by *Dewar* and *Gleicher*[88] the Hückel rule may be regarded as valid for up to the 22 π-electron system; consequently the question of whether the aromaticity observed in the prototype *(71)* also extends to its nearest homologues should depend mainly on the geometry of the perimeter.



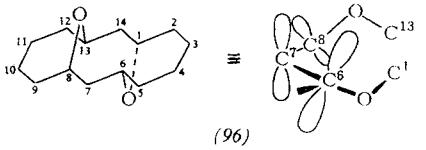
(71) *(93)* *(94)*

As soon as the number of bridges is greater than one, geometrical isomerism occurs, with the result that *(93)* can exist in a *syn* and an *anti* form, while *(94)* can exist in three forms (*syn-syn*, *anti-anti* and *syn-anti*). *Dreiding* and *Stuart-Briegleb* models of the homologues of *(71)* show that these molecules, unlike the flexible annulenes[89], have relatively rigid ring skeletons, and that substantial planarity of the perimeter is possible only in the *syn* and all-*syn* forms. The Stuart models indicate that there is no mutual steric hindrance of the *syn*-oxygen atoms, which would lead to bending of the carbon skeleton. Since the increase in the carbon perimeter from 10 to 14 or 18 C atoms is accompanied by an appreciable relief of strain in the C–O–C angle, the C skeleton can in fact be flatter in *syn-(93)* and *syn-syn-(94)* than in the parent compound *(71)*[90].

In the compounds in which we are interested, *i.e.* 1,6;8,13-bisoxido[14]annulenes, the $2p_z$-orbitals on C^6, C^7, and C^8 (like those on C^1, C^{14}, and C^{13}) can assume an approximately parallel position in the *syn* form *(95)*, whereas in the *anti* form *(96)* the $2p_z$-orbitals on C^6 and C^7 as well as those on C^7 and C^8 exhibit appreciable twisting in relation to each other. Thus the resonance stabilization should undoubtedly be highest in the *syn* form.



(95)



(96)

The qualitative validity of the views deduced from the Hückel rule and from molecular models concerning the homologues of 1,6-oxido[10]annulene *(71)* is demonstrated by attempts to synthesize *syn-* and *anti-*1,6; 8,13-bisoxido[14]annulene.

In view of the synthesis of *(71)* from 1,4,5,8-tetrahydronaphthalene, the most suitable starting compound for the synthesis of the two bisoxido[14]-annulenes *(101)* and *(105)* appeared to be 1,4,5,8,9,10-hexahydroanthracene *(97)*[91]. Reaction of the tetraene *(97)* with two equivalents of perbenzoic acid leads almost quantitatively to 1,4,5,8,9,10-hexahydro-4a,9a; 8a,10a-bisoxidoanthracene, which, according to the NMR spectrum, consists of the *syn (102)* and the *anti* isomer *(98)* (molar ratio approximately 60:40), since the central CH_2-protons give rise both to an AB-system (*syn* form) and to a singlet (*anti* form). The isomer mixture could be separated by fractional crystallization. Treatment of the *syn-* and *anti-*diepoxides *(102)* and *(98)* with bromine gives the corresponding tetrabromo adducts *(103)* and *(99)* (the configurational relationship between the remote bromine atoms is uncertain). The dehydrobromination of the two tetrabromides with potassium t-butoxide in tetrahydrofuran at 0 °C leads to a surprising result.

Whereas *(99)* lost four moles of hydrogen bromide to form the colorless bis(arene oxide) *(100)*, the reaction of *(103)* led directly to the desired *syn*-bisoxido[14]-annulene *(105)*, which was obtained as a stable carmine compound. Thus in the latter case the dehydrobromination was followed by dehydrogenation, evidently by atmospheric oxygen. The *syn* configuration of the bisoxido[14]annulene is shown, not only by the

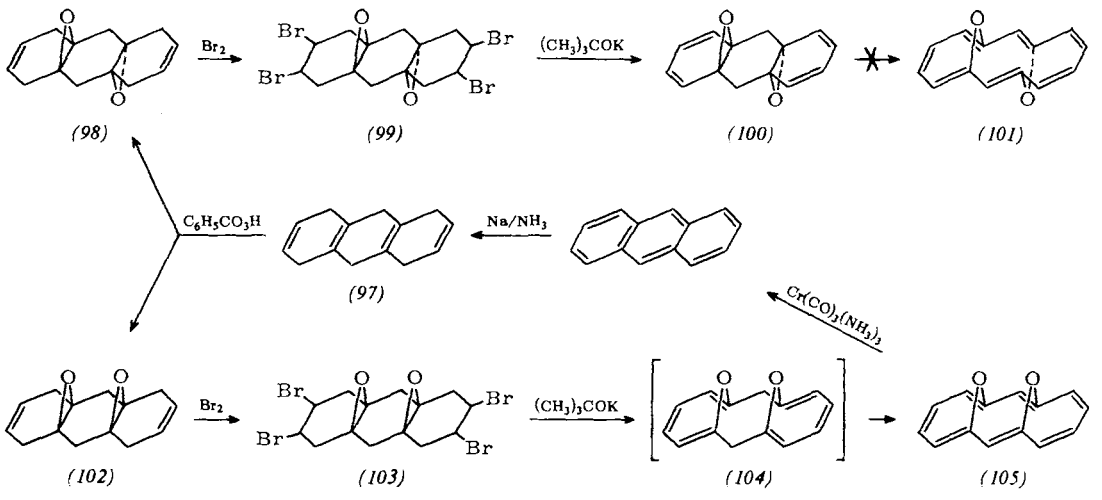
[87] *W. Bremser, H.T. Grunder, E. Heilbronner*, and *E. Vogel*, Helv. chim. Acta, *50*, 84 (1967).

[88] *M. J. S. Dewar* and *G. J. Gleicher*, J. Amer. chem. Soc. *87*, 685 (1965).

[89] *Y. Gaoni, A. Melera, F. Sondheimer*, and *R. Wolovsky*, Proc. chem. Soc. (London) *1964*, 397; *I. C. Calder* and *F. Sondheimer*, Chem. Commun. *1966*, 904; *G. Schröder* and *J. F. M. Oth*, Tetrahedron Letters *1966*, 4083.

[90] Cf. the X-ray analysis of 1,6-methano[10]annulene-2-carboxylic acid [*M. Dobler* and *J. D. Dunitz*, Helv. chim. Acta *48*, 1429 (1965)].

[91] *J. Runge*, Z. Chem. *2*, 374 (1962); *A. J. Birch, P. Fitton, D. C. C. Smith, D. E. Steere*, and *A. R. Stelfox*, J. chem. Soc. (London) *1963*, 2209; *E. Vogel, M. Biskup, A. Vogel, U. Haberland*, and *J. Eimer*, Angew. Chem. *78*, 642 (1966); Angew. Chem. internat. Edit. *5*, 603 (1966).



synthesis [92], but also by the dipole moment of 3.25 D, which is of the expected order of magnitude [93]. In the meantime, it has been possible to detect spectroscopically the dihydro precursor of *(105)*. This is not the bis(arene oxide) corresponding to *(100)*, but the bisoxepin *(104)*.

The compound *(100)* has so far resisted all attempts to dehydrogenate it to *anti*-bisoxido[14]annulene *(101)*; this indicates that *(101)*, unlike the *syn*-isomer, has no appreciable resonance stabilization. A 1,6;8,13-bisoxido[14]annulene of unknown configuration [94], which was found to be identical with *(105)*, had been previously obtained from the mixture of *syn*- and *anti*-diepoxides *(102)* and *(98)* by reaction with *N*-bromosuccinimide and treatment of the crude bromination product with potassium t-butoxide in tetrahydrofuran.

A chemical proof of the structure of *syn*-bisoxido[14]-annulene *(105)*, which, however, does not take into account the configuration, is based on its reaction with $Cr(CO)_3(NH_3)_3$, which leads to deoxygenation and formation of anthracene in yields of up to 95 % [65]. This reaction should be useful in the determination of the structures of substitution products of *(105)*.

The NMR spectrum (Fig. 7) of *syn*-bisoxido[14]-annulene *(105)* shows a singlet at $\tau = 2.06$ (relative intensity 2) for the protons H^7 and H^{14} and an AA'BB' system ($\tau_A = 2.25$ and $\tau_B = 2.40$, relative intensity 8), which corresponds to the protons H^2 to H^5 and H^9 to H^{12}. The fact that the proton resonances occur at relatively low field strengths, together with the symmetry of the spectrum, points to a ring current in the peripheral 14 π-electron system. With 1,6-oxido[10]-annulene *(71)* as the reference substance, an estimate of the chemical shift from Pople's point-dipole model [81] gives $\tau_C = 1.92$, $\tau_A = 2.27$, and $\tau_B = 2.65$, in good agreement with the experimental values. The spin-spin interactions found for *(105)* are in remarkable agreement with those of *(71)* (cf. Section VI); $J_{AB} = 9.0$, $J_{BB'} = 9.2$, $J_{AB'} = 0.3$ and $J_{AA'} = 1.1$ Hz. Since the vicinal coupling constants J_{AB} and $J_{BB'}$ are practically identical, it is probable (as in the cases of *(70)* and *(71)* [90]) that the lengths of the C–C bonds in question do not differ appreciably.

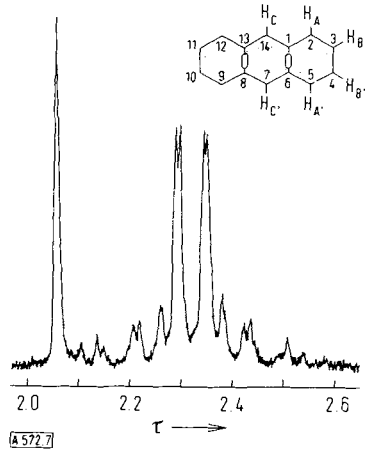


Fig. 7. ^1H–NMR spectrum of *syn*-1,6; 8,13-bisoxido[14]annulene (in $CDCl_3$; 60 MHz; internal standard: tetramethylsilane).

The electronic spectrum of *syn*-bisoxido[14]annulene *(105)* shows a four-band system, as is reported for the aromatic 14 π-electron system *trans*-15,16-dimethyldihydropyrene [95]. The maxima, which occur at slightly lower wavelengths than for the dihydropyrene derivative, are located at 306 (ε = 169000), 345 (14400), 382 (8500), and 555 mμ (775), the band at 555 mμ exhibiting vibrational fine structure. Though the C_{14} perimeter in bisoxido[14]annulene cannot become completely planar and electronic interaction of the oxygen atoms with the 14 π-electron system is not ruled out, the energy transitions calculated by the Pariser-Parr method for an unperturbed 14 π-electron system are surprisingly well satisfied. This is particularly true of the transition at the longest wavelength, whose expected value of 2.17 eV (≡ 572 mμ) corresponds to the band between 543 and 565 mμ [96].

[92] Oscillation of the bridge oxygen atoms through the peripheral C_{14} ring seems unlikely on steric grounds [the rotation of optically active methyl 1,6-methano[10]annulene-2-carboxylate remains unchanged even on prolonged heating at 240 °C (experiments by *W. Schröck*, unpublished)].

[93] According to measurements by *W. Bremser*, unpublished.

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The IR spectrum, which contains relatively few bands owing to the symmetry of the compound, contains only one band at 1536 cm^{-1} in the C—C stretching region, which practically coincides with the analogous absorption of 1,6-oxido[10]-annulene (1538 cm^{-1}).

The aromatic character shown by the spectra of *(105)* is reflected in the considerable thermal stability of the compound and in its insensitivity to oxygen. Moreover, preliminary experiments indicate that *(105)* gives substitution products under the action of various electrophilic reagents.

The substantial similarity between the spectral and chemical properties of 1,6-oxido[10]annulene and *syn*-1,6; 8,13-bisoxido[14]annulene provides a firm experimental basis for the idea of an homologous series of bridged annulenes having aromatic character within the range of validity of the Hückel rule.

VIII. Procedures

Oxepin-Benzene Oxide:

A slurry of pulverized 1,2-epoxy-4,5-dibromocyclohexane *(17)*[14] (12.7 g, 50 mmole) in ether (25 ml) is added over a period of 10 min to a suspension of freshly prepared sodium methoxide (8.1 g, 150 mmole) in boiling ether (30 ml). After the reaction mixture has been refluxed for a further 5 min it is cooled in ice, and then 30 ml of water is added. The ethereal phase is washed with 2×20 ml of water and the combined washes extracted with 20 ml of ether (to recover any entrained oxepin-benzene oxide). The ethereal phase and the ether extract (from the washes) are then combined and dried over $MgSO_4$. The oxepin-benzene oxide is recovered by distillation using a 15 cm Vigreux column; the ether is distilled off first and the oxepin-benzene oxide finally recovered by distillation under vacuum (water pump). Yield: 3.85 g (80 %) of orange oxepin-benzene oxide (b.p. 27 °C/14 mm, 38 °C/30 mm; n_D^{20} = 1.5163). The product may be distilled under normal pressure (b.p. 124 °C) in an apparatus that has been treated with alkali.

2,7-Dimethyloxepin:

A solution of 4,5-dibromo-1,2-epoxy-1,2-dimethylcyclohexane *(28)* (20 g) (prepared from 1,2-epoxy-1,2-dimethylcyclohex-4-ene[97] and bromine in methylene chloride at −78 °C, m.p. 85—86 °C) in ether (30 ml) is added to a stirred suspension of sodium methoxide (14 g, 260 mmole) in boiling ether (30 ml). The reaction mixture is refluxed for 2 h, cooled on ice, and water (50 ml) is then added. The product is recovered as in the previous procedure. Yield: 7.3 g (84 %) yellow-orange 2,7-dimethyloxepin (b.p. 49—50 °C/11 mm; n_D^{20} = 1.5045).

8,9-Indan Oxide:

A solution of 5,6-dibromo-8,9-epoxy-4,7-dihydroindan *(51)*, $n = 3$, (14.8 g) (prepared from 8,9-epoxy-4,7-dihydroindan[98] and bromine in methylene chloride at −78 °C: m.p. 87 to 88 °C) in anhydrous ether (150 ml) is added to a stirred suspension of potassium t-butoxide (25 g, 220 mmole) in anhydrous ether (225 ml) at 0 °C over a period of 1 h.

After the reaction mixture has been stirred for 5 h at room temperature and then for 15 min at 40 °C, it is cooled on ice and 2 N KOH (40 ml) is added. Since the product is unstable towards water in neutral solution, it is washed twice with 2 N KOH (40 ml); it is subsequently recovered in the normal way. Yield: 5.7 g (85 %) of 8,9-indan oxide as a colorless liquid (b.p. 30—31 °C/0.4 mm; n_D^{20} = 1.5255).

Thanks are due to M. Biskup, R. Schubart, W. A. Böll, M. Wiesel, F.-G. Klärner, and R. Sundermann for their enthusiastic cooperation. We are grateful to H. Friebolin, Freiburg, for recording the low-temperature NMR spectra. Acknowledgment is also due to the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for their generous support of our work.

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Translated by Express Translation Service, London

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The Norcaradiene Problem

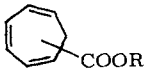
BY G. MAIER [*]

Dedicated to Professor R. Criegee on the occasion of his 65th birthday

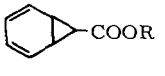
Compounds having the norcaradiene structure are stable if one of the double bonds of the norcaradiene also belongs to a benzene ring or if C atoms 1 and 6 are fixed in position by a bridge. A similar effect that favors the norcaradiene form is produced by the incorporation of nitrogen atoms in positions 3 and 4. Cycloheptatriene and most of the simply substituted tropilidenes exist exclusively in the monocyclic triene form. It has been possible in some cases to detect a valence-tautomeric equilibrium between the norcaradiene and the cycloheptatriene ring system. Non-classical stabilization of compounds having norcaradiene or cycloheptatriene structure in the sense of a pseudoaromatic "homobenzene" is only very slight, if it occurs at all.

I. Introduction

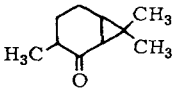
Following a suggestion by his tutor *Curtius*[1], *Buchner*[2–10] attempted to identify the products formed in the thermal decomposition of diazoacetic ester in benzene. He found a mixture of esters ("Buchner esters") that appeared to contain the ester *(2)* of bicyclo[4.1.0]hepta-2,4-dienecarboxylic acid, as well as esters *(1)* of three isomeric cycloheptatrienecarboxylic acids (R = CH_3, C_2H_5).



(1)



(2)

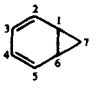


(3)

The ester *(2)*, which is formed as the only product in the photolysis of diazoacetic ester in benzene[11,12] may be regarded as a three-, six-, or seven-membered ring derivative. Chemical proof was provided for all three ring systems: Oxidation of the carboxylic acid of *(2)* with potassium permanganate gave *trans*-cyclopropane-1,2,3-tricarboxylic acid[9]; the amide obtained by reaction of *(2)* with ammonia gave phenylacetic acid on treatment with concentrated sulfuric acid[9]; and the ester *(2)* could be converted into esters of three isomeric cycloheptatrienecarboxylic acids[5,7]. Because of its similarity to the structure of carone *(3)*, as established by *von Baeyer*[13], the carbon skeleton *(4)* on which the ester *(2)* is based was named norcaradiene.

The structure of the seven-membered ring esters *(1)* was established by hydrolysis and reduction to cycloheptanecarboxylic acid, which could be prepared independently from cycloheptanone[6].

Though the unsubstituted norcaradiene was unknown, *Willstätter*[14] obtained the isomeric cycloheptatriene *(5)* by an unambiguous route from cycloheptanone, and found it to be identical with the "tropilidene" obtained by *Ladenburg*[15] from atropine.



(4)



(5)



(6)

Thus both the norcaradiene and the cycloheptatriene ring systems were apparently capable of existing, and neither appeared to show any tendency to change spontaneously into the other. Compounds of the norcaradiene type, *e.g.* the ester *(2)*, were reported to undergo cleavage of the three-membered ring with formation of the cycloheptatriene derivative when heated[5–7,9] or when treated with bases[4,6,9].

[*] Priv.-Doz. Dr. G. Maier
Institut für Organische Chemie der Technischen Hochschule
Richard-Willstätter-Allee
75 Karlsruhe (Germany)

[1] *E. Buchner* and *Th. Curtius*, Ber. dtsch. chem. Ges. *18*, 2377 (1885).

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This view was subsequently generally accepted as correct. It was only when *Meerwein* [16] and *Doering* [17, 18] studied the photolysis of diazomethane in benzene that doubts began to arise. While *Meerwein*, on the basis of hydrogenation experiments, regarded the reaction product as a mixture of cycloheptatriene and norcaradiene, *Doering* reported that the only product apart from a little toluene was cycloheptatriene, whereas norcaradiene *(4)* should have been formed by analogy with the formation of *(2)* from benzene and diazoacetic ester.

Doering repeated *Buchner*'s experiments and found [19] (see also [20, 21]) that all Buchner esters have the same basic structure, and may be regarded as the four positionally isomeric cycloheptatriene esters. Thus *Buchner* had not obtained a norcaradiene derivative.

II. Statement of Problem

Three basic limiting cases may be discussed for the relationships between the norcaradiene and the cycloheptatriene ring systems:

a) Both compounds with norcaradiene structures and compounds with cycloheptatriene structures can exist. These are to be regarded as independent entities; the energy barrier between the two systems is so high, that no interconversion takes place.

b) Norcaradiene and cycloheptatriene are related by a valence-tautomeric equilibrium similar to that known for some time for the system bicyclo[4.2.0]octa-2,4-diene/cycloocta-1,3,5-triene [22].

c) Norcaradiene is to be regarded as a pseudoaromatic planar compound [19], in which the 1,6 bond is fully uncoupled, and overlap of the orbitals of C-1 and C-6 with those of the two double bonds leads to the formation of a "homobenzene" *(6)* [23]. The structures *(4)* and *(5)* would then be resonance structures of the resonance hybrid *(6)*, the bond lengths and angles being assumed to be equal.

On the basis of the papers published up to 1960, strong arguments could be advanced for each of these three possibilities. The results of catalytic hydrogenation supported case a) [11, 16] (see also [24]), since compounds assumed to have the norcaradiene structure take up only two moles of hydrogen, while compounds having the cycloheptatriene structure take up three. The acid obtained by hydrolysis of the ester *(2)* reacted with bromine to give a tetrabromide, which was stable toward permanganate [9]. The ozonization of *(2)*, which is reported to give a diozonide, also supports the norcaradiene structure [25]. The NMR spectra of tropilidene and its simple substitution products, on the other hand, are indicative of a cycloheptatriene structure [26].

The fact that compounds to which a cycloheptatriene structure had been definitely assigned react in the bicyclic form in many reactions, *e.g.* in the Diels-Alder synthesis [11, 21, 27–29], could be taken as evidence of the existence of a valence-tautomeric equilibrium [case b)]. However, it is possible that transition into the bicyclic system takes place only under the influence of the attacking agent [30]. This view is supported by the fact that the enol esters of eucarvone, which, from their NMR spectra, must be monocyclic, give good yields of caronic acid on ozonolysis [31].

The NMR spectra of the Buchner esters and the value of about 7 kcal/mole found for the stabilization energy of tropilidene from heats of hydrogenation (based on the heat of hydrogenation of cycloheptene) [32, 33] led *Doering* to accept the pseudoaromatic structure *(6)* [case c)]. This view is compatible with *Winstein*'s concept of homoaromaticity [23, 34].

Further support for these considerations was provided by the analysis of the vibration spectra of tropilidene, which also indicates a planar, quasiaromatic structure, but does not discount the possibility that the methylene group lies slightly out of the plane of the ring [35]. In order to decide between the above alternatives, it will be necessary, not only to establish the general structure of the compounds in question, but also to clarify any relationships existing between the valence tautomers. The degree of delocalization of the 1,6 bond in compounds having the norcaradiene structure, or the degree of 1,6 overlap in substances having the cycloheptatriene ring structure, would also have to be known.

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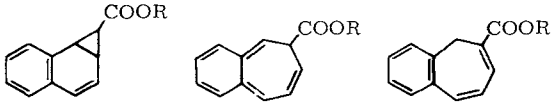
III. The Norcaradiene/Cycloheptatriene System

The easiest way to obtain more definite information would be by direct investigation of a system in which both the monocyclic cycloheptatriene form and the bicyclic norcaradiene form can exist, and in which both are present in sufficiently high concentrations. Until recently, however, this was not possible. More recent investigations have shown that cycloheptatriene and its simple substitution products exist entirely in the monocyclic form.

Compounds having an intact norcaradiene structure could be obtained only by the use of special expedients, either by inclusion of one of the two double bonds of the norcaradiene in an aromatic ring or by bridging of carbon atoms 1 and 6 with an additional ring.

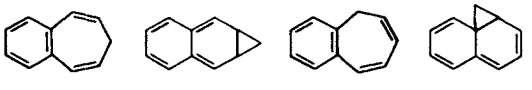
a) Benzo Derivatives

Buchner [36] found that the decomposition of diazoacetic ester in naphthalene leads to the adduct *(7)* [30,37]. The transition into the cycloheptatriene derivative *(8)* involves dearomatization of the benzene ring. Consequently, the isomerization takes place only at high temperatures. On rearomatization, *(8)* is then converted into *(9)* with a hydrogen shift, which is probably rate-determining.

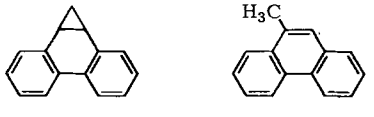


(7) *(8)* *(9)*

Conversely, if one of the double bonds of the cycloheptatriene also belongs to a benzene ring, only the triene form is found. It is therefore not surprising that the benzocycloheptatrienes *(10)* and *(12)* [39] do not change into the norcaradiene derivatives *(11)* and *(13)*, since this would involve the formation of a quinoid ring from a benzoid ring. On the contrary, compounds



(10) *(11)* *(12)* *(13)*



(14) *(15)*

of the type *(11)* or *(13)* isomerize spontaneously into the benzocycloheptatrienes [40].

Dibenzonorcaradiene *(14)* should be particularly stable toward isomerization into the cycloheptatriene system. It is found, in fact, that *(14)* does not form dibenzocycloheptatriene when heated, but yields 9-methylphenanthrene *(15)* instead [38,41,55]. The ease of conversion into the phenanthrene derivative is also indicated by the fact that *(14)* can transfer the methylene group to olefins under the action of light [42]. The adduct of dichlorocarbene and 9-methoxyphenanthrene loses methyl chloride when heated, with formation of a dibenzotropone [43]. The patterns outlined here are confirmed by the behavior of the adducts of methylene with anthracene [44].

Several highly condensed aromatic compounds have so far been converted into benzonorcaradienes. This is usually achieved by thermal decomposition of diazoacetic ester in the presence of the corresponding aromatic compound [30,36,37,41,45–53] (see also [40]); this method can sometimes be used with heterocyclic compounds [46,54]. The photolytic [37] or copper salt-catalysed [38,41,44,52,55] decomposition of diazo compounds, and even the addition of dihalogenocarbene in the case of activated aromatic compounds [43] have also been successfully used. These compounds cannot provide any information on the question of whether the norcaradiene system exists in a valence-tautomeric equilibrium with the cycloheptatriene system. The fused benzene rings can stabilize one tautomer to such an extent that no equilibrium can be detected at low temperatures.

The benzonorcaradienes also provide no indication of appreciable delocalization of the 1,6 bond of norcaradiene. This would lead to flattening of the ring, and, in the extreme case, the two geminal cyclopropane protons should give only one signal in the NMR spectrum. However, this is not so. The position and splitting in the NMR spectrum of the cyclopropane protons in the adduct of methylene and naphthalene [37] clearly indicate the structure *(16a)* ≡ *(16c)* [56]. However the two

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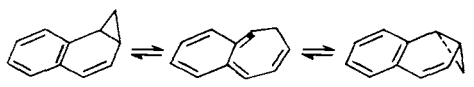
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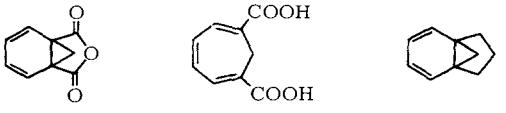


(16a) *(16b)* *(16c)*

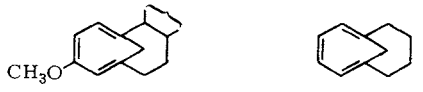
geminal cyclopropane protons in *(16a)* give a single signal when this substance is heated to 180 °C. This is regarded as evidence that a valence-tautomeric equilibrium is established between the forms *(16a)*, *(16b)*, and *(16c)*. An equilibrium of this type is also suggested for a derivative of *(16a)* [57]. The activation energy of 19.4 kcal/mole found for this reaction [56] seems surprisingly low in view of the fact that the benzene ring must be dearomatized in the formation of *(16b)*.

b) Bridged Systems

The anhydride *(17)* prepared by *Eschenmoser* [58] in connection with his colchicine synthesis [59] and the hydrocarbon *(19)* described by *Vogel* [60] are examples of another, very elegant method of fixing the norcaradiene structure. In these compounds the carbon atoms 1 and 6 of the norcaradiene are held in position by an additional five-membered ring. In contrast to its anhydride *(17)*, the dicarboxylic acid exists entirely in the monocyclic form *(18)*. However, compounds containing a six-membered ring bridge, *e.g.* *(20)* [61,62], *(21)* [63], or their derivatives [64], must be regarded as derivatives of cycloheptatriene.



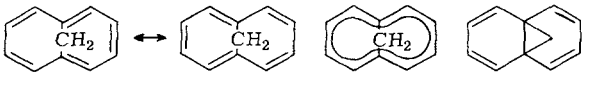
(17) *(18)* *(19)*



(20) *(21)*

In norcaradiene derivatives that are stabilized by a bridge, the two geminal three-membered ring protons are not identical, and very different τ values are found in the NMR spectrum, the higher τ value being assigned to the *endo* proton (see Section IVc). Information can also be obtained from the coupling between the methylene protons. While the absolute value for norcaradiene derivatives is 3–5 Hz, that for cycloheptatrienes is 7–12 Hz [60–71]. The UV spectra [60–71] and the ^{13}CH coupling constants [65,72] can also be used as evidence of structure.

An interesting bridged system is 1,6-methanocyclodecapentaene (1,6-methano[10]annulene) *(22)* [73]. All the properties of this compound [72], particularly the NMR spectrum, which shows 8 protons in the aromatic hydrogen atom region at $\tau = 2.5$–3.2 and a sharp singlet at $\tau = 10.5$ and which may be regarded as indicative of the existence of a ring current, suggest that the compound is best described by the two resonance structures *(22)* and *(23)* or by the formula *(24)*. The chemical properties, the ^{13}CH coupling constant of the methylene group, the UV spectrum, and the X-ray analysis of methanocyclodecapentaene-2-carboxylic acid [74], which showed that localized single and double bonds are not present although the perimeter is not quite planar, are all in agreement with this structure.



(22) *(23)* *(24)* *(25)*

There is no indication of any valence-tautomeric equilibrium with the norcaradiene form *(25)*. The same is true of the substitution products of *(22)* [64,65, 68,70,72,75], *anti*-1,6;8,13-bismethano[14]annulene [67], and the hydrocarbon *(26)* [66]. On the other hand compound *(28)* [69,71] and the adduct *(27)* [67] of *(22)* and dimethyl acetylenedicarboxylate exist in the norcaradiene form.

The four membered ring homologue *(29)* of *(22)* also has the tricyclic structure, probably for steric reasons [63,76].

The existence of the methylenenorcaradiene derivative *(30)* [77], which does not isomerize into *(31)*, even when heated at 275 °C, shows that norcaradiene struc-

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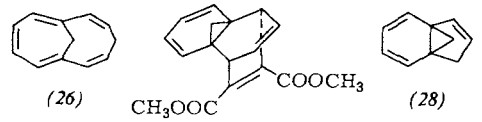
[73] *E. Vogel* and *H. D. Roth,* Angew. Chem. *76,* 145 (1964); Angew. Chem. internat. Edit. *3,* 228 (1964).

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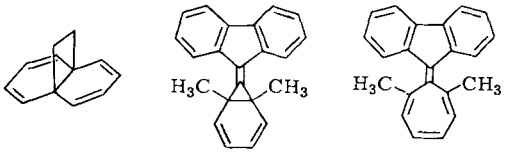
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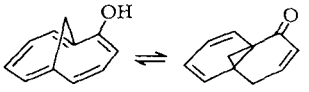
(26) (27) (28)



(29) (30) (31)

tures can be stabilized by other steric effects as well as by a "bracket effect".

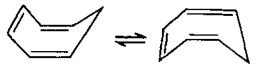
A valence-tautomeric equilibrium between compounds having cycloheptatriene and norcaradiene structures coupled with a keto-enol tautomerization has been found between the alcohol *(32)* and the ketone *(33)* [68].



(32) (33)

c) The System Norcaradiene/Cycloheptatriene (Unsubstituted)

Tropilidene (cycloheptatriene) clearly has the monocyclic structure *(5)*. Hydrogenation yields cycloheptane [24], and oxidation with CrO_3/pyridine leads to tropone [78]. The NMR spectrum is particularly informative. At room temperature the two methylene hydrogen atoms give only one triplet signal; this could be regarded as evidence of a planar structure. In addition to the coupling constant for the geminal methylene protons, the coupling constants of the olefinic protons can also be used as evidence of structure [79,80]. Both methods indicate the monocyclic structure. The NMR spectrum is temperature-dependent, and the methylene protons give separate signals at −140 °C [81, 82]. This shows that cycloheptatriene has a boat configuration and undergoes a rapid ring inversion *(34a)* ⇌ *(34b)*.



(34a) (34b)

The boat form of cycloheptatriene is also indicated by IR-spectroscopic findings for [7-D]-cycloheptatriene [83], the microwave spectrum of cycloheptatriene [84], and the characteristic thermal [85,86] and photochemical [87,88] transannular hydrogen shifts of [D]-cycloheptatriene. The absolute proof is provided by electron diffraction diagrams [89]. According to X-ray analysis [90], the seven-membered ring in the tricarbonylmolybdenum complex of cycloheptatriene has a similar boat form, but in this case the six unsaturated carbon atoms lie almost in the same plane. In contrast to the angled structure of cycloheptatriene, the tropyl radical [95,96] and the tropilidene anion [97–99] have a highly symmetrical structure analogous to that of the planar tropylium ion [91–94].

No valence-tautomeric equilibrium has so far been detected between cycloheptatriene and norcaradiene. Even the dilatometric method used so successfully by *Huisgen* for the cyclooctatetraene/bicyclooctatriene system fails in this case [100]. The existence of an equilibrium with an extremely small quantity of norcaradiene, which cannot be detected directly, can only be indirectly deduced from the course of many chemical reactions of tropilidene, *e.g.* the Diels-Alder reaction [27,28,101–104] (many dienophiles also react with the triene form [105–107]) or the isomerization to form toluene [108,109], but mainly by analogy with the results obtained with substituted cycloheptatrienes (see next section).

While the thermal isomerization of cycloheptatriene into norcaradiene, according to *Woodward* and *Hoff-*

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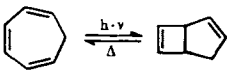
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mann's rules [110], can be disrotatory and can therefore proceed very readily, the transition from cycloheptatriene to bicyclo[3.2.0]heptadiene *(35)* would require a greater activation energy for the thermal reac-



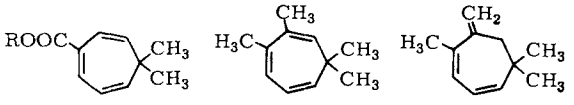
(5) *(35)*

tion, but should proceed smoothly under the action of light. Cycloheptatriene can in fact be smoothly converted into *(35)* by exposure to light, but the thermal isomerization of *(35)* into cycloheptatriene takes place only under drastic conditions [111–114].

d) The System Norcaradiene/Cycloheptatriene (Substituted)

Most investigations on the norcaradiene problem have been carried out on simply substituted derivatives. Substituted cycloheptatrienes are best prepared by thermal [1–9, 24, 40, 115–124], photolytic [11, 16–18, 40, 123], or catalytic [125–128] decomposition of diazo compounds in the presence of aromatic compounds or from eucarvone [26, 29, 31] or tropylium salts [91, 129, 130]. Apart from diazo compounds, other sources of carbenes may also be used [131, 132].

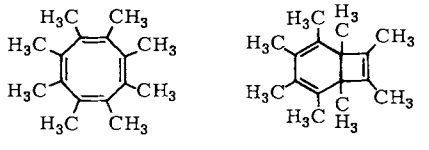
The structures of the substituted cycloheptatrienes can again be determined from their chemical and spectral properties. The boat conformation is shown by X-ray analysis of a derivative of 7,7-dimethylcycloheptatriene-3-carboxylic acid *(36)* [133, 134], which is a typical cyclic polyolefin with alternating bond lengths. The 1,6 distance is 2.42 Å, so that a norcaradiene structure can be ruled out. A 1,6 overlap can occur, if at all, only "under the boat". Nevertheless, a value of 1/3 of the 2,3 overlap in butadiene is calculated for this overlap. The fact that the substituted tropilidene *(37)* is only 1.3 kcal/mole more stable than the isomer *(38)* shows that a 1,6 overlap, which is impossible in *(38)*, makes no appreciable contribution to the stabilization of *(37)* [135].



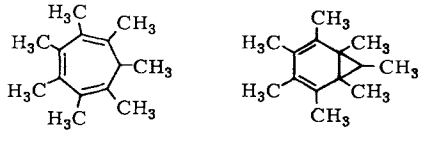
(36) *(37)* *(38)*

Compounds of the type *(37)* give an NMR spectrum that contains only one signal for the protons of the two geminal methyl groups. The derivative with a t-butyl group in position 2 gives two signals below −86 °C [136]. It was shown in this way for the first time that tropilidenes undergo a fast ring inversion at room temperature.

The question of the existence of a valence-tautomeric cycloheptatriene-norcaradiene equilibrium could not be answered until very recently. According to investigations by *Criegee*, an accumulation of methyl groups can favor bicyclic valence isomers rather than the monocyclic isomers. Thus octamethylcyclooctatetraene *(39)*, in contrast to the unmethylated parent compound [137, 138], can be converted into the bicyclic isomer *(40)* by heating [139, 140]. It therefore seemed pertinent to determine whether heptamethylcycloheptatriene *(41)* has a greater tendency than the unsubstituted cycloheptatriene to change into the norcaradiene derivative *(42)*. This isomerization did not



(39) *(40)*



(41) *(42)*

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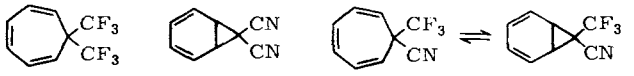
[138] *R. Huisgen* and *F. Mietzsch*, Angew. Chem. *76*, 36 (1964); Angew. Chem. internat. Edit. *3*, 83 (1964).

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take place [124]; however, the increased rate of the Diels-Alder reaction compared with that of tropilidene indicates that the bicyclic form is more strongly favored. Heptaphenyltropilidene also has the monocyclic structure [141].

Investigations carried out by *Ciganek* show that a valence-tautomeric equilibrium can, in principle, be assumed for all these compounds. Whereas 7,7-bis(trifluoromethyl)cycloheptatriene *(43)* exists exclusively in the open triene form [122, 142], the UV spectrum indicating a somewhat flatter boat than in cycloheptatriene, only the bicyclic form *(44)* can be detected in the case of the corresponding dicyano compound [40]. The structure *(44)* is based on the chemical behavior and on the spectra. A detailed analysis of the NMR spectrum of *(44)* [143] and an X-ray analysis of the compound methylated in positions 2 and 5 [144] confirm the assignment of this structure.



(43) *(44)* *(45)* *(46)*

In view of these findings, it is not surprising that the temperature-dependence of the NMR spectrum of 7-cyano-7-trifluoromethylcycloheptatriene *(45)* indicates an equilibrium with the valence tautomer *(46)* [24].

Substituted tropilidenes undergo a variety of thermal rearrangements, depending on the conditions. The very readily induced ring inversion (activation energy about 6 kcal/mole [81, 82]) is followed at higher temperatures by the valence tautomerism mentioned above (calculated activation energy 11 ± 4 kcal/mole [145]); a further temperature rise leads to the 1,5 hydrogen shifts discussed earlier in connection with deuteriocycloheptatriene (E_A = 31 kcal/mole) [85, 86, 123, 146 to 152]. At sufficiently high temperatures, even the carbon skeleton can rearrange. Thus tropilidene isomerizes at 400 °C to give toluene (E_A = 51 kcal/mole [109]).

Berson studied the pyrolysis of 3,7,7-trimethyltropilidene *(47)* at 300 °C [145, 153]. Analysis of the pyrolysis products of 1,5-dideuterated *(47)* shows that the atoms 1 to 6 of the starting material always remain in their original sequence on pyrolysis, and that C-7, with its geminal methyl groups, is simply inserted between any two adjacent atoms of this sequence. The simplest explanation for this is that *(47)* and the two other tropilidenes that can result from rearrangement establish an equilibrium *via* the corresponding norcaradienes, the isopropyl residue formally migrating around a quasi-toluene ring as in *(48)*.



(47) *(48)*

Photolytically induced isomerizations into bicyclo[3.2.0]-heptatriene derivatives [155] and hydrogen shifts [87, 88, 123, 154] (which, according to *Woodward* and *Hoffmann*'s selection rules, must be either 1,7 or 1,3 shifts, in contrast to the thermally induced 1,5 shifts) as well as photolytically induced *Wagner-Meerwein* rearrangements [155] and rearrangements proceeding *via* tropylium ions (by primary removal of a hydride ion [146]) have also been observed with substituted tropilidenes.

IV. Systems Containing Hetero Atoms

a) Oxepin-Benzene Oxide

On the one hand the oxepins are of interest in connection with the norcaradiene problem, particularly because of the possibility of valence tautomerism with the corresponding bicyclic oxides, and on the other owing to their cyclic 8 π-electron system and the associated question of the aromaticity of these compounds [156]. The first oxepin derivatives, which became known mainly as a result of the work of *Dimroth*, were 4,5-benzoxepin *(49)* and its derivatives [157, 158-161]. 2,3-Benzoxepin has recently been synthesized [162]. The pigment flavanonol is also regarded as an oxepin derivative [163]. By analogy with benzocycloheptatriene *(10)*, compounds of the type *(49)* will have no great tendency to form the valence-tautomeric naphthalene oxides. Conversely, the norcaradiene-like form can again be stabilized by a "bracket effect", as in the compound *(50)* [164].

[141] *M. A. Battiste*, Chem. and Ind. *1961*, 550.

[142] *D. M. Gale*, *W. J. Middleton*, and *C. G. Krespan*, J. Amer. chem. Soc. *87*, 657 (1965).

[143] *C. Ganter* and *J. D. Roberts*, J. Amer. chem. Soc. *88*, 741 (1966).

[144] *C. J. Fritchie*, Acta crystallogr. *20*, 27 (1966).

[145] *J. A. Berson* and *M. R. Willcott*, J. Amer. chem. Soc. *88*, 2494 (1966).

[146] *K. Conrow*, J. Amer. chem. Soc. *83*, 2343 (1961).

[147] *G. Büchi* and *E. M. Burgess*, J. Amer. chem. Soc. *84*, 3104 (1962).

[148] *A. P. Ter Borg* and *H. Kloosterziel*, Recueil Trav. chim. Pays-Bas *82*, 741 (1963).

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[150] *T. Nozoe* and *K. Takahashi*, Bull. chem. Soc. Japan *38*, 665 (1965).

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[152] *R. K. Lustgarten* and *H. G. Richey*, Tetrahedron Letters *1966*, 4655.

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[157] *K. Dimroth* and *A. Freyschlag*, Angew. Chem. *65*, 95 (1957).

[158] *K. Dimroth* and *A. Freyschlag*, Chem. Ber. *90*, 1623 (1957).

[159] *K. Dimroth* and *G. Pohl*, Angew. Chem. *73*, 436 (1961).

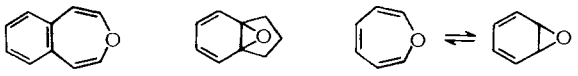
[160] *K. Dimroth*, *G. Pohl*, and *H. Follmann*, Chem. Ber. *99*, 634 (1966).

[161] *R. Huisgen*, *E. Laschtuvka*, *I. Ugi*, and *A. Kammermeier*, Liebigs Ann. Chem. *630*, 128 (1960).

[162] *E. Vogel*, *M. Biskup*, *W. Pretzer*, and *W. A. Böll*, Angew. Chem. *76*, 785 (1964); Angew. Chem. internat. Edit. *3*, 642 (1964).

[163] *T. Kubota*, *N. Ichikawa*, *K. Matsuo*, and *K. Shibata*, Tetrahedron Letters *1966*, 4671.

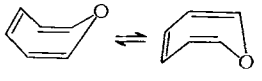
[164] *E. Vogel*, *W. A. Böll*, and *H. Günther*, Tetrahedron Letters *1965*, 609.



(49) (50) (51) (52)

It is possible that naphthalene oxides occur as intermediates in the isomerization of benzoxepins into phenol derivatives [161, 165]. A valence-tautomeric equilibrium has been definitely detected for the parent compound *(51)* and its methyl derivatives [164, 166]. These compounds are readily obtainable by double dehydrobromination of dibromides. Thus when 1,2-epoxy-4,5-dibromocyclohexane is treated with suitable bases, it forms a yellow oil, which clearly has the seven-membered ring structure *(51)* on the basis of its chemical properties (heating to 70 °C or treatment with acids yields phenol; catalytic hydrogenation leads to oxepane; the Diels-Alder reaction leads to adducts derived from benzene oxide) and its spectra [80, 164, 166]. Another synthesis of the oxepin system has been described by *Prinzbach* [166a].

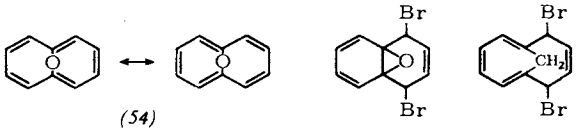
The temperature-dependence of the NMR spectrum of *(51)* and the solvent-dependence of the UV spectrum indicate a valence-tautomeric equilibrium between oxepin *(51)* and benzene oxide *(52)*, the position of the equilibrium being strongly dependent on the solvent (about 30% as benzene oxide in isooctane, and about 90% in water/methanol). The chemical and spectral properties of *(51)*, by analogy with those of cyclooctatetraene and in agreement with the Hückel rule, indicate that oxepin may be regarded as a typical polyolefin with no appreciable "aromatic" stabilization. The valence tautomerism *(51)* $\rightleftharpoons$ *(52)* is faster [164, 167] ($E_{A\ (51)\rightarrow (52)} = 7.2 \pm 1.0$; $E_{A\ (52)\rightarrow (51)} = 9.1 \pm 0.8$ kcal/mole) than that described for the system *(45)/(46)*. The analysis of the NMR spectrum [167] indicates that oxepin also exists as a boat form *(53)*; this fact suggests that there is again a very rapid interconversion between the two identical conformers *(53a)* and *(53b)*, and shows that there can be no delocalization, so that olefinic reactions are to be expected.



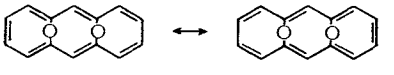
(53a) (53b)

Methyl groups in positions 2 and 7 favor the monocyclic form, probably because of steric repulsion. Thus 2,7-dimethyloxepin exists only as the triene; the monocyclic and bicyclic forms of 2-methyloxepin have almost the same energy [168].

On the other hand, 1,6-oxidocyclodecapentaene *(54)* could, according to the Hückel rule, be aromatic. In fact the NMR spectrum of *(54)* (A_2B_2 system, centered at $\tau = 2.5$ [162, 169]) indicates a ring current; the UV spectrum corresponds to that of 1,6-methanocyclodecapentaene. The chemical behavior of *(54)*, *e.g.* on electrophilic substitution, agrees with this. *(54)* reacts with bromine to form an addition product whose spectra indicate that it must have the benzene oxide structure *(55)* [64]. This is surprising, since the corresponding carbocyclic compound *(56)* exists in the cycloheptatriene form. Evidently the equilibrium can in general be displaced in favor of the norcaradiene form by an additional six-membered ring; however, this effect is not sufficiently strong in *(56)*, since the position of the valence-tautomeric equilibrium in the cycloheptatriene is too unfavorable. As in 1,6-oxido-[10]annulene *(54)*, a ring current must also be assumed to be present in 1,6;8,13-bisoxido[14]annulene *(57)* [170].



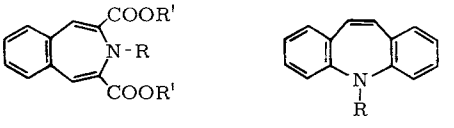
(54) (55) (56)



(57)

b) Azepine-Benzene Imine

The principle of "freezing" individual double bonds by incorporation in a benzene ring has also been used successfully in the azepine series. Typical examples are the monobenzo and dibenzo derivatives *(58)* [171–173] and *(59)* [174–176].



(58) (59)

The seven-membered ring in these compounds is probably again nonplanar, so that the 8 π coupling must be extremely small. It should be noted that *(58)*, R = Br, is very stable, and can probably be regarded as a derivative of the azatropylium ion. Mononuclear azepine derivatives are obtained by the thermal or photolytic decomposition of azido compounds in the

[165] *H. Hofmann*, Angew. Chem. *77*, 864 (1965); Angew. Chem. internat. Edit. *4*, 872 (1965).

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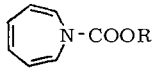
[174] *E. D. Bergmann* and *M. Rabinovitz*, J. org. Chemistry *25*, 827 (1960).

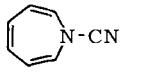
[175] *R. Huisgen*, *E. Laschtuvka*, and *F. Bayerlein*, Chem. Ber. *93*, 392 (1960).

[176] *W. Schindler* and *H. Blattner*, Helv. chim. Acta *44*, 753 (1961).

presence of aromatic compounds[177–179] (cf. the reaction with diazo compounds). Thus irradiation of ethyl azidoformate in benzene yields ethyl azepine-*N*-carboxylate *(60)*[180]. The same products are also obtained with ethoxycarbonylnitrene formed by α-elimination[181]. The chemical and spectral behavior clearly indicate the structure *(60)*. It is not yet clear whether or not *(60)* is in equilibrium with small amounts of the benzene imine derivative *(61)*. An electron-attracting substituent on the nitrogen appears to be essential to the stability of the azepine system; *N*-methylazepine *(67)*, which can be obtained from *(60)* by reduction with $LiAlH_4$, is thermally very unstable[182]. Thus azepine experiences only very little (if any) "aromatic" stabilization. This is supported by the fact that compounds that formally can enolize to form hydroxyazepines exist only in the keto form[57, 183, 184].

The azepines are sensitive to acids. Thus *N*-cyanoazepine *(62)*[179] rearranges in the presence of acids to form phenyl cyanamide. Isomerizations of this type may proceed *via* the azanorcaradienes, *e.g.* in this case *(63)*.

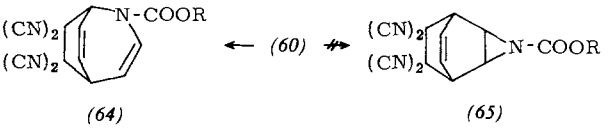
(60)  *(61)*

(62)  *(63)*

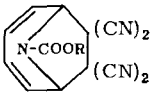
The same is true of the reductive elimination of nitrogen to form aromatic compounds[185].

On the other hand, it is surprising that the ester *(60)* of azepine-*N*-carboxylic acid does not give the adduct *(65)*, as would be expected by analogy with cycloheptatriene or oxepin, or the compound *(66)*, as was originally assumed[186], but that the compound *(64)* is formed instead[187–189].

The structure *(64)* is based on the X-ray analysis of its derivatives[190–191]. The formation of adducts of the type *(64)* can be explained by the assumption that the triene form is much more stable than the norcaradiene form in azepines. If this is so, the 1,4-addition to the triene form will predominate, whereas if the monocyclic and bicyclic tautomers are roughly equally stable, as in the case of the carbocyclic cycloheptatrienes, 1,4-addition to the norcaradiene form will take place[189].

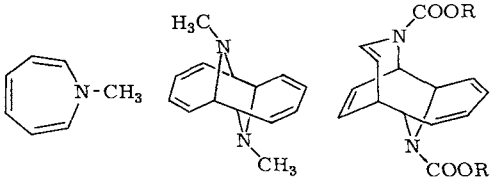


(64) ← *(60)* → *(65)*



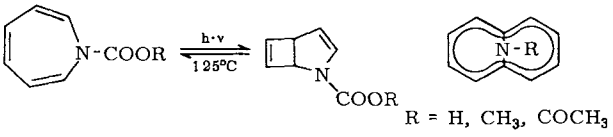
(66)

The yellow *N*-methylazepine *(67)* dimerizes rapidly above 0 °C to give *(68)*[182]. *(60)* and *(62)* give similar dimers when heated[192, 193]. According to the Woodward-Hoffmann rule, a 6 + 6 addition cannot take place directly[194], but must proceed in several steps. This is confirmed by the fact that a 4 + 6 addition product *(69)* has been found as an intermediate[192].



(67) *(68)* *(69)*

Like cycloheptatriene (Section IIIc) and 2,7-dimethyloxepin[190], *(60)* is converted by exposure to light into the valence-isomeric 2-azabicyclo[3.2.0]heptadiene derivative *(70)*, which in turn is reconverted into *(60)* by heating[190].



(60) *(70)* *(71)*

The spectra of the nitrogen-bridged cyclodecapentaenes *(71)*[162, 195] are in agreement with those of the methylene and oxygen analogues.

[177] *K. Hafner*, *D. Zinser*, and *K.-L. Moritz*, Tetrahedron Letters *1964*, 1733.

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[183] *W. Theilacker*, *K. Ebke*, *L. Seidl*, and *S. Schwerin*, Angew. Chem. *75*, 208 (1963); Angew. Chem. internat. Edit. *2*, 154 (1963).

[184] *P. Rosenmund* and *W. H. Haase*, Chem. Ber. *99*, 2504 (1966).

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[187] *J. H. Van Den Hende* and *A. S. Kende*, Chem. Commun. *1965*, 384.

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[191] *I. C. Paul*, *J. E. Baldwin*, and *R. A. Smith*, J. Amer. chem. Soc. *88*, 3653 (1966).

[192] *L. A. Paquette* and *J. A. Barrett*, J. Amer. chem. Soc. *88*, 2590 (1966).

[193] *A. L. Johnson* and *H. E. Simmons*, J. Amer. chem. Soc. *88*, 2591 (1966).

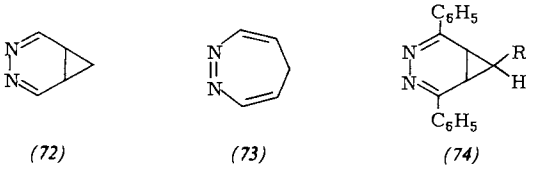
[194] *H. Hoffmann* and *R. B. Woodward*, J. Amer. chem. Soc. *87*, 2046, 4389 (1965).

[195] *E. Vogel*, *W. Pretzer*, and *W. A. Böll*, Tetrahedron Letters *1965*, 3613.

No compound having a definite benzene imine structure has so far been found, but there are indications of a valence-tautomeric equilibrium between *N*-methylazepine *(67)* and *N*-methylbenzeneimine [182].

c) 3,4-Diazanorcaradiene—3,4-Diazacycloheptatriene

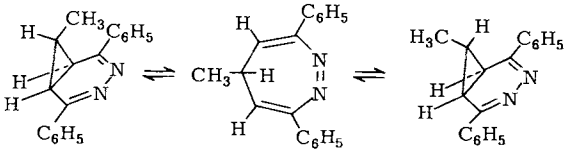
Norcaradiene derivatives can be stabilized, not only by "freezing" a double bond (by incorporation in an aromatic ring) or by the "bracket effect", but also by the incorporation of nitrogen atoms into the norcaradiene ring in positions 3 and 4. It can be calculated that in the system 3,4-diazanorcaradiene *(72)*/3,4-diazacycloheptatriene *(73)*, the bicyclic valence tautomer must be thermodynamically more stable than the monocyclic form.



(72) *(73)* *(74)*

In fact, 2,5-diphenyl-3,4-diazanorcaradiene *(74)*, R = H, and its substitution products are stable at room temperature [196–201]. The bicyclic structure is evidenced on the one hand by the spectra, and on the other by the chemical behavior of these compounds. Compounds of the type *(74)*, R = H, CH_3, COC_6H_5, form 4-alkyl-3,6-diphenylpyridazines when treated with acid, and reaction with manganese dioxide, ozone, or peroxy acids leads almost quantitatively to dibenzoylcyclopropanes [198, 199, 202]. Similar results were also obtained with the four-membered ring homologues of *(74)* [203–205].

The monocyclic triene form is present in such small concentrations in the diaza series that it cannot be detected directly. However, a valence-tautomeric equilibrium has been found between the diazanorcaradienes *(75a)* and *(75b)* and the diazacycloheptatriene *(76)*. As would be expected, *(74)* with R = CH_3 forms two *cis-trans* isomers *(75a)* and *(75b)*; in solution, the



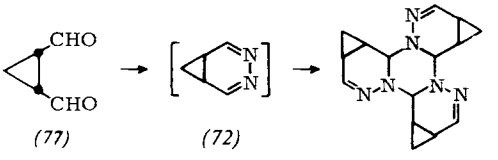
(75a) *(76)* *(75b)*

equilibrium mixture contains equal amounts of the two compounds. This equilibration ($E_{A\ (75a)\rightarrow(75b)}$ = 22.0±2.5; $E_{A\ (75b)\rightarrow(75a)}$ = 24.5±2.5 kcal/mole [202]) is most easily formulated as proceeding *via* the triene *(76)*.

Delocalization of the 1,6 bond definitely does not take place in the diazanorcaradienes. This conclusion is based mainly on the NMR spectra: the three-membered ring protons of *(74)*, R = H, give an AB_2X spectrum (τ_A = 7.91, τ_B = 7.38, τ_X = 9.77; J_{AB} = 9.0, J_{BX} = 4.8, J_{AX} = 3.5 Hz). The great difference in the positions of the signals for the two geminal cyclopropane protons indicates that the three-membered ring is twisted well out of the plane of the six-membered ring. It can be deduced from the coupling constants that the proton corresponding to the high τ value lies above the dihydropyridazine ring.

The UV spectra of the diphenyldiazanorcaradienes differ markedly from those of suitable model substances, such as 3,7-diphenyl-1,2-diazacyclohepta-2,7-diene, and can be used for the identification of these systems.

As long as only 2,5-diphenyl-substituted 3,4-diazanorcaradienes are known, it will remain uncertain whether the stability of the bicyclic tautomers is really due to the nitrogen atoms, since it could also result from the conjugative effect of the phenyl groups. The same is true of diazanorcaradienes substituted in positions 2 and 5 by other groups containing double bonds (*e.g.* ester groups [201]).



(77) *(72)* *(78)*

Attempts were therefore made to prepare the unsubstituted parent compound *(72)*. Condensation of cyclopropane-*cis*-1,2-dicarbaldehyde *(77)* [206] with hydrazine leads not to *(72)*, but to a mixture of three isomeric substances, the composition and molecular weight of which indicate that they must be trimers of diazanorcaradiene. These can be separated chromatographically; each component, when treated with acid, yields the original mixture. The trimers of *(72)* presumably have the constitution *(78)* [206]. However, this structure indicates that in the diazanorcaradiene *(72)* postulated as the intermediate, the bicyclic valence tautomer is again more stable than the monocyclic form.

To avoid trimerization, attempts were made to synthesize 2,5-dimethyldiazanorcaradiene by preparation of *cis*-1,2-diacetylcyclopropane and *cis*-1,2-dimethyl-1,2-diacetylcyclopropane *(79)* and reaction of these with hydrazine [207]. *(79)* gave a compound having the correct empirical formula, but with double the expected molecular weight. The spectra of this compound show that a methyl group has reacted in the dimerization. The IR spectrum contains no NH band; therefore the methyl group has not added across the C=N double bond of a second molecule of *(81)* to give *(82)*. On the contrary, all the available evidence indicates that the dimer has the structure *(83)*. The same compound is formed in the reaction of pyridazinone *(80)* with methyl-lithium.

[196] *G. Maier*, Chem. Ber. *95*, 611 (1962).

[197] *G. Maier*, Angew. Chem. *75*, 920 (1963); Angew. Chem. internat. Edit. *2*, 621 (1963).

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[199] *G. Maier*, Chem. Ber. *98*, 2446 (1965).

[200] *R. G. Amiet, R. B. Johns*, and *K. R. Markham*, Chem. Commun. *1965*, 128.

[201] *J. Sauer* and *G. Heinrichs*, Tetrahedron Letters *1966*, 4979.

[202] *G. Maier* and *U. Heep*, unpublished.

[203] *G. Maier*, Chem. Ber. *99*, 1229 (1966).

[204] *G. Maier*, Chem. Ber. *99*, 1232 (1966).

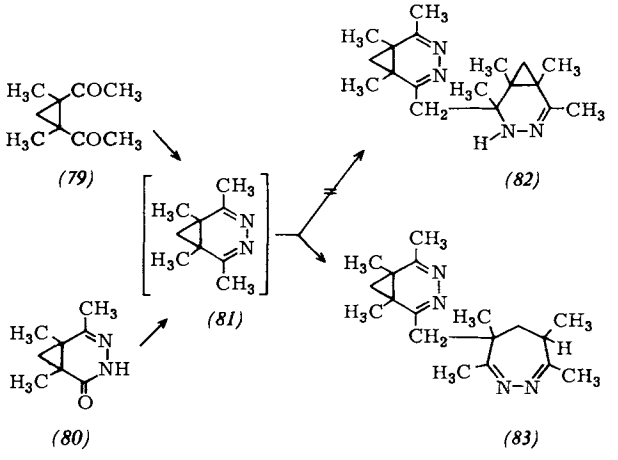
[205] *G. Maier* and *F. Seidler*, Chem. Ber. *99*, 1236 (1966)

[206] *G. Maier* and *T. Sayrac*, Angew. Chem. *78*, 981, 1103 (1966); Angew. Chem. internat. Edit. *5*, 959 (1966).

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Since one half of the molecule *(83)* contains the diazanorcaradiene ring system, it may be concluded that the stabilization of the bicyclic form is due to the nitrogen atoms, and that conjugation with the phenyl groups is of little importance.

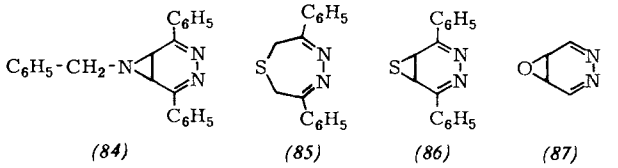
The conjugation with the phenyl groups is the dominant factor when they are in the positions 1 and 6. In such systems the valence-tautomeric equilibrium is strongly in favor of the monocyclic form [207a].



(79) *(80)* *(81)* *(82)* *(83)*

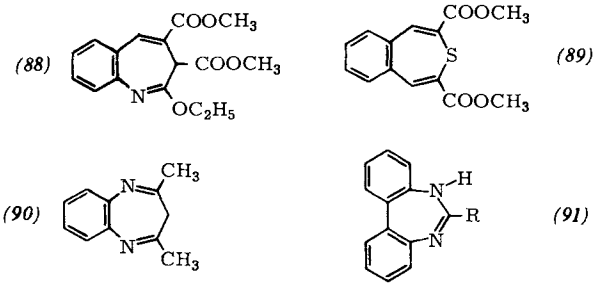
d) Other Systems

The above conclusion remains valid even when an additional hetero atom is incorporated in position 7 of the diazanorcaradiene ring system. Like the compound *(74)*, the 3,4,7-triaza derivative *(84)* is also a relatively stable substance, which can again be detected only in the bicyclic form [208]. Though the *S*-analogue *(86)* has not yet been obtained, the easy elimination of the sulfur atom with formation of 3,6-diphenylpyridazine on bromination of *(85)* suggests intermediate formation of *(86)* [209]. A derivative of pyridazine oxide *(87)* has also been described in the literature [210]; however, doubt has recently been cast on the suggested structure [211].



(84) *(85)* *(86)* *(87)*

Mono- and dibenzo derivatives of azepine, thiepin, and the diazepines are known; examples are the compounds *(88)* [213], *(89)* [214], and *(90)* [212, 215–217] and compounds of the type *(91)* [218–219]. Since at least one of the double bonds in these compounds also belongs to an aromatic ring, valence tautomerization to form norcaradiene derivatives is hindered. However, the ease of elimination of the sulfur atom in *(89)* [220] does suggest a valence-tautomeric equilibrium.



(88) *(89)* *(90)* *(91)*

1,2-Diazepines appear to be stabilized even without condensation with a benzene ring, and exist in the monocyclic form [201]. It is interesting that these compounds, when their structures are such that tautomerization is possible (*e.g.* migration of the hydrogen from the carbon to the nitrogen), prefer the 3*H* form and not the 1*H* form; this is further evidence that the resulting 8 π-electron system is not appreciably stabilized. Quantum-mechanical calculations [221], according to which the 1*H*-azepine is less stable than the isomeric azatropilidenes with the nitrogen in the double bond, support this experimental evidence. The calculations also show that electron-attracting substituents on the nitrogen can stabilize 1*H*-azepines.

As in the carbocyclic norcaradienes (see Section IIIa), systems with hetero atoms should permit stabilization of the bicyclic tautomers by fixation of the double bond. This is so *e.g.* in the compound *(92)* [222], which in analogy to *(7)* can be transformed thermally to a benzodiazepine [222a]. The action of light on *N*-oxides of heterocyclic compounds should give compounds in which the norcaradiene system includes an oxaziridine ring. One of many compounds of this type [223, 224-226] is the product *(93)*, reportedly formed by the action of light on 2-phenylquinoline *N*-oxide. However, this compound is probably only an intermediate in the photolysis. The product isolated was benzoxazepine *(95)* [227], the formation

[207a] *M. A. Battiste* and *T. J. Barton*, Tetrahedron Letters, *1967*, 1227.

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[213] *H. Plieninger* and *D. Wild*, Chem. Ber. *99*, 3070 (1966).

[214] *K. Dimroth* and *G. Lenke*, Chem. Ber. *89*, 2608 (1956).

[215] *J. Thiele* and *G. Steimmig*, Ber. dtsch. chem. Ges. *40*, 955 (1907).

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[220] *A. Schönberg* and *M. B. E. Fayez*, J. org. Chemistry *23*, 104 (1958).

[221] *H. Volz*, personal communication.

[222] *G. F. Field, W. J. Zally*, and *L. H. Sternbach*, Tetrahedron Letters *1966*, 2609.

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[223] *C. Kaneko, S. Yamada*, and *I. Yokoe*, Tetrahedron Letters *1966*, 4701.

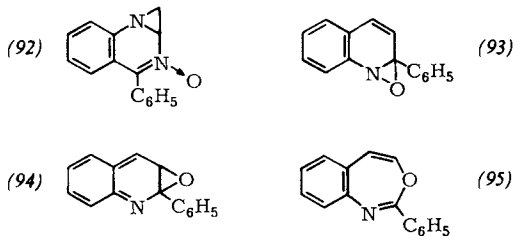
[224] *C. Kaneko, S. Yamada*, and *M. Ishikawa*, Tetrahedron Letters *1966*, 2145.

[225] *E. C. Taylor, B. Furth*, and *M. Pfau*, J. Amer. chem. Soc. *87*, 1401 (1966).

[226] *O. Buchardt* and *C. Lohse*, Tetrahedron Letters *1966*, 4355.

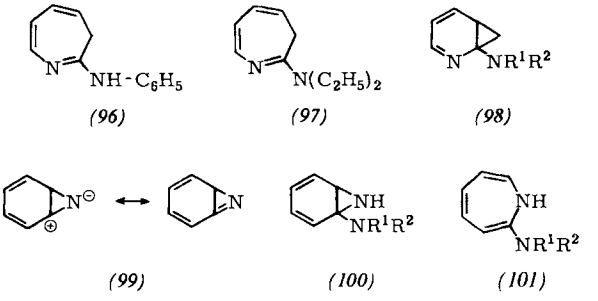
[227] *O. Buchardt*, Tetrahedron Letters *1966*, 6221.

of which can be explained by the isomerization of *(93)* into the norcaradiene derivative *(94)*, which immediately forms *(95)*.



The photolytically induced ring contraction of pyridine *N*-oxide to form pyrrole-2-carbaldehyde is also formulated as proceeding *via* primary formation of an oxazanorcaradiene derivative followed by valence tautomerization [228].

Stabilization by a condensed benzene ring does not occur with the azatropilidenes that are formed during the thermal or photolytic decomposition of aromatic azides in the presence of amines. Thus when phenyl azide is heated in aniline, "dibenzamil" is formed [229]; this was recognized as an azepine derivative [230, 231] having the structure *(96)* [186, 232]. The photolysis of phenyl azide in aniline yields the same substance, while the compound *(97)* is formed in diethylamine [233]. Trimethyl derivatives of this ring system can be obtained by ring expansion of 2,4,6-trimethylphenol [234]. In this case it is again found that the 3*H*-azepine system shows no tendency to change into the tautomeric 1*H*-azepine system. (1*H*-azepine structures are ruled out by the fact that the IR spectrum of compounds such as *(97)* does not contain an



NH band). A choice can be made between the six other possible structures on the basis of the NMR spectra. There is no evidence of a valence-tautomeric equilibrium, probably because the amidine resonance is lost on transition from *(96)* to *(98)*, $R^1 = H$, $R^2 = C_6H_5$. A 7-azanorcaradiene may occur as an intermediate in the formation of the compounds *(96)* and *(97)*. It is assumed [232, 235, 236] that the phenyl azide is converted *via* phenylnitrene into the dehydroazanorcaradiene *(99)*, which adds the base to give a 7-azanorcaradiene derivative *(100)*. *(100)* should then undergo valence tautomerization to form the 1*H*-azepine *(101)*, from which the final product is formed by hydrogen shift.

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Translated by Express Translation Service, London

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[230] *R. Huisgen*, *D. Vossius*, and *M. Appl*, Angew. Chem. *67*, 756 (1955).

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[233] *R. A. Odum* and *M. Brenner*, J. Amer. chem. Soc. *88*, 2074 (1966).

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Recent Chemistry of Bullvalene[1]

BY G. SCHRÖDER AND J. F. M. OTH [*]

Dedicated to Professor R. Criegee on the occasion of his 65th birthday

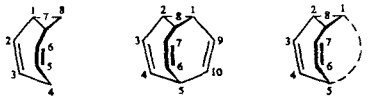
The essential structural element of bullvalene is the homotropilidene system. Thus in any discussion of the chemistry of bullvalene, all bridged homotropilidenes must also be considered. The present article deals with new syntheses and with the thermal behavior of the homotropilidene system and of bullvalene. Emphasis is also placed on the syntheses and the NMR-spectroscopic behavior of complexed bullvalene, of monosubstituted, disubstituted, and fused bullvalenes, and of some benzobullvalene derivatives.

I. Introduction

The fundamental work of *Doering* and *Roth*[2] in the discovery of a fast and reversible valence isomerization (or a "degenerate Cope rearrangement") in bicyclo-[5.1.0]octa-2,5-diene *(1)*, which is also known as homotropilidene, together with the discussion of the fascinating properties of bullvalene *(2)*, is one of the milestones of organic chemistry and forms the basis of the present review.

Two years ago we published[3] our first review on molecules exhibiting fast and reversible valence isomerization, which are also described as molecules with fluctuating bonds. The present article is confined to only a part, though a very important part, of this class of compounds.

The essential structural element of bullvalene *(2)* is the homotropilidene system *(1)*. Consequently, all bridged homotropilidenes *(3)* are considered in the discussion of bullvalene.



(1) *(2)* *(3)*

[*] Priv.-Doz. Dr. G. Schröder
Institut für Organische Chemie
der Technischen Hochschule
Richard-Willstätter-Allee
75 Karlsruhe (Germany)

Dr. J. F. M. Oth
Union Carbide European Research Associates
95, Rue Gatti de Gamond
Brussels-18 (Belgium)

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II. New Syntheses of the Homotropilidene System and of the Bullvalene Skeleton

a) Tricyclo[3.3.0.0^{2,8}]octa-3,6-diene ("Semibullvalene") [4]

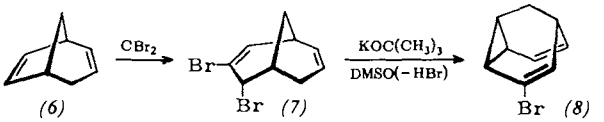
The photolysis of a 1 to 2 % solution of barrelene *(4)* in isopentane, in the presence of 3 to 8 % of acetone as a sensitizer, leads to the formation of "semibullvalene" *(5)* and traces of cyclooctatetraene.



(4) *(5)*, 25-46% 1-2%

b) 3-Bromotricyclo[3.3.1.0^{2,8}]nona-3,6-diene [5]

The addition of dibromocarbene to bicyclo[3.2.1]octa-2,6-diene *(6)* under the conditions for the preparation of dibromocarbene (basic medium) yields the dibromide *(7)*, which loses HBr in the presence of a strong base to form *(8)*.



(6) *(7)* *(8)*

c) Tricyclo[3.3.1.0^{2,8}]nona-3,6-diene [6,7]

The Wolff-Kishner reduction of the tricyclic ketone *(9)*[6] or the base-catalysed decomposition of the tosylhydrazone *(11)*[7] leads *inter alia* to tricyclo-

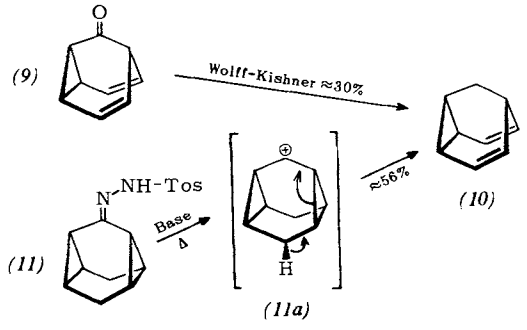
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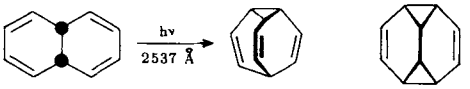
[3.3.1.$0^{2,8}$]nona-3,6-diene *(10)*. Following the mechanism of the Bamford-Steven reaction[8], *(11)* should give the cation *(11a)*, which is stabilized by loss of a proton to form *(10)*[7].



d) New Syntheses of Bullvalene

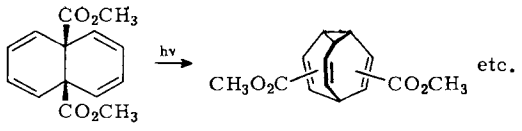
The two syntheses of bullvalene which were developed several years ago[9,10] may now be supplemented by the following additional syntheses:

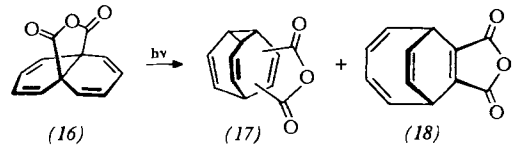
1. When 9,10-dihydronaphthalene *(12)* in deaerated pentane is irradiated by a low-pressure UV lamp at 0 °C, a mixture of four compounds is formed. One of these compounds is bullvalene[11].



As a result of theoretical considerations by *Hoffmann* and *Woodward*[12], the synchronous photochemical conversion of *(12)* into tetracyclo[4.4.0.$0^{2,10}0^{5,7}$]deca-3,8-diene *(13)* has now become understandable; *(13)* plays a part in speculations on the mechanism of this new synthesis of bullvalene [11,14b].

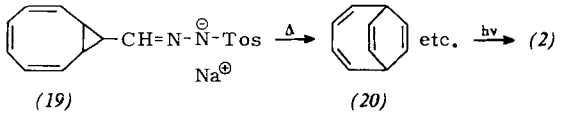
2. Almost simultaneously with the work of *Doering* and *Rosenthal*[11], *Vogel et al.*[13] reported work which was mechanistically closely related to the former, and which led to the synthesis of disubstituted bullvalenes. On irradiation of dimethyl *cis*-9,10-dihydronaphthalene-9,10-dicarboxylate *(14)* in methanol by a low-pressure mercury lamp, one of the products is a photoisomer, which must have the structure of a dimethyl bullvalenedicarboxylate *(15)*. The anhydride



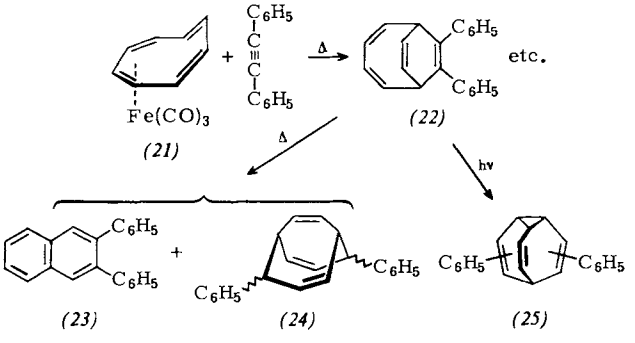


(16) corresponding to *(14)* is converted by UV irradiation in ether solution into two photoisomeric anhydrides for which the structures *(17)* and *(18)* are proposed.

3. Bicyclo[4.2.2]deca-2,4,7,9-tetraene *(20)*, which is formed together with $C_{10}H_{10}$ isomers on thermal decomposition of the sodium tosylhydrazone *(19)*, is converted surprisingly smoothly into bullvalene on UV irradiation[14a].



4. Tricarbonylcyclooctatetraeneiron *(21)* reacts with alkynes at high temperatures (boiling mesitylene) to form derivatives of bicyclo[4.2.2]deca-2,4,7,9-tetraene[15]. Thus the products obtained with tolan include a hydrocarbon $C_{22}H_{18}$ (35 %) whose NMR spectrum is compatible with the structure *(22)*. *(22)* decomposes at about 180 °C to give mainly 2,3-diphenylnaphthalene *(23)* and diphenylbicyclo[3.3.2]deca-2,6,9-triene *(24)*. The evidence for the structure *(24)* is based essentially on the NMR spectrum of this compound. UV irradiation of *(22)* yields unchanged starting material, together with a viscous oil having the composition $C_{22}H_{18}$ and which gives temperature-dependent NMR spectra. The oil evidently contains diphenylbullvalene *(25)*.



Replacement of an isolated double bond in *(20)* by a cyclobutene ring leads to a hydrocarbon $C_{12}H_{12}$ *(27)*[16], which might, by analogy with the behavior of *(20)*, be expected to undergo isomerization to *(26)*[17] under the action of UV light.

[8] *L. Friedman* and *H. Shechter*, J. Amer. chem. Soc. *81*, 5512 (1959).

[9a] *G. Schröder*, Angew. Chem. *75*, 722 (1963); Angew. Chem. internat. Edit. *2*, 481 (1963); [9b] Chem. Ber. *97*, 3140 (1964).

[9b] *G. Schröder*, Chem. Ber. *97*, 3140 (1964).

[10] *W. v. E. Doering* and *G. Klumpp*, personal communication.

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[12] *R. Hoffmann* and *R. B. Woodward*, J. Amer. chem. Soc. *87*, 2046 (1965).

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[14a] *M. Jones jr.* and *L. T. Scott*, J. Amer. chem. Soc. *89*, 150 (1967).

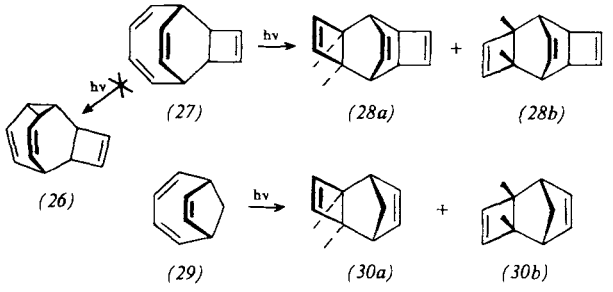
[14b] *W. v. E. Doering* and *J. W. Rosenthal*, Tetrahedron Letters *1967*, 349, isolated *(20)* on UV irradiation of *(12)*.

[15] *U. Krüerke*, Angew. Chem. *79*, 55 (1967); Angew. Chem. internat. Edit. *6*, 79 (1967).

[16] *G. Schröder* and *W. Martin*, Angew. Chem. *78*, 117 (1966); Angew. Chem. internat. Edit. *5*, 130 (1966).

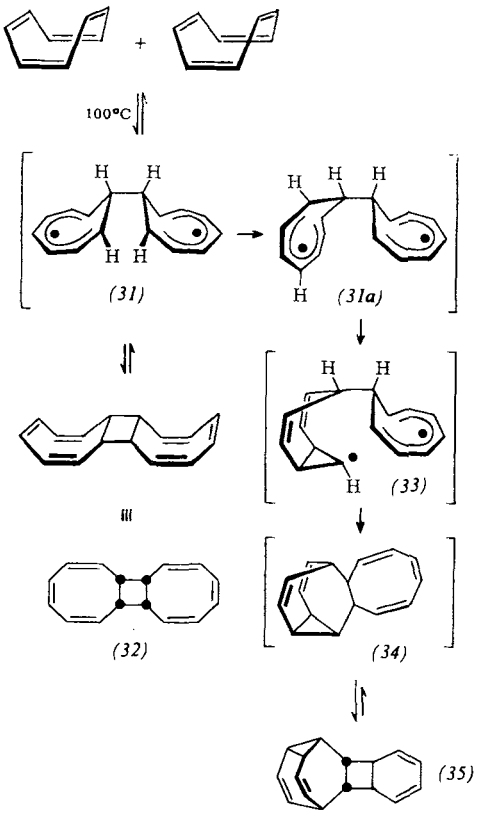
[17] *G. Schröder*, Chem. Ber. *97*, 3131 (1964).

However, the result actually observed is ring contraction with formation of roughly equal quantities of the two isomers *(28a)* and *(28b)* [18]. This result is underlined by the fact that UV irradiation of bicyclo[4.2.1]nona-2,4,7-triene *(29)* leads *inter alia* to the *exo*- and *endo*-tricyclononadienes *(30a)* and *(30b)* [19].



Of the five known syntheses of the bullvalene skeleton, by far the highest yields are obtained by that based on the formation of a homotropilidene system on thermal dimerization of cyclooctatetraene [9]. This is the only synthesis that permits a relatively fast and simple preparation of bullvalene on the 100 g scale (assuming that cyclooctatetraene is readily obtainable in large quantities).

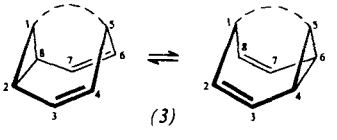
It is of interest in this connection to consider the mechanism of the dimerization of cyclooctatetraene. Earlier attempts [9b, 20] to explain this reaction were based on an incorrect structure for the dimer *(32)* and are consequently no longer tenable. In our new hypothesis, we assume that the first step is analogous to that of a 1,2/1,2 cycloaddition [21] and leads to the biradical *(31)*. Further reaction of *(31)* leads to branching. The activation required for the formation of the dimer *(32)*, which is a symmetrical tricyclic compound with an all-*cis* configuration of the cyclobutane ring [16], is relatively low; *(32)* is formed in preference to all other dimers [18]. *(31)* either decomposes reversibly into two molecules of cyclooctatetraene or undergoes irreversible rearrangement into *(35)*, presumably *via* the intermediates *(31a)*, *(33)*, and *(34)*. This interpretation agrees with the experimental observation that when pure *(32)* is heated to about 100 °C it forms (a) cyclooctatetraene, which under suitable reaction conditions (slightly reduced pressure) is removed from the reaction vessel immediately on formation, and (b) the dimer *(35)* [22]. This shows that *(32)* is at least one of the precursors of *(35)*.



III. Reversible and Irreversible Thermal Rearrangements of Molecules Containing the Homotropilidene System

The reversible thermal rearrangements of molecules containing the homotropilidene system have relatively low activation energies E_a (see Table 1) and have been described by the concept of fluctuating

Table 1. Kinetic parameters of the valence isomerization in bridged homotropilidenes *(3)*. (The values of $\log_{10}A$ and E_a were calculated by the method of least squares (Arrhenius equation). The errors correspond to the mean square deviations; the systematic errors were not taken into account. A = frequency factor.)



Compound	k (sec^{-1}) −40 °C	k (sec^{-1}) 0 °C	log A	E_a (kcal mole^{-1})	$\Delta H\neq$ (kcal mole^{-1})	$\Delta S\neq$ (cal deg^{-1} mole^{-1})
(2) [23–25]	20	790	12.11 ± 0.08	11.5 ± 0.1	10.9 ± 0.1	− 4.8 ± 0.4
(37) [26]	6150	332500	15.0 ± 0.4	12.6 ± 0.4	12.0 ± 0.4	+11.0 ± 0.4
(10) [27]	990000	26000000	15.7 ± 0.3	10.4 ± 0.3	9.8 ± 0.3	+11.5 ± 0.3
(5)	faster than *(10)*					

[18] *G. Schröder* and *W. Martin*, unpublished.

[19] *L. C. Cannell*, Tetrahedron Letters *1966*, 5967.

[20] *G. Schröder*: Cyclooctatetraen. Verlag Chemie, Weinheim/Bergstr., 1965.

[21] *J. D. Roberts* u. *C. M. Sharts*, Org. Reactions *12*, 1 (1962).

[22] *B. Flügel*, Diploma Thesis, Technische Hochschule Karlsruhe, 1964.

[23] *J.-M. Gilles* and *J. F. M. Oth*, Communication No. 389 at the 8th European Congress on Molecular Spectroscopy, August 14–20, 1965, Copenhagen, Denmark.

[24] *M. Saunders*, Tetrahedron Letters *1963*, 1699.

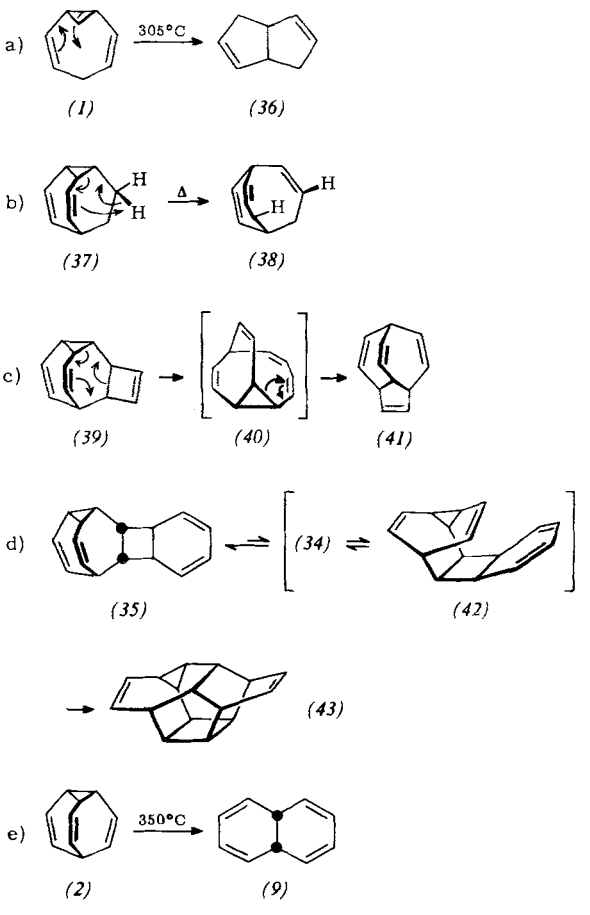
[25] *A. Allerhand* and *H. S. Gutowsky*, J. Amer. chem. Soc. *87*, 4092 (1965).

[26] *J. F. M. Oth* and *J.-M. Gilles*, unpublished.

[27] Modified values after *J. H. Hartenstein*, personal communication. The contribution of the spin-spin couplings to the line width of the mixed resonance signals of olefinic and cyclopropyl protons was taken into account; *J. F. M. Oth* and *J.-M. Gilles*, unpublished.

bonds [3]. The fast and reversible valence isomerizations in *(3)* (the broken line represents a bridge between C-1 and C-5) are generally fairly easily recognized from the temperature-dependence of the NMR spectra. The activation energies E_a for the bond shifts decrease with decreasing distance between C-1 and C-5 in *(3)*.

At higher temperatures (between 100 and 400 °C, depending on the molecular structure), the reversible reactions in *(3)* are replaced by irreversible reactions. In the examples a) to e) discussed here these irreversible reactions lead to definite secondary products.



a) Homotropilidene *(1)* undergoes an irreversible vinylcyclopropane → cyclopentene rearrangement [28] at about 305 °C to give bicyclo[3.3.0]octa-2,6-diene *(36)* [2].

b) In dihydrobullvalene *(37)*, on the other hand, the 1,5-homodienyl hydrogen shift predominates; the product is *(38)* [29].

c) Pyrolysis of *(39)*, a homotropilidene system bridged by a cyclobutene ring, leads smoothly to the isomer *(41)*, the formation of which is explained as follows: Valence isomerization in *(39)* (as indicated by the arrows) yields a vinylogue *(40)* of bullvalene, which subsequently undergoes a vinylcyclopropane rearrangement to form *(41)* [29].

d) The dimeric cyclooctatetraene *(35)* reacts readily with dienophiles [17]. In our opinion, this behavior is compatible only with an *anti* configuration on the cyclobutane ring. Thus consideration of models shows that if the configuration were *syn*, steric interactions in the resulting Diels-Alder adducts should lead to unusually high strain, which would greatly impede the formation of these products. At about 100 to 110 °C, *(35)* rearranges (yield $\geqslant$ 80 %) to form the known [30] dimeric cyclooctatetraene *(43)* [31]. A simple valence isomerization in *(35)* leads first to *(34)*, which, in principle, exists in equilibrium with *(35)* and *(42)*. However, the steric requirements for an intramolecular Diels-Alder reaction to form *(43)* are satisfied only in *(42)*.

e) Bullvalene *(2)*, which in the dissolved state can be described by 1.2×10^6 structurally equivalent valence isomers, and whose ten carbon atoms are continuously exchanging places and neighbors at room temperature [2], undergoes a thermally irreversible rearrangement at about 350 °C to form 9,10-dihydronaphthalene *(9)* [11]. Two mechanisms are at present under discussio for this reaction [11].

IV. New Bullvalene Derivatives

a) Bullvalene-Ag^+ Complexes

Bullvalene *(2)* forms complexes of various compositions with $AgNO_3$ and $AgBF_4$ [25]. The results of X-ray structural analysis of a complex $(C_{10}H_{10})_3AgBF_4$ *(44)* are shown in Figure 1 [32].

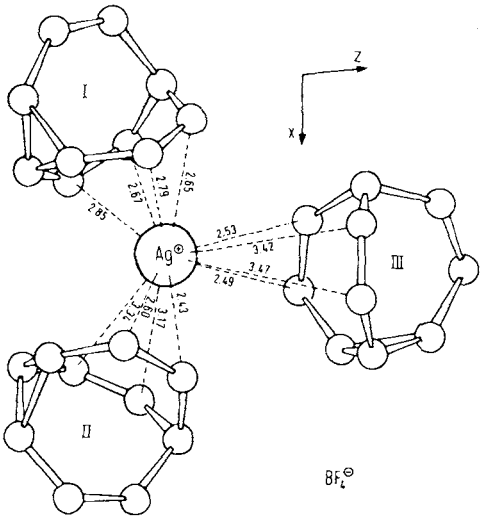


Fig. 1. Structure of an $Ag^+(C_{10}H_{10})_3$ unit. (Examined parallel to the *b* axis; the Ag^+—C(sp^2) distances are given in Å units).

The degree of complexing of the silver ion with the olefinic double bond varies. With each of the molecules II and III in *(44)*, we find a stronger (distance

[28] *C. G. Overberger* and *A. E. Borchert*, J. Amer. chem. Soc. *82*, 1007, 4896 (1960).

[29] *J. Meinwald, J. N. Labows jr., H. Röttele*, and *G. Schröder*, J. Amer. chem. Soc. *89*, 612 (1967).

[30] *H. W. Moore*, J. Amer. chem. Soc. *86*, 3398 (1964).

[31] *H. W. Moore*, personal communication; *G. Schröder*, unpublished.

[32] *M. G. Newton* u. *I. C. Paul*, J. Amer. chem. Soc. *88*, 3161 (1966).

2.51 Å) and a weaker (distance 3.35 Å) interaction between the silver ion and the double bonds; roughly equally strong complexing of two double bonds is found only in I. The structure *(44)* has the highest $Ag^{\oplus}$-olefin coordination number so far observed by X-ray crystallography. In the crystalline complex *(44)* [33], the fast and reversible valence isomerization in the bullvalene molecule appears to be frozen (diagram recorded at 4 °C).

In solution and in the presence of silver ions, bullvalene (0.32 g of bullvalene in 1 ml of 7.15 M $AgNO_3$ in D_2O) shows an apparent activation energy $E_a = 15.1 \pm 0.8$ kcal/mole for the valence isomerization in the homotropilidene system [25]. The value for uncomplexed bullvalene is about 2.3 kcal/mole lower [3, 23–25]. There are two explanations for this difference:

(i) The valence isomerization takes place only in uncomplexed bullvalene, which is formed by dissociation of the silver complex; the dissociation constant should be expected to increase with rising temperature.

(ii) The valence isomerization takes place in the silver complex, but at a lower rate and with a higher activation energy than in free bullvalene.

It is possible that both of these mechanisms are involved [25].

b) Monosubstituted Bullvalenes

In principle, any substituted bullvalene represents a system of 1.2×10^6 valence isomers, but in contrast to the parent compound, these isomers are not all structurally equivalent. Thus for a monosubstituted bullvalene there are four possible positional isomers, which can be interconverted at room temperature. The equilibrium between these four positional isomers (cf. Fig. 2), which is dynamic at high temperatures, is frozen at very low temperatures [3, 34]. It was of interest to us

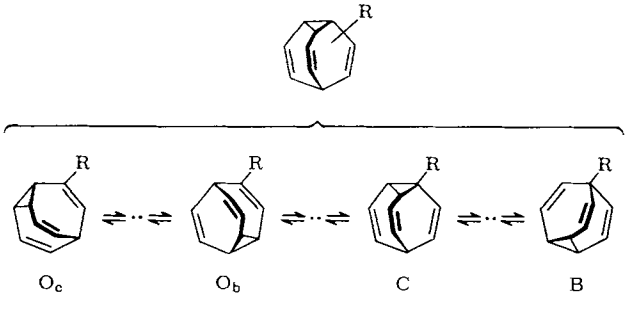
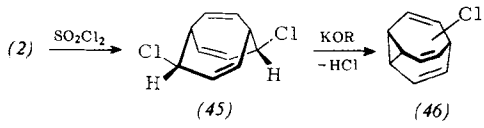


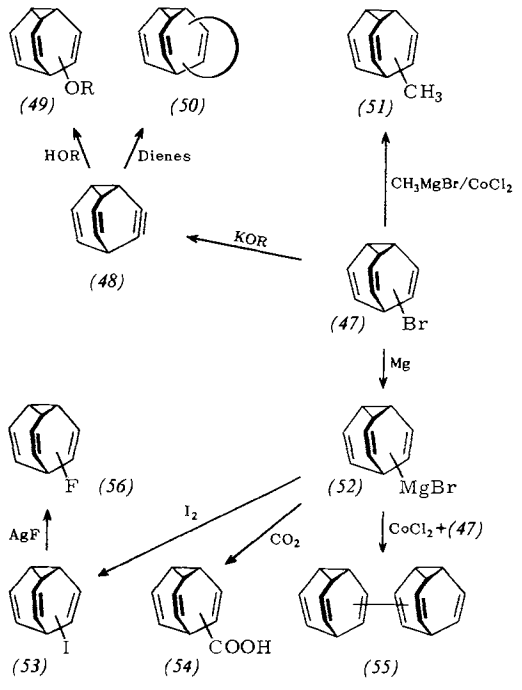
Fig. 2. The four positional isomers of monosubstituted bullvalenes [35].

to learn how the kinetic parameters of the valence isomerization, and hence also the equilibrium composition [34], could be influenced by variation of the substituent R.

The synthesis of chlorobullvalene *(46)* [36] proceeds by stereoselective chlorination of *(2)*. In the presence of KOR, HCl is eliminated from the bicyclic *trans*-dichloride *(45)* with reformation of the homotropilidene system; the product is *(46)*.



At present, bromination of bullvalene is still the best route to monosubstituted bullvalene derivatives. Bromobullvalene *(47)* can be obtained in good yields from the resulting dibromide by treatment with bases [34] and is the key substance for the preparation of other monosubstituted bullvalenes (see Scheme 1).



Scheme 1. Substituted bullvalenes prepared from bromobullvalene.

(47) reacts smoothly with potassium alkoxides to form alkoxybullvalenes *(49)* (60–90%) [34], the reaction proceeding *via* a didehydrobullvalene *(48)* [36], since Diels-Alder adducts *(50)* (17–80%) are formed in the presence of reactive dienes [36]. Methylbullvalene *(51)* can be obtained in moderate yields (32%) by treatment of *(47)* with CH_3MgBr in the presence of $CoCl_2$ [36]. Reaction with Mg turnings leads to the versatile Grignard compound *(52)*, which reacts (i) with *(47)* in the presence of $CoCl_2$ to form bibullvalenyl *(55)* (17%), (ii) with CO_2 to form bullvalene carboxylic acid *(54)* (40%), and (iii) with iodine to form iodobullvalene *(53)* (38%) [36]. *(53)* is in turn the starting material for the preparation of fluorobullvalene *(56)* (52%, in pyridine) [36]. *(56)* is remarkable in that the valence isomers in this case can be studied on the basis of two temperature-dependent NMR signals (H and F).

All substituted bullvalenes give temperature-dependent NMR spectra. The spectra recorded at high temperatures reflect the dynamic situation (*i.e.* the fast

[33] For the thermal behavior of crystalline bullvalene, see *J. D. Graham* and *E. R. Santee jr.*, J. Amer. chem. Soc. *88*, 3453 (1966).

[34] *J. F. M. Oth, R. Merényi, J. Nielsen*, and *G. Schröder*, Chem. Ber. *98*, 3385 (1965).

[35] The meanings of the abbreviations are: C, substituent on the cyclopropane ring; O_c and O_b, substituent on the olefinic double bond nearer to the cyclopropane ring and nearer to the bridgehead respectively; B, substituent on the bridgehead; see also [34].

[36] *H. Röttele*, Dissertation, Technische Hochschule Karlsruhe, 1967.

and reversible valence isomerizations), while those recorded at low temperatures correspond to the static situation (*i.e.* the frozen equilibrium mixtures)[3]. Two examples are described below.

a) In bibullvalenyl *(55)*, $C_{20}H_{18}$, there are not four (the number for monosubstituted bullvalenes), but ten positional isomers to be considered (the second bullvalenyl residue, like the first, has four different positions). The temperature-dependent NMR spectra of *(55)* are shown in Fig. 3. At higher temperatures only one resonance signal is found for the eighteen protons,

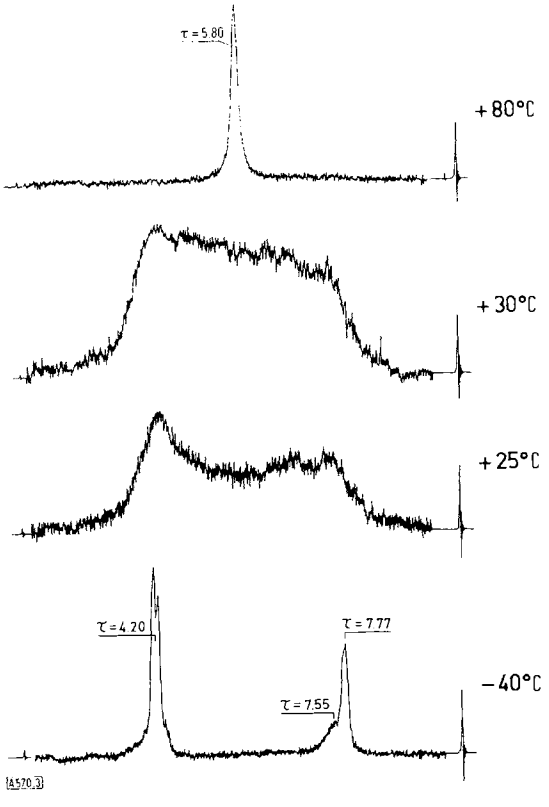


Fig. 3. ^{1}H—NMR spectra of bibullvalenyl *(55)* in CS_2. (Internal standard: tetramethylsilane, $\tau = 10$.)

i.e. the eighteen protons are all NMR-spectroscopically equivalent. In the bibullvalenyl molecule, the valence isomerizations in the two linked bullvalenyl residues proceed more or less independently of one another. The low-temperature spectrum (−40 °C) indicates a ratio of ten olefinic to eight aliphatic bullvalenyl protons, *i.e.* the equilibrium mixture (as was to be expected from earlier investigations on monosubstituted bullvalenes[3,34]) consists mainly of the isomers O_b–O_b, O_b–O_c, O_c–O_c in which the two halves of the molecule are joined *via* two olefinic C atoms.

In all the monosubstituted bullvalenes studied so far (see Table 2), with the exception of fluorobullvalene *(56)*, the substituent preferentially occupies an olefinic position (O_c and/or O_b). The low-temperature spectrum of *(56)* (Fig. 4) shows that an isomer with the substituent in an aliphatic position (B or C; see Fig. 2) predominates in the equilibrium mixture, since the ratio of olefinic to aliphatic bullvalenyl protons is 6:3.

The olefinic proton signal appears as a doublet at $\tau = 4.11$ in the low-temperature spectrum. At 20 MHz, this low-temperature resonance signal has the same habit, with no change in the splitting. Thus the doublet

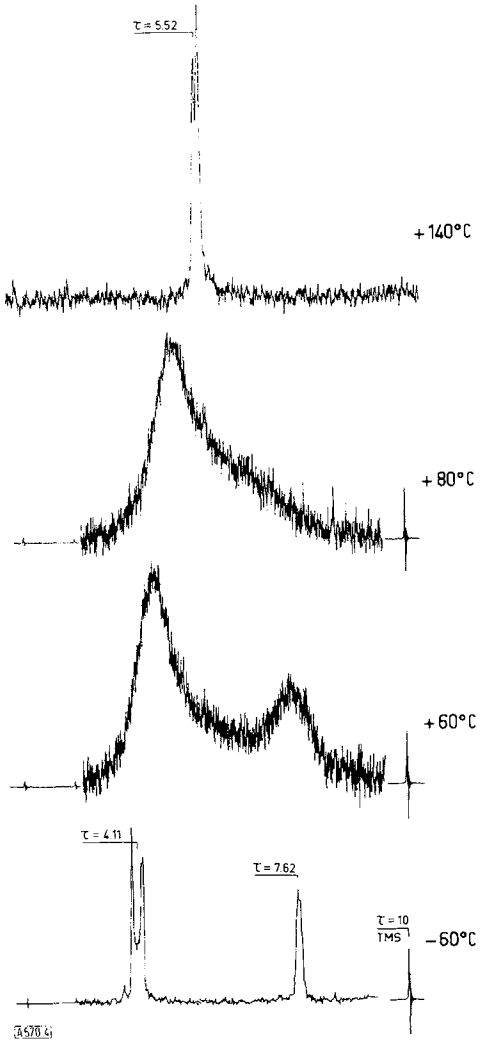


Fig. 4. ^{1}H—NMR spectra of fluorobullvalene *(56)* in $CDCl_3$. (Internal standard: tetramethylsilane, $\tau = 10$.)

is due to spin-spin coupling between the olefinic protons and the fluorine nucleus in the B position (see Fig. 2). The chemical shifts of the O_b and O_c protons and the coupling constants between these protons and the fluorine nucleus ($J_{FHO_b} \approx J_{FHO_c} \approx$ 14 Hz) are almost identical. The simple symmetrical signal of the aliphatic protons can again be explained only if the fluorine is in the B position. The high-temperature spectrum (+140 °C) consists of a doublet centered at $\tau = 5.52$. All the protons are now NMR-spectroscopically equivalent and coupled with the fluorine nucleus (mean value of the coupling constants $J_{HF} \approx 6$ Hz).

Figure 5 shows the ^{19}F—NMR spectra of *(56)* at −53 and 40 °C. At −53 °C, the spectrum contains a pseudoheptet centered at $\delta = -12.26$ (internal standard: C_6F_6). The multiplet loses its fine structure when the temperature is raised, and the spectrum also shows line broadening and a downfield shift.

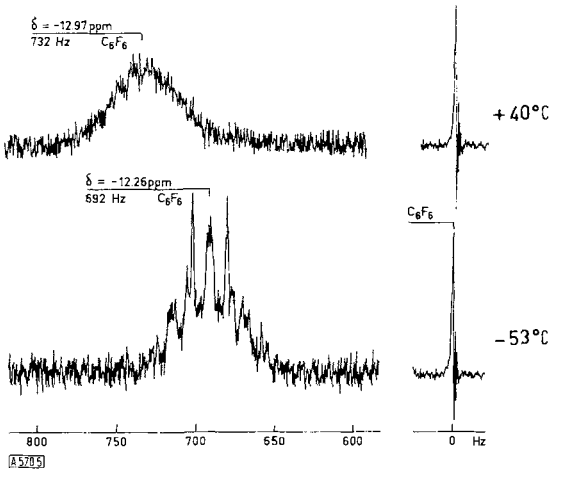


Fig. 5. ^{19}F—NMR spectra of fluorobullvalene *(56)* in $CDCl_3$. (At 56.4 Mc/s; internal standard: C_6F_6).

It is intended [37] to carry out a quantitative calculation of the ^1H and ^{19}F nuclear resonance spectra of fluorobullvalene *(56)*, which should contribute toward a deeper understanding of the dynamic equilibria.

Some important NMR-spectroscopic results for substituted bullvalenes are listed in Table 2. The second column shows the chemical shifts (τ scale) of the singlet observed for the bullvalenyl protons, and the third column gives the corresponding half-widths. All substituted bullvalenes exhibit greater half-widths than bullvalene itself. It may therefore be concluded that, on average, the bonds in substituted bullvalenes fluctuate more slowly than in bullvalene itself. It can be seen from the fourth column that, as expected, the O isomers are generally preferred [3, 34], except in fluorobullvalene, in which the B isomer is surprisingly found to have a lower energy than any of the other three.

c) Disubstituted Bullvalenes

Table 2 contains data for three disubstituted bullvalenes. For a disubstituted bullvalene with two identical substituents, there are twelve possible positional isomers (three of which correspond to pairs of antipodes) (cf. Fig. 6) and 27 isomerization processes. The twelve positional isomers can, in principle, be thermally interconverted under relatively mild conditions. This dynamism is peculiar to molecules having the bullvalene skeleton.

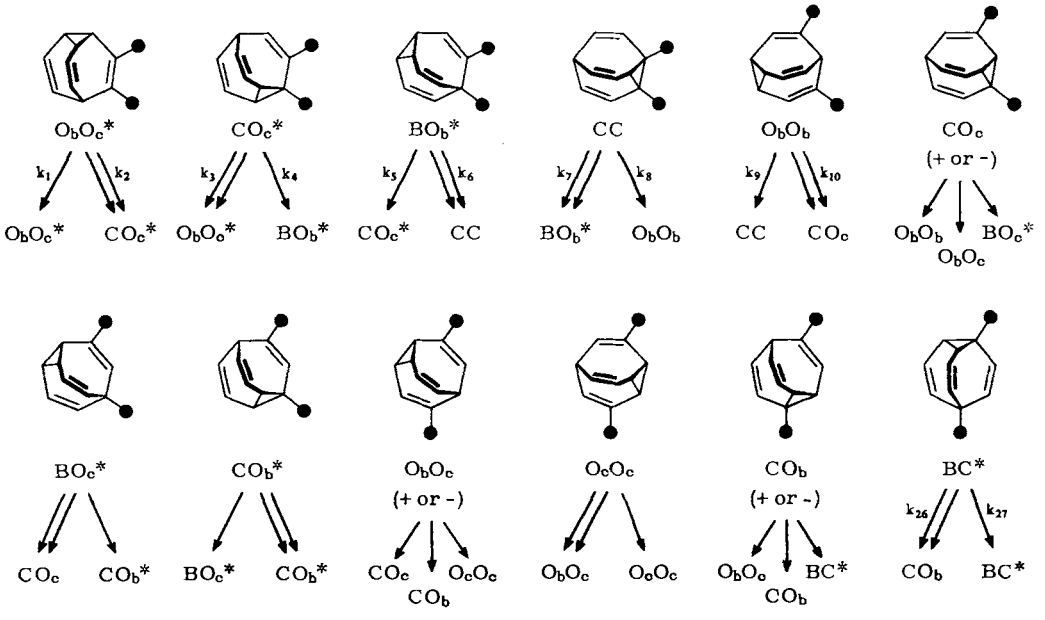


Fig. 6. Positional isomerism of disubstituted bullvalenes [38].

Table 2. ^1H—NMR-spectroscopic data for mono- and disubstituted bullvalenes (cf. Fig. 2 and 6).

Substituent R		τ at 80 °C	Δν [Hz] at 80 °C	Preferred isomer [38]
H	*(2)*	5.78	2.8	--
F	*(56)*	5.52 (140 °C)	83	B
Cl	*(46)*	5.76	7.4	O
Br	*(47)*	5.73	7.4	O
I	*(53)*	5.73	7.2	O
C_6H_5 [39]		5.75	6.0	O_b
$C_{10}H_9$	*(55)*	5.80	7.0	O
CO_2H	*(54)*	5.44	12.6	O
CO_2CH_3 [36]		5.48	9.6	O_b
CH_3	*(51)*	5.95	5.4	O
$OC(CH_3)_3$	*(49)*	5.97	19.1	O_b and O_c
$OCH(CH_3)_2$	*(49)*	6.00	41.0	O_b
OCH_2CH_3	*(49)*	6.00	55.0	O_b
OCH_3	*(49)*	6.02	72.0	O_b
2 Br	*(58)*	5.69	35	O_bO_c and O_cO_c
2 $OC(CH_3)_3$	*(59)*	6.08	97	O_bO_c and O_cO_c
2 CO_2CH_3	*(15)*	5.25	24	O_bO_b

Dibromo- *(58)* and bis(t-butoxy)bullvalene *(59)* were synthesized and studied by our research group [40], and bis(methoxycarbonyl)bullvalene *(15)* by *Vogel* [13]. The bromination of *(47)* yields a tribromide whose NMR spectrum agrees with the structure *(57)*. Treatment of *(57)* with potassium t-butoxide in t-butanol/benzene leads to elimination of HBr and formation

[37] *J. F. M. Oth* and *J.-M. Gilles*.

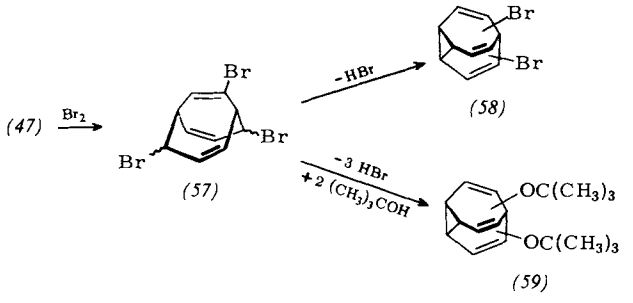
[38] The meanings of the abbreviations are as follows: C, O_c, O_b, and B as in [35]; the asterisk "*" denotes structures in which both substituents are situated on the same arm of the bullvalene skeleton. (An arm is a chain of bridgehead, olefinic, olefinic and cyclopropane carbon atoms.)

[39] *G. Schröder*, Angew. Chem. *77*, 682 (1965); Angew. Chem. internat. Edit. *4*, 695 (1965).

[40] *J. F. M. Oth, R. Merényi, G. Engel*, and *G. Schröder*, Tetrahedron Letters *1966*, 3377.

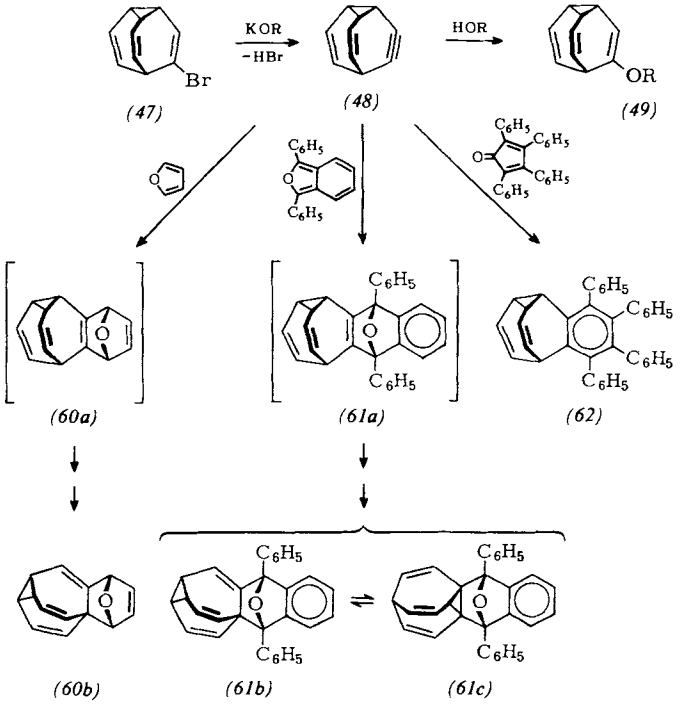
of the dibromide *(58)*, whereas dry potassium t-butoxide in benzene gives *(59)*.

As can be seen from Table 2, each of the three disubstituted bullvalenes gives a singlet (the half-widths being different) for the eight bullvalenyl protons at high temperatures. O,O-Isomers predominate in the equilibrium mixture.



d) Fused Bullvalenes, Benzobullvalenes [36,41]

Bromobullvalene *(47)* and potassium alkoxides react (preferably in dimethyl sulfoxide) to form alkoxybullvalenes *(49)* in good yields [34]. Extensive investigation of the preparation and behavior of 1,2-dehydrobenzene [42] and other cyclic dehydro compounds [43] suggest that these reactions should be formulated as proceeding by an elimination-addition mechanism. The decisive intermediate is 3,4-didehydrobullvalene *(48)* [44]. It is to be expected that *(48)* behaves as a reactive dienophile and reacts in the presence of dienes to form the corresponding adducts (see Scheme 2).

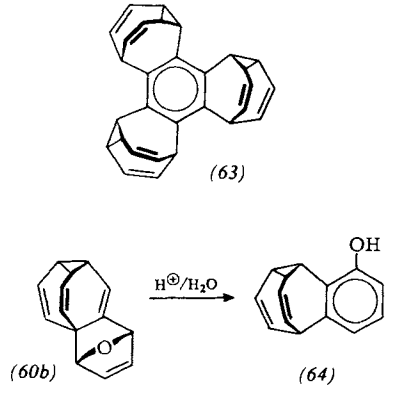


Scheme 2. Reactions of 3,4-didehydrobullvalene.

When the reaction of *(47)* with KOR is carried out in furan, the products include not only *(49)*, but also the furan adduct *(60)* (16 %) and small quantities of trimeric didehydrobullvalene *(63)* [36]. When the reaction of *(47)* with bases is carried out in benzene with the addition of 2,5-diphenyl-3,4-benzofuran, or in dioxane with the addition of tetracyclone, the adducts *(61)* and *(62)* can be isolated in yields of 76 % and 46 % respectively.

The evidence for the structures *(60)* to *(62)* is based particularly on the temperature-dependent NMR spectra. It is clear from these spectra that the adducts of *(48)* and the two furans do not have the structures *(60a)* and *(61a)* expected from a Diels-Alder reaction. This seems surprising at first sight, but can be explained as follows. The rapid bond shifts in the bullvalene skeleton allow the molecules to "collapse" into the structures having the lowest energy, *i.e.* into *(60b)* and into *(61b)* and *(61c)* [41]. The strain (Pitzer and/or Baeyer strain) in *(60b)* and in *(61b)* and *(61c)* is obviously less than in the corresponding isomers *(60a)* and *(61a)*.

In the light of *Wittig*'s work on the behavior of cyclohexyne [45] and 1,2-cyclohexadiene [46], we regard the formation of *(63)* as further evidence of the intermediate formation of *(48)*.



Hydrolysis of the furan adduct *(60b)* leads to smooth rearrangement with formation of 6-hydroxytetracyclo[6.3.3.$0^{2,7}0^{9,14}$]tetradeca-2(7),3,5,10,12-pentaene *(64)*.

α) NMR-Spectroscopic Behavior of Fused Bullvalenes [41]

The valence isomerizations in fused bullvalenes *(60)* and *(61)* are treated like those in disubstituted bullvalenes (cf. Fig. 6). Owing to ring strain, however, all

[41] *G. Schröder, H. Röttele, J. F. M. Oth*, and *R. Merényi*, Chem. Ber., in press; *J. F. M. Oth, R. Merényi, H. Röttele*, and *G. Schröder, ibid.*, in press.

[42] See, *e.g.*, *G. Wittig*, Angew. Chem. *77*, 752 (1965); Angew. Chem. internat. Edit. *4*, 731 (1965).

[43] For the detection of a dehydrocycloheptatriene derivative, see *W. Tochtermann, K. Oppenländer*, and *U. Walter*, Chem. Ber. *97*, 1318 (1964).

[44] The systematic name for bullvalene *(2)* is tricyclo[3.3.2.$0^{2,8}$]-deca-3,6,9-triene, corresponding to the numbering given on p. 414, and not tricyclo[3.3.2.$0^{4,6}$]deca-2,7,9-triene [2, 3]. We are grateful to Dr. *R. Cruse*, Freiburg, for pointing this out.

[45] *G. Wittig* and *U. Mayer*, Chem. Ber. *96*, 342 (1963).

[46] *G. Wittig* and *P. Fritze*, Angew. Chem. *78*, 905 (1966); Angew. Chem. internat. Edit. *5*, 846 (1966).

the isomers in Figure 6 except the first four must be ruled out. The two substituted carbon atoms are always *ortho* to each other, since k_8 (Fig. 6) is practically zero. The relatively complex temperature-dependent NMR spectra of *(60)* can be best explained by the valence isomerizations $BO_b^* \rightleftharpoons CC \rightleftharpoons BO_b^*$ as shown in Fig. 7, provided that the percentage of CC is assumed to be small [41].

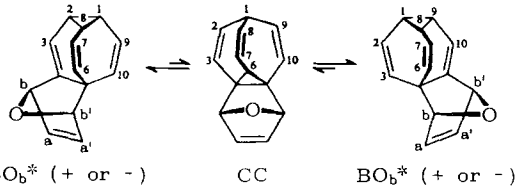


Fig. 7. Valence isomerizations in the 3,4-didehydrobullvalene-furan adduct *(60)*.

The adduct *(61)* in solution is in principle described by the same equilibria; the percentage of the two BO_b^* isomers is now about 54%, and that of the CC isomer is about 46% [41].

Since the valence isomerizations in the fused bullvalenes *(60)* and *(61)* are very limited, the eight bullvalenyl protons no longer give one singlet in the high-temperature NMR spectrum.

To illustrate this, let us consider the temperature-dependent NMR spectra of the furan adduct *(60)*

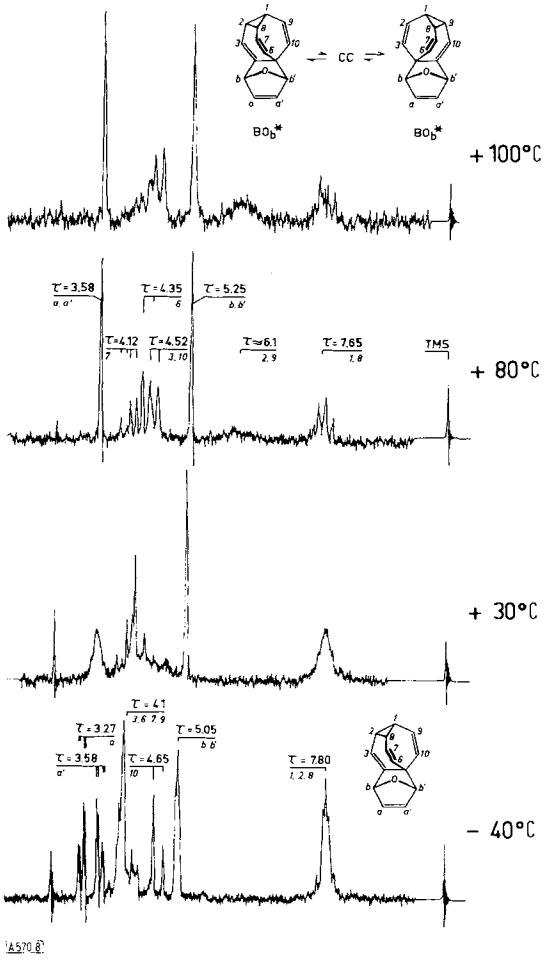


Fig. 8. ^1H—NMR spectra of the 3,4-didehydrobullvalene-furan adduct *(60)*.

(Fig. 8) in more detail. The low-temperature spectrum (−40 °C) shows three aliphatic and five olefinic bullvalenyl protons, the three aliphatic protons giving the signal centered at $\tau = 7.80$ and the five olefinic protons the signals between $\tau = 3.7$ and $\tau = 4.8$. The "non-bullvalenyl" olefinic protons aa′ give an AB quartet at $\tau_a = 3.27$ and $\tau_{a'} = 3.58$ ($J_{aa'} = 5.8$ Hz). Each of these signals is split into a doublet as a result of coupling with the protons b and b′ ($J_{ab} = 1.5$ Hz). The bridgehead protons bb′ appear as a pseudo-triplet at $\tau = 5.05$.

The ratio of three aliphatic to five olefinic protons and the habit of the resonance signals of the protons aa′ and bb′ show unmistakably that only the isomers BO_b^* and CO_c^* must predominate in the equilibrium mixture of *(60)*. However, the CO_c^* isomer can be ruled out, since it is not in agreement either with the changes in the NMR spectrum when the temperature is raised or with the high-temperature spectrum [41]. BO_b^* is the predominant isomer in the adduct *(60)*.

The bullvalenyl proton signals in the low-temperature spectrum of *(60)* are assigned as follows: The doublet centered at $\tau = 4.65$ represents proton no. 10 [47] ($J_{9,10} = 11$ Hz), protons 3, 6, 7, and 9 give the group of signals centered at about $\tau = 4.1$, and the aliphatic bullvalenyl protons 1, 2, and 8 give the signal at $\tau = 7.80$.

The temperature-dependence of the NMR spectra of *(60)* and the habit of the high-temperature spectrum can be best explained by the valence isomerizations $BO_b^* \rightleftharpoons CC \rightleftharpoons BO_b^*$ (see Fig. 7) (the two BO_b^* isomere are related as mirror images), provided that the percentage of CC is assumed to be small. It is then understandable why the resonance signal of the a and a′ protons at low temperatures represents an AB system and why the a and a′ protons are NMR-spectroscopically equivalent at higher temperatures (one resonance signal at $\tau = 3.58$). Similar considerations apply to the resonance signals of the b and b′ protons. The shape of the signals of the a, a′, b, and b′ protons corresponds to the calculated spectrum of an A_2X_2 system with $J_{AX} = J_{ab} = 1.5$ Hz, $J_{AA} = J_{aa'} = 5.8$ Hz, and $J_{AX'} = J_{XX'} = J_{ab'} = J_{bb'} = 0$ Hz. The presence of a band centered at $\tau = 6.1$ and having a relative intensity of 2 in the spectrum at +80 °C and +100 °C can also be explained on the basis of the same valence isomerization. This τ value approximately corresponds to the average of the chemical shifts of protons 2 and 9 ($\tau_{calc.} = 5.95$). It is also clear that protons 3 and 10 give a doublet centered at $\tau = 4.52$ ($J_{2,3} = J_{9,10} = 9$ Hz) and having a relative intensity of 2.

The signals of protons 7 ($\tau = 4.12$), 6 ($\tau = 4.35$) and 1 and 8 ($\tau = 7.65$) should be independent of temperature. The small changes in their chemical shifts can be explained by a temperature-dependent solvent effect. The percentage of the CC isomers in the equilibrium is certainly very small (< 5%), since a distinct shift of the signals due to protons 6 and 8 would otherwise be observed in the high-temperature spectrum. The low concentration of the CC isomer is also confirmed by the absence of two sharp bands for the a and a′ and the b and b′ protons (a and a′ as well as b and b′ are identical in the CC isomer) in the low-temperature spectrum.

Furthermore, the CC isomer can occur in two configurations, with either the oxygen atom or the double bond of the substituted dihydrofuran system situated above the cyclopropane ring of the bullvalene skeleton. The two CC isomers are described as CC_{endo} and CC_{exo}, corresponding to the position of the oxygen atom relative to the cyclopropane ring. Only the CC_{endo} isomer participates in the NMR-observed exchange process; this can be explained by steric effects. Valence iso-

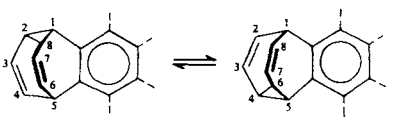
[47] Numbering of the left-hand formula in Fig. 7.

merizations involving the CO_c^* and $O_bO_c^*$ isomers can be ruled out. If these isomers were involved, much stronger mixing of the bullvalenyl proton signals should occur.

β) NMR-Spectroscopic Behavior of Benzobullvalenes

In the benzobullvalenes, one double bond of the bullvalene is blocked by incorporation into a benzene ring. Thus we have a homotropilidene system bridged by a benzene residue. The temperature-dependence of the NMR spectra of the benzobullvalenes can only be explained by a valence isomerization involving two $O_bO_c^*$ isomers.

The spectra of *(62)*, *(63)*, and *(64)* at +70 °C are in fact similar to the high-temperature spectra of other bridged homotropilidene systems [3]. An important signal in this case, which is centered at $\tau = 6.1$ ppm, results from the averaging of the chemical shifts of two cyclopropyl (nos. 2 and 8) and two olefinic protons (nos. 4 and 6) (Fig. 9, left-hand formula).



$O_bO_c^*$ $O_bO_c^*$

Fig. 9. Valence isomerizations in benzobullvalene.

One of us (G. S.) is grateful to the Badische Anilin- & Soda-Fabrik AG., the Deutsche Forschungsgemeinschaft, and the Fonds der chemischen Industrie for their generous support of his investigations.

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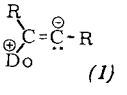
Additions to the Activated CC Triple Bond

BY E. WINTERFELDT [*]

The possibilities of additions to the activated CC triple bond are discussed with the aid of a number of examples. The additions of donors that contain no active hydrogen are generally initiated via a dipolar primary complex, which can undergo stabilization by rearrangement, cyclization, or addition reactions. Preparative aspects of these reactions are also discussed. They offer routes for the preparation of heterocycles, particularly pyrrole and thiophene derivatives.

I. Introduction

The high reactivity of the CC triple bond toward nucleophilic reagents is of great significance in many preparatively interesting reactions and also in important industrial processes. This reactivity is even greater in conjugated polyynes. A survey of addition reactions of these compounds has already been published [1]. Since reviews have also appeared concerning their 1,3-dipolar additions [2] and on their diene reactions [3], the present article will deal only with nucleophilic additions to CC triple bonds activated by acceptor groups. Triple bonds polarized by functional groups of this type are very reactive, and are attacked, often surprisingly readily, by many nucleophiles. The adducts are obtained directly, when possible, and generally in very high yields. Otherwise the primary complex of the general type *(1)* is stabilized by rearrangement or cyclization, or by further reaction with a second mole of the acetylene derivative. This offers a simple route to a wide range of heterocyclic compounds.



(1)

R = CO_2R'; CN; CF_3; SO_2R'

II. Additions of Compounds containing Mobile Hydrogen

1. Addition of Alcohols

The addition of alcohols and phenols can be catalysed both by alkoxides [4] and by tertiary amines [5]; the addition is predominantly *trans* [4,6], and in the case of dimethyl acetylenedicarboxylate it leads to enol

[*] Priv.-Doz. E. Winterfeldt
Organisch-Chemisches Institut der Technischen Universität
Hardenbergstr. 34
1 Berlin 12 (Germany)

[1] *F. Bohlmann*, Angew. Chem. *69*, 82 (1957).

[2] *R. Huisgen*, Angew. Chem. *75*, 604, 742 (1963); Angew. Chem. internat. Edit. *2*, 565, 633 (1963).

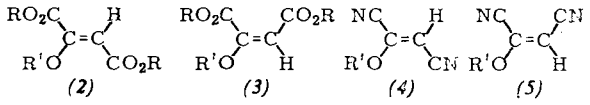
[3] *J. Sauer*, Angew. Chem. *78*, 233 (1966); Angew. Chem. internat. Edit. *5*, 211 (1966).

[4] *S. I. Miller*, J. Amer. chem. Soc. *78*, 6091 (1956).

[5] *E. Winterfeldt*, Chem. Ber. *97*, 1952 (1964).

[6] *E. Winterfeldt*, Chem. Ber. *99*, 450 (1966).

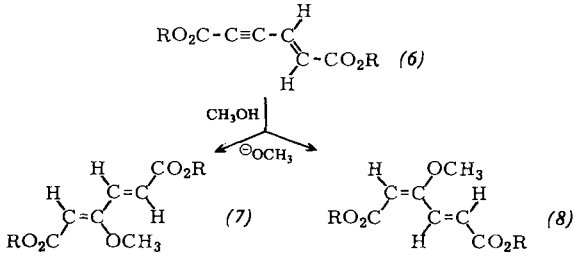
ethers of the type *(2)*. Thermal additions (≈ 180 °C), on the other hand, lead mainly to the *cis* derivative *(3)*. Similar results are obtained in additions to methyl



(2) *(3)* *(4)* *(5)*

propiolate. Dinitriles of the type *(5)* predominate in the products obtained from dicyanoacetylene and the corresponding primary or secondary alcohols even at room temperature [7]. Whereas t-butyl alcohol does not add to acetylenedicarboxylic acid, even under drastic conditions, the addition to dicyanoacetylene proceeds at room temperature in the presence of weak bases, *trans* addition to form the product *(4)* being predominant. The configurations in the diesters *(2)* and *(3)* can be established readily by NMR spectroscopy, since products of the type *(2)* show a distinctly negatively shielded proton at $\tau = 3.9$, while products of the type *(3)* give a signal at $\tau = 4.8-4.9$ [6]. In the nitriles, as measurements on *cis,trans*-isomeric compounds have shown [8], the resonance of the proton in compounds having the configuration *(4)* is shifted by only 0.1–0.2 ppm towards lower fields. Since this difference is in full agreement with the values found for other compounds, an assignment is again possible in this way.

These results suggest that the *trans*-addition product should predominate in the catalytic addition of alcohols; however, the sodium methoxide-catalysed addition of methanol to the diester *(6)* shows that this rule is not generally valid.

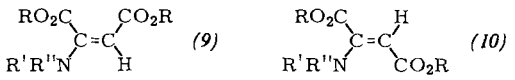


(6) *(7)* *(8)*

In this case the kinetically controlled reaction leads to equal quantities of the *cis,trans*-isomeric enol ethers *(7)* and *(8)* [7]. An unambiguous assignment of the configurations is again possible on the basis of NMR measurements.

2. Addition of Amines

The addition of primary and secondary amines proceeds extremely rapidly and smoothly with formation of enamines of the types *(9)* and *(10)* (R′ = H, R″ = alkyl or aryl, or R′ and R″ = alkyl or aryl).



(9) *(10)*

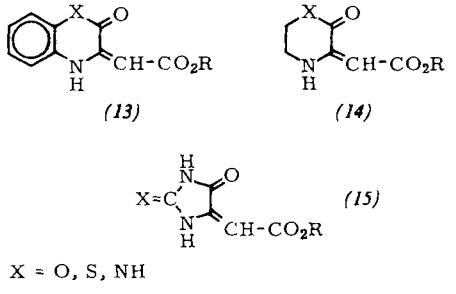
This *cis* addition plays a dominant role in these reactions [6,9,9a]. Though the proportion of the *cis* configuration is already very high in the case of primary amines, it is even higher for secondary amines. However, it is found that the steric course depends on many factors, including the constitution of the acetylene compound and of the amine, as well as on the manner in which the two reactants are brought together [7]. When the amine is added very slowly to the solution of the acetylene compound, the addition can proceed exclusively in the *cis* direction. This can be demonstrated for the dinitrile *(11)*, owing to the stability of the reaction products. Whereas a mixture of the dinitriles *(11)* and *(12)* is formed when the reactants are brought together rapidly, slow addition with cooling leads exclusively to the *cis*-addition product *(11)*. With the diester, it must be assumed that during slow addition, the very small quantities of *trans* adduct that are observed on direct combination in an NMR tube at low temperatures [9,9a,16] undergo very rapid isomerization.

The configuration can again be determined from the NMR spectrum; however, the IR spectra were also used for the adducts with primary amines, since the configuration *(10)* can be recognized by the presence of a hydrogen bond. The results of the NMR analysis of adducts with secondary amines are confirmed by dipole-moment measurements.



(11) *(12)*

o-Substituted aniline derivatives add readily to form products of the type *(13)* [10].



(13) *(14)* *(15)*

X = O, S, NH

This principle is generally applicable to the synthesis of six-membered heterocyclic compounds *(14)* [11]. Substituted imidazolidones *(15)* are obtained in this way by the use of guanidines as bifunctional components [12]. When the reaction with aniline is carried out in the presence of Cu(I), a mixture of *(16)* and *(17)* is obtained, depending on the conditions [13].

The addition of phenylhydroxylamine to dimethyl acetylenedicarboxylate follows a rather unusual course [14]. It proceeds *via* an intermediate *(18)* which,

[7] *E. Winterfeldt, W. Krohn,* and *H. Preuss,* Chem. Ber. *99,* 2572 (1966).

[8] *A. N. Kurtz, W. E. Billups, R. B. Greenlee, H. F. Hamil,* and *W. T. Pace,* J. org. Chemistry *30,* 3141 (1965).

[9] *R. Huisgen, K. Herbig, A. Siegl,* and *H. Huber,* Chem. Ber. *99,* 2526 (1966).

[9a] *E. W. Truce* and *D. G. Brady,* J. org. Chemistry *31,* 3543 (1966).

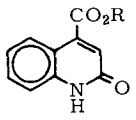
[10] *Y. Iwanami,* J. chem. Soc. Japan, pure Chem. Sect. (Nippon Kagaku Zassi) *82,* 634 (1964).

[11] *Y. Iwanami et al.,* Bull. Soc. Chem. Japan *37,* 1740, 1745 (1964).

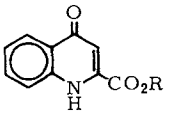
[12] *Y. Iwanami, H. Saaki,* and *H. Sakata,* J. chem. Soc. Japan, pure Chem. Sect. (Nippon Kagaku Zassi) *85,* 704 (1964).

[13] *J. Reisch,* Angew. Chem. *75,* 1203 (1963); Angew. Chem. internat. Edit. *2,* 741 (1963).

[14] *C. Agosta,* J. org. Chemistry *26,* 1724 (1961).

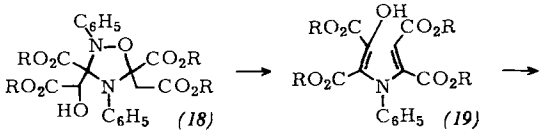


(16)

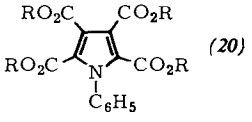


(17)

though unstable, can be isolated in the crystalline form; the stable end product obtained after two days at 35 °C is the 2:1 adduct *(19)*, the structure of which is confirmed by independent synthesis and conversion into the pyrrole derivative *(20)*.



(18) (19)

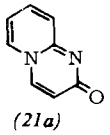


(20)

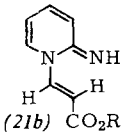
In the reaction with 2-aminopyridine, the ring nitrogen takes part in the addition, and the two products *(21a)* and *(21b)* [15] are obtained.

In connection with investigations on the mechanism of the addition of amines, *Huisgen* and *Herbig* examined the stabilities of *(9)* and *(10)*. The "maleic acid derivatives" of the type *(9)* are more stable than the "fumaric acid derivatives" of the type *(10)*; the isomerization is catalysed by protons [16]. A thorough investigation of the stabilities of the configurations was also carried out by *Reimlinger*, who demonstrated the *cis* addition of pyrazole to dimethyl acetylenedicarboxylate [17].

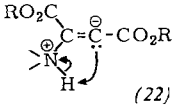
It has been suggested [6] that the direct, uncatalysed addition of amines (and alcohols) may proceed by an intramolecular cyclic proton shift from the primary complex *(22)*, and this was confirmed in a recent kinetic study by *Huisgen et al.* [16a] on the addition of ethylenimine to dimethyl acetylenedicarboxylate.



(21a)



(21b)



(22)

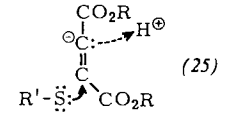
3. Addition of Thiols

In a series of fundamental investigations, *Truce* [18] established the *trans*-addition mechanism for the catalysed addition of thiols. As in the addition of alcohols and amines, two configurations [*(23)* and *(24)*] are to be expected.



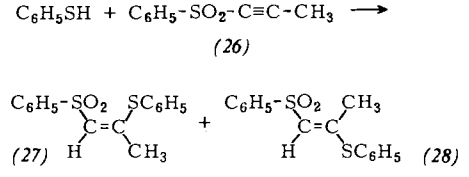
(23) (24)

Truce was able to prove that the addition products have the "fumaric acid" configuration *(24)*, and he formulated the reaction as proceeding *via* the complex *(25)*, though it is not certain whether the alkylthioalkenyl ion exists as such for a definite period, or whether the proton capture takes place simultaneously with the addition of the thiolate ion.



(25)

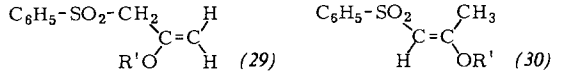
The addition of thiols such as thiophenol to phenyl 1-propynyl sulfone *(26)* has also been studied [19, 19a], and in agreement with *Truce*'s results, *trans* addition to form *(27)* is again observed.



(26) (27) (28)

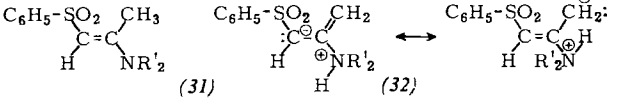
Products such as *(27)* can also be isomerized into the thermodynamically more stable compounds *(28)*. The reaction of sodium sulfinates R–SO–ONa with *(26)* also leads to the *trans*-addition product.

The additions of phenyl propadienyl sulfone, phenyl 1-propynyl sulfone, and phenyl 2-propynyl sulfone all give the same mixture, *i.e.* the compounds *(29)* and *(30)*.



(29) (30)

(29) is the product of the kinetically controlled reaction, and subsequently isomerizes to form *(30)*. Thus in this case isomerization is faster than addition, and the thermodynamically stable end product is *(30)*. The addition of amine, irrespective of the solvent, also leads almost exclusively to the *cis* adduct *(31)*, which is given by all three isomers as the only reaction product. However, *Truce* recently showed by NMR measurements at −25 °C that, because of the stabilization of the transition state, this reaction also proceeds as a pure *trans* addition, but that very rapid isomerization then ensues to give the thermodynamically stable product with the *trans* arrangement of the donor and acceptor groups [9a]. A considerable solvent-dependence is found, a very low reaction rate being recorded (as expected) in benzene, and a very much higher rate in methanol.



(31) (32)

Labeling with deuterium shows that the proton probably migrates after the addition of the amine [to form the primary betaine *(32)*]. With the primary amine benzylamine, the product is again a mixture of the *cis* and *trans* adducts, in which the *trans* adduct *(33)* predominates because it is stabilized by hydrogen bonding [19a].

[15] *I. J. Pachter*, J. org. Chemistry *26*, 4157 (1961).

[16] *K. Kerbig, R. Huisgen*, and *H. Huber*, Chem. Ber. *99*, 2546 (1966).

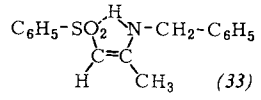
[16a] *R. Huisgen*, personal communication.

[17] *H. Reimlinger* and *C. H. Moussebois*, Chem. Ber. *98*, 1805 (1965).

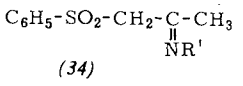
[18] *W. E. Truce, G. H. Klein*, and *R. B. Kruse*, J. Amer. chem. Soc. *83*, 4636 (1961).

[19] *J. M. Stirling*, J. chem. Soc. (London) *1964*, 5856.

[19a] *C. H. McMullen* and *C. J. M. Stirling*, J. chem. Soc. (London) *B 1966*, 1217.



(33)



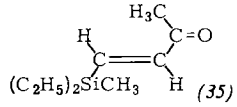
(34)

Additions of semicarbazide and phenylhydrazine yield the normal phenylsulfonylacetone derivative *(34)*.

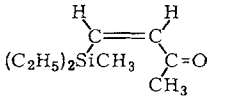
4. Additions of Substances of the Type H-X

Kinetic studies on the addition of hydrobromic [20] and hydriodic [21] acids have also been recently carried out. It was confirmed that the adducts are in the "fumaric acid configuration"; the reaction is interpreted as nucleophilic addition.

The addition of trialkylsilanes to butynone [22] yields a mixture of the *cis,trans*-isomeric addition products *(35)* and *(36)*.

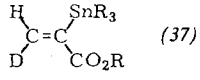


(35)



(36)

A kinetic study of the addition of deuterium trialkylstannates ($DSn(R)_3$) showed that the reaction with methyl propiolate proceeds by *trans* addition to give the compound *(37)*, and that the addition of the hydride ion is the rate-determining step [23]. Similar results were obtained in a study of the hydroplumbation of the activated CC triple bond [24].

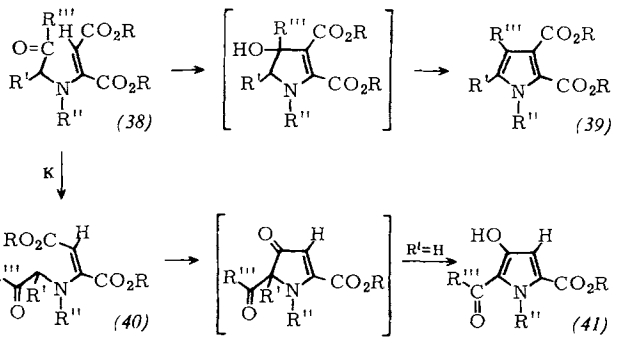


(37)

The addition of phosphines will be discussed in connection with the phosphorus derivatives.

5. Preparative Uses

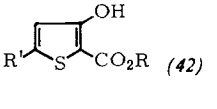
The main preparative application is the preparation of pyrroles and thiophenes by the addition of amines and thiols. Thus *Hendrickson* [25] described a general and smooth synthesis of pyrroles (Scheme 1), which was extended by *Pandit* and *Huisman* to polycyclic compounds [26].



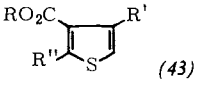
(38) (39) (40) (41)

After isomerization of *(38)* to *(40)*, however, the latter undergoes Dieckmann cyclization to form the hydroxypyrrole *(41)* [27].

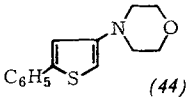
Similar reactions can be used for the preparation of thiophenes. *Fiesselmann* and *Schiprak* reported the formation of esters *(42)* of hydroxythiophenecarboxylic acids by addition of methyl thioglycolates to dimethyl acetylenedicarboxylate [28]. This method was then used by other authors for the synthesis of other thiophene derivatives of this type [29]. *Bohlmann* and *Bresinsky* [30] showed that, depending on the conditions, it is possible to obtain either the thiophene derivatives *(42)* or (by direct artack on the carbonyl group of the ketone) the derivatives *(43)*.



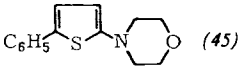
(42)



(43)



(44)



(45)

The combined action of morpholine and sulfur on alkynyl ketones also leads to thiophene compounds. Thus 4-phenylbutynone gives a mixture of the two morpholinothiophenes *(44)* and *(45)* [31].

III. Additions of Donors containing No Active Hydrogen

1. Addition of Aromatic Tertiary Amines

Diels and *Alder* showed many years ago that aromatic amines, *e.g.* pyridine, react smoothly with dimethyl acetylenedicarboxylate to form adducts [32].

However, the structure of the products [*(48)* is formed as the stable end product *via* an unstable primary

[20] *I. V. Smirnov-Zamkov* and *G. A. Piskovitina*, Ukrainskij chim. Ž. *30*, 1076 (1964); Chem. Abstr. *62*, 5160e (1965).

[21] *G. F. Dvorka* and *E. A. Shilov*, Kinetika i Katalyz *37*, 40 (1965); Chem. Abstr. *62*, 16009h (1965).

[22] *N. L. Masljakovskii* and *L. F. Celpanova*, Ž. obšč. Chim. *35*, 2009 (1965).

[23] *A. J. Leusink* and *J. W. Marsmann*, Recueil Trav. chim. Pays-Bas *84*, 1123 (1965).

[24] *A. J. Leusink* and *G. J. M. van der Kerk*, Recueil Trav. chim. Pays-Bas *84*, 1617 (1965).

[25] *J. B. Hendrickson*, *R. Rees*, and *J. F. Templeton*, J. Amer. chem. Soc. *86*, 107 (1964).

[26] *U. K. Pandit* and *H. O. Huisman*, Recueil Trav. chim. Pays-Bas *85*, 311 (1966).

[27] *E. Winterfeldt* and *H. J. Dillinger*, Chem. Ber. *99*, 1558 (1966).

[28] *H. Fieselmann* and *P. Schiprak*, Chem. Ber. *87*, 835, 841 (1954).

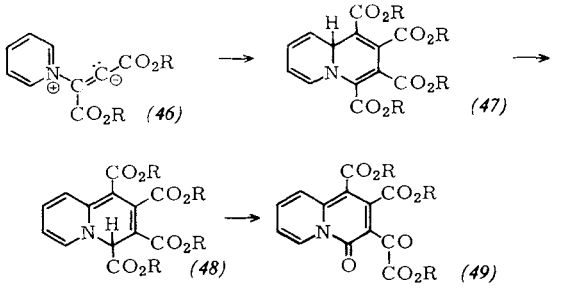
[29] *A. Courtin*, *E. Class*, and *H. Erlenmeyer*, Helv. chim. Acta *47*, 1748 (1964).

[30] *F. Bohlmann* and *E. Bresinsky*, Chem. Ber. *97*, 2109 (1964).

[31] *T. Bacchetti*, *A. Alemagna*, and *B. Danieli*, Tetrahedron Letters *1965*, 2001.

[32] *O. Diels* and *K. Alder*, Liebigs Ann. Chem. *498*, 16 (1932).

product having the structure *(47)*] was conclusively proved very much later [33]. The mode of formation of a by-product of this reaction ["Kashimoto compound" *(49)*] was also established recently [34].



(46) *(47)* *(48)* *(49)*

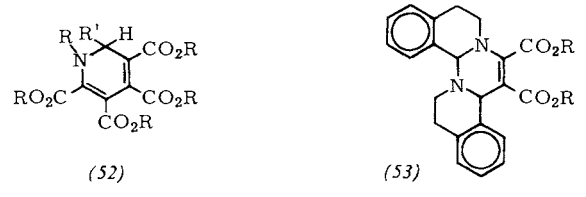
In connection with the mechanism of this reaction, apart from the work of *Jackmann et al.* [35], special mention should be made of the investigation of the interception of the enoxide ion in *(46)* with CO_2 by *Acheson* and *Plunkett* [36]. The products obtained are the *cis,trans*-isomeric betaines *(50)* and *(51)*.



(50) *(51)*

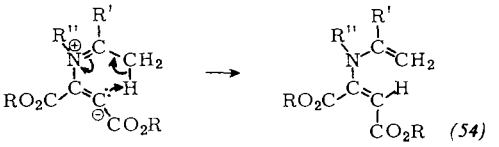
Pyridine and quinoline derivatives have also been used in this reaction [33]. An excellent survey of the spectral data for the resulting compounds has been published by *Acheson* [37].

Huisgen and *Herbig* have also used imines as donors, and have shown that the products *(52)* are formed [38]. The second addition step is classified by these authors as a 1,4-dipolar addition. In the presence of a suitable excess of the imine, the 1,4-dipole can also be intercepted by this component. Thus under these conditions dihydroisoquinoline gives the pentacyclic compound *(53)*.



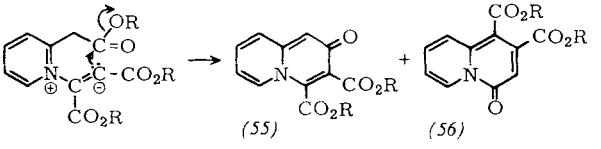
(52) *(53)*

In the reaction with ketimines (Schiff bases), the primary complex is stabilized by prototropy to form enamine derivatives of the type *(54)* if protons are available in the α position.



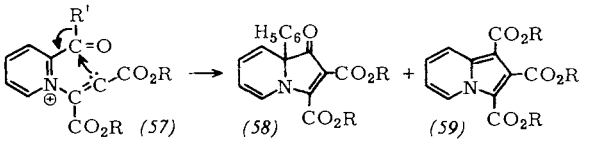
(54)

Attempts to stabilize the enoxide ion in the primary complex *(46)* by attack on the electrophilic center of a carbonyl group led, in the case of ethyl pyridylacetate, to the 2*H*- or 4*H*-quinolizones *(55)* or *(56)*, the main product in polar solvents being *(55)*, and in nonpolar solvents *(56)* [39].



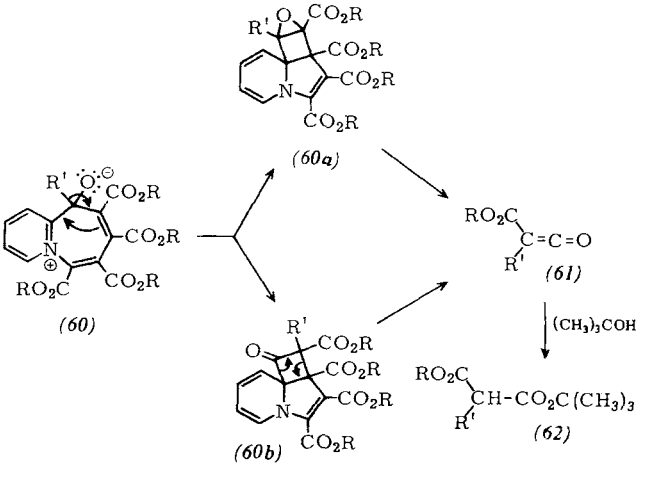
(55) *(56)*

If the carbonyl group is directly attached to the ring, this reaction, with R′ = C_6H_5, yields the rearrangement product *(58)* *via* *(57)*, but the main product in every case is the indolizinetricarboxylate *(59)* and is completely independent of the residue R′.



(57) *(58)* *(59)*

The formation of these substances is explained by primary addition to give the 2:1 complex *(60)*. The simultaneous formation of the ketene *(61)* can be deduced from the fact that the mono-t-butyl ester *(62)* is obtained when the reaction is carried out in t-butanol.



(60a) *(60)* *(61)* *(60b)* *(62)*

It was not possible to decide whether *(60a)* or *(60b)* occurs as the intermediate, though the route *via* *(60b)* seems more plausible.

The addition products with aromatic heterocycles can be used for the synthesis of cycloazines. Thus *Acheson* showed that the "2nd stable adduct" obtained by *Diels* and *Möller* [40] from dimethyl acetylenedicarboxylate and *trans*-stilbazole results from the

[33] For a review, see *R. M. Acheson*, Advances heterocyclic Chem. *1*, 125 (1963).

[34] *R. M. Acheson, D. M. Goddall*, and *D. A. Robinson*, J. chem. Soc. (London) *1965*, 2633.

[35] *L. M. Jackmann, A. W. Johnson*, and *J. C. Tebby*, J. chem. Soc. (London) *1960*, 1579.

[36] *R. M. Acheson* and *A. O. Plunkett*, J. chem. Soc. (London) *1964*, 2676.

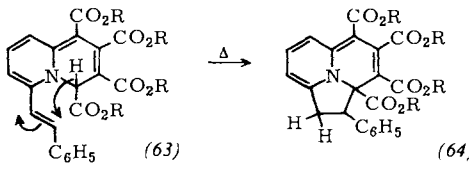
[37] *R. M. Acheson, R. S. Feinberg*, and *J. M. F. Gagan*, J. chem. Soc. (London) *1965*, 948.

[38] *R. Huisgen* and *K. Herbig*, Liebigs Ann. Chem. *688*, 98 (1965); *J. M. F. Gagan*, J. chem. Soc. (London) *C 1966*, 2221.

[39] *E. Winterfeldt*, Chem. Ber. *98*, 3537 (1965).

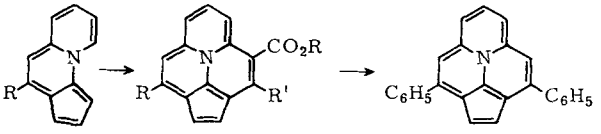
[40] *O. Diels* and *F. Möller*, Liebigs Ann. Chem. *516*, 45 (1935).

thermal isomerization of the "1st stable adduct" *(63)* and has the constitution *(64)* [41].



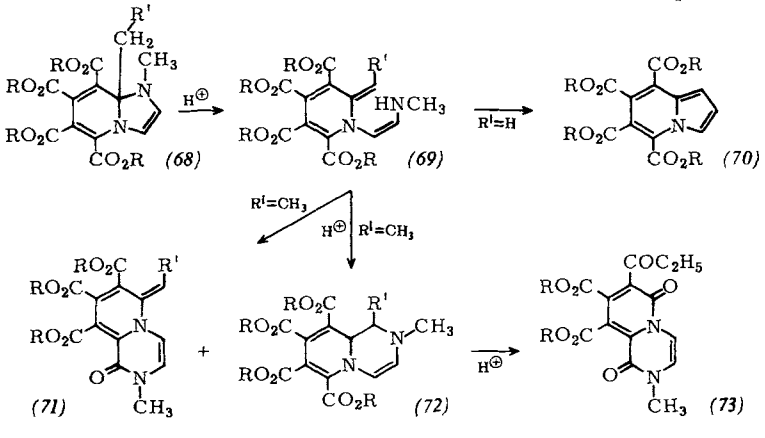
(63) *(64)*

Gibson and *Leaver* converted the quinolizine derivative *(65)* into the tetracyclic product *(66)* (R′ = CO_2CH_3, R = CH_3) by addition of dimethyl acetylenedicarboxylate. This interpretation is supported by the fact that with the phenyl compound *(65)* (R = C_6H_5) and methyl phenylpropiolate, subsequent decarboxylation gave a compound *(67)*, the symmetry of which is apparent from its NMR spectrum [42].



(65) *(66)* *(67)*

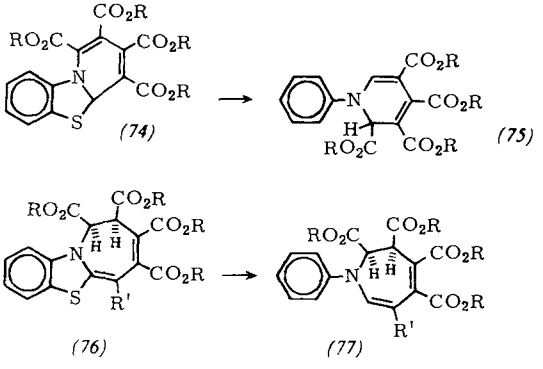
The reaction with imidazoles and thiazoles, which had also been considered earlier by *Diels* and *Alder* [45] proceeds fundamentally in accordance with the same reaction scheme [43,44]. This was confirmed by *Crabtree* and *Johnson*, who also described interesting secondary reactions [47]. Thus it is found that the adduct *(68)* with R′ = H is converted *via (69)* into the indolizine *(70)* by the action of acids. A similar primary adduct is obtained when R′ = CH_3; however, it does not lose methylamine on treatment with acids, but recyclizes to form the compounds *(71)* and *(72)*. Both products give *(73)* when heated with concentrated hydrochloric acid.



(68) *(69)* *(70)* *(71)* *(72)* *(73)*

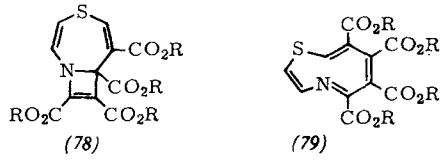
Thiazoles and oxazoles react similarly (for a survey of the spectral data see [46]).

The benzothiazole derivative *(74)* can be desulfurized with Raney nickel to give the dihydropyridine derivative *(75)*. 2-Alkyl derivatives of benzothiazole also add two moles of the ester to form the azepine derivatives *(76)*, which can be desulfurized with Raney nickel to give *(77)*.



(74) *(75)* *(76)* *(77)*

Similar results are also reported by a second research team, but it cannot be established whether the reactions of thiazole and its 2- and 4-methyl derivatives in dimethylformamide yield *(78)* or *(79)* [44].



(78) *(79)*

The simultaneous action of pyridine and CH acids on dimethyl acetylenedicarboxylate has also been studied in detail [47,48]. The first results were again reported by *Diels et al.* [49]; it was later found that the reaction with cyanoacetic ester leads to the blue salt *(81) via* the primary adduct *(80)*.

The primary adduct *(80)* can be protonated at room temperature to give *(82)*, with simultaneous hydration of the nitrile group. *(82)* cyclizes when heated to form *(83)*. The cyclopentadienone obtained by protonation of *(81)* is assigned a dimeric structure. The results obtained with malonodinitrile are completely analo-

[41] *R. M. Acheson* and *R. S. Feinberg*, Chem. Commun. *1965*, 342.

[42] *W. K. Gibson* and *D. Leaver*, Chem. Commun. *1965*, 11.

[43] *A. Crabtree* and *A. W. Johnson*, J. chem. Soc. (London) *1962*, 1510.

[44] *D. H. Reid et al.*, Tetrahedron Letters *1964*, 1797.

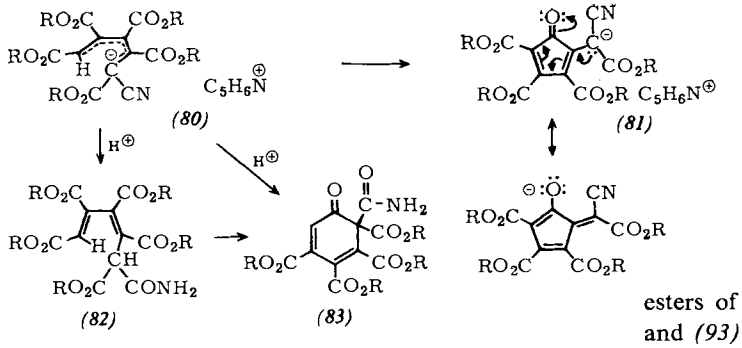
[45] *O. Diels* and *K. Alder*, Liebigs Ann. Chem. *498*, 1 (1932).

[46] *R. M. Acheson*, *M. W. Foxton*, and *O. R. Miller*, J. chem. Soc. (London) *1966*, 3200.

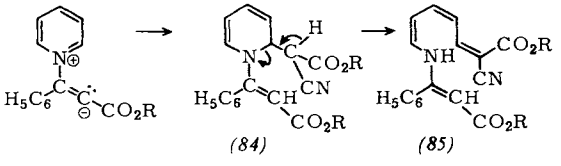
[47] *P. Bamfield*, *A. Crabtree*, and *A. W. Johnson*, J. chem. Soc. (London) *1965*, 4355.

[48] *E. Le Goff* and *R. B. La Count*, J. org. Chemistry *29*, 423 (1964).

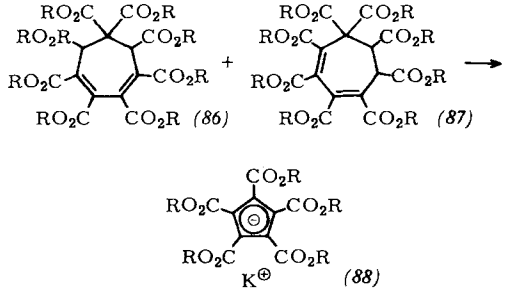
[49] *O. Diels*, Chem. Ber. *75*, 1452 (1942); *O. Diels* and *U. Kock*, Liebigs Ann. Chem. *556*, 38 (1944).



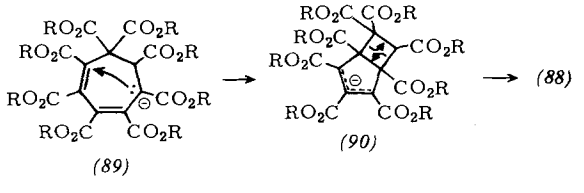
gous. An attempt to apply these reactions to methyl phenylpropiolate results in cleavage of the pyridine ring *via (84)*, with formation of *(85)*.



The reaction with diesters of malonic acid in the presence of pyridine leads to entirely different structures, *i.e.* to the cycloheptadienes *(86)* and *(87)*.

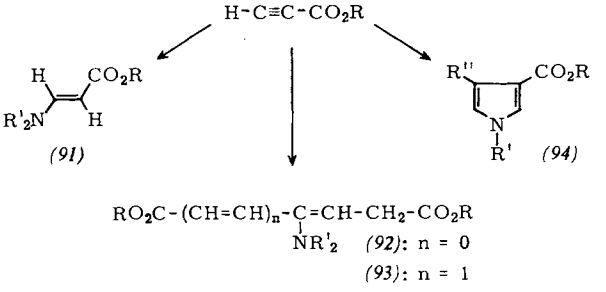


When heated with potassium acetate, these compounds lose the malonate component and form the potassium salt *(88)*. The acid of this salt is as strong as nitric acid. The formation of the anion is explained by deprotonation to form *(89)* followed by transannular Michael addition to give *(90)*, which is thought to undergo subsequent loss of the malonate component to form *(88)*.

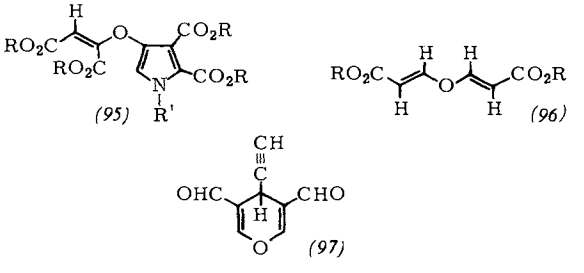


2. Addition of Tertiary Amines

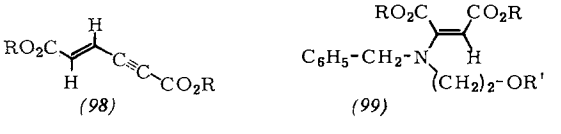
Non-aromatic tertiary amines can also be made to react, but in this case it is necessary to use dilute solutions and low temperatures because of the higher basicity of these compounds. Thus the reaction of methyl propiolate with β-aminocarbonyl compounds leads to *(91)* by Hofmann degradation, that with esters of α-amino acids and their vinylogues to *(92)* and *(93)* by rearrangement and prototropy, and that with α-amino ketones in dimethyl sulfoxide to pyrroles *(94)* [5].



Analogous products are obtained with dimethyl acetylenedicarboxylate [50]. In this case, however, pyrrole derivatives are also formed in the reaction with esters of α-amino acids, but these immediately react further to yield *(95)* [27].



Trialkylamines add only in the presence of their salts to give esters of dialkylaminomaleic acid [51]. These tertiary amines can therefore be advantageously used as catalysts for additions to CC triple bonds. This permits the addition, not only of alcohols (see Section III 1), but also of water; in the case of methyl propiolate, double addition takes place with formation of *(96)*, while with propargyl aldehyde, addition and condensation leads to *(97)* [52]. The reaction of methyl propiolate with tertiary amines with rigorous exclusion of water leads to *(98)*.



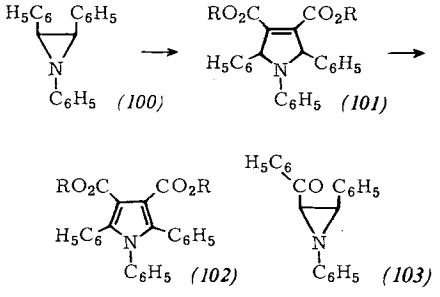
Whereas the reaction of *N*-benzylaziridine with diethyl acetylenedicarboxylate in alcohol results almost exclusively in cleavage of the C–N bond and formation

[50] *E. Winterfeldt*, unpublished.

[51] *R. J. Alaimo* and *D. G. Farnum*, Canad. J. Chem. *43*, 700 (1965).

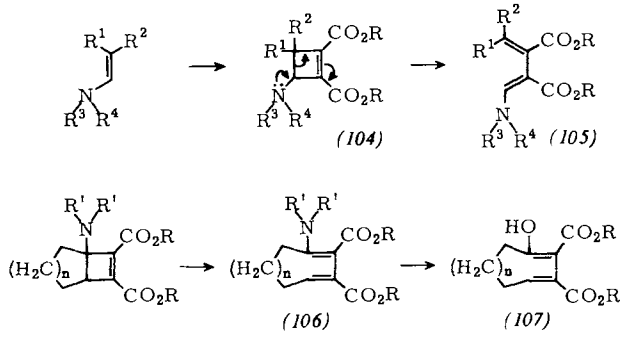
[52] *E. Winterfeldt*, Chem. Ber. *97*, 1959 (1964).

of ethers of the type *(99)* [27], reactions involving the cleavage of the C–C bond have been reported for the substituted aziridines *(100)* and *(103)*. Thus the reaction of *(100)* in toluene yields the pyrroline *(101)*, which can be converted into the pyrrole *(102)* by treatment with chloranil [53]. *(103)* reacts similary [54].



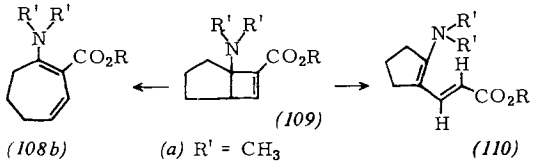
(100) *(101)* *(102)* *(103)*

The reaction of enamines with the activated triple bond was studied simultaneously by several research groups [55]. The reaction generally proceeds *via* the four-membered ring adduct *(104)*, which undergoes ring cleavage to form the dienamine *(105)*. Cyclic enamines undergo ring expansion *via* a similar intermediate, with formation of *(106)*.



(104) *(105)* *(106)* *(107)*

The hydrolysis of this reaction product leads to the enol ester *(107)*. The cyclobutene structure of *(104)* has been confirmed, *inter alia*, by hydrogenation to form the corresponding cyclobutane [55c]. The reactions of enamines with methyl propiolate can also be explained by this scheme, but in this case *Brannock et al.* found a dependence on the ring size of the enamine and on the structure of the amine component [56]. Thus *(109a)* gives the Stork adduct *(110)* when simply allowed to stand at room temperature, while *(109b)* and *(109c)* are converted into the cycloheptadienes *(108b)* and *(108c)* when heated at 90 °C.

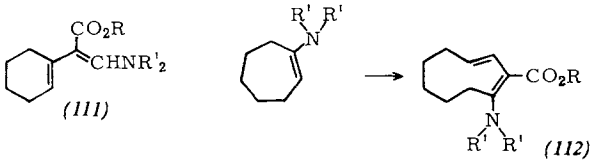


(108b) *(a)* R' = CH_3 *(109)* *(110)*

(108c) *(b)* R', R' = $-(CH_2)_4-$

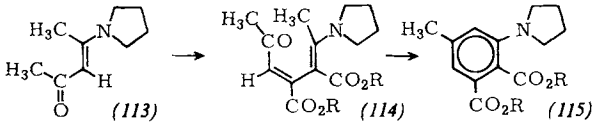
(c) R', R' = $-(CH_2)_5-$

Whereas cyclohexenamines unexpectedly give the substituted aminoacrylates *(111)*, cycloheptenamine gives the normal ring-expansion product *(112)*.



(111) *(112)*

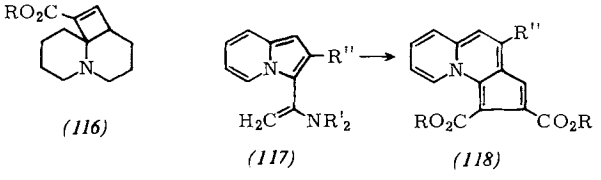
Enamines derived from β-dicarbonyl compounds, *i.e.* vinylogous amides and urethanes also undergo this reaction [55c]. Thus the pyrrolidinopentenone *(113)* first reacts normally to form *(114)*, which then undergoes spontaneous cyclization to form the aromatic compound *(115)*.



(113) *(114)* *(115)*

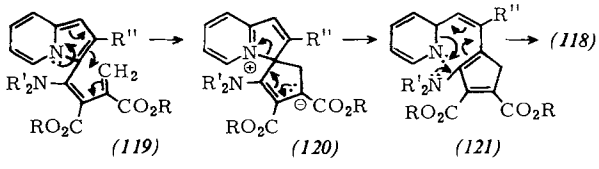
According to *Huebner et al.*, the addition of vinylogous urethanes also proceeds *via* a four-membered ring adduct, but the authors do not rule out the normal Michael reaction.

This reaction has been used *e.g.* for ring expansion in the steroid series [55a] and for the synthesis of a tricyclic ester *(116)* from 2,3,6,7,8,9-hexahydro-4*H*-quinolizine [57].



(116) *(117)* *(118)*

In one case of the attempted preparation of cycloazines, the indolizine derivative *(117)* gives the cyclopentaquinolizine derivative *(118)* [58]. This previously unknown indolizine-quinolizine rearrangement probably also proceeds *via* a cyclobutene derivative, since it is possible to isolate the primary adduct *(119)* at room temperature; *(119)* forms *(118)* when heated in toluene, *(120)* and *(121)* being proposed as intermediates.



(119) *(120)* *(121)* *(118)*

Alkynylamines also add smoothly to dimethyl acetylenedicarboxylate, and benzene derivatives of the type *(122)* are formed, even at room temperature [59].

An interesting reaction of acetylenedicarboxylic acid with ethynyl alkyl ethers has been described by *Arens*

[53] *H.W. Heine* and *R. Peavy*, Tetrahedron Letters *1965*, 2123.

[54] *A. Padwa* and *L. Hamilton*, Tetrahedron Letters *1965*, 4363.

[55] a) *G. A. Berthold* and *G. F. Uhlig*, J. org. Chemistry *29*, 1459 (1964); b) *K. C. Brannock, R. D. Burpitt, V. W. Goodlett*, and *J. G. Thweatt, ibid. 29*, 1464 (1964); c) *C. F. Huebner et al., ibid. 29*, 3134 (1964); d) *A. K. Bose, G. Mina, M. S. Manhas*, and *E. Rzucidlo*, Tetrahedron Letters (London) *1963*, 1467.

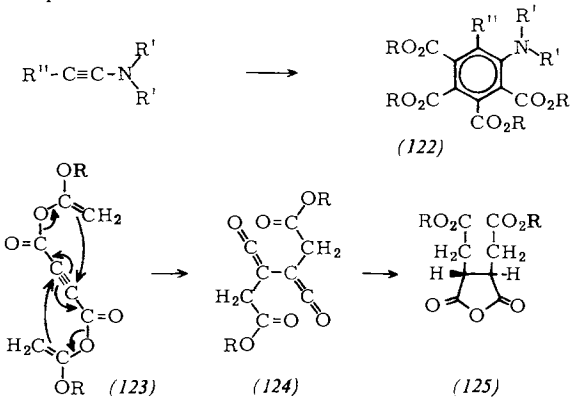
[56] *K. C. Brannock, R. D. Burpitt, V. W. Goodlett*, and *J. G. Thweatt*, J. org. Chemistry *29*, 818 (1964).

[57] *W. Knoblauch*, Dissertation, Technische Universität Berlin, 1965.

[58] *W. K. Gibson* and *D. Leaver*, J. chem. Soc. (London) *1966*, 330.

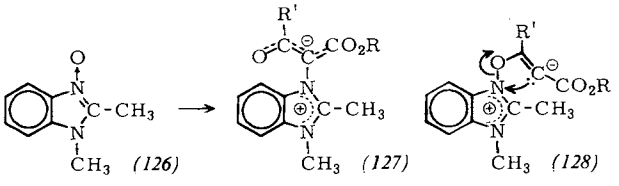
[59] *J. Ficini* and *C. Barbara*, Bull. Soc. chim. France *1964*, 871; *H. G. Viehe, F. Fuks*, and *M. Reinstein*, Angew. Chem. *76*, 571 (1964); Angew. Chem. internat. Edit. *3*, 581 (1964).

and *Cley*[60]. The ketene acetal *(123)* formed at −10 °C in diethyl ether rearranges spontaneously into the diketene *(124)*, which gives the anhydride *(125)* in the presence of water.



(122) *(123)* *(124)* *(125)*

Though the reaction of aromatic *N*-oxides with activated acetylene derivatives normally proceeds by 1,3-cycloaddition[61], *Takahashi* and *Kano* have described a case that does not fit directly into this scheme[62]. The reaction of the *N*-oxide *(126)* with methyl propiolate or dimethyl acetylenedicarboxylate in chloroform at room temperature yields a betaine, which is assigned the structure *(127)*, R′ = H or CO_2R, on the basis of the degradation products obtained on acid hydrolysis.

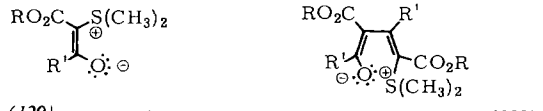


(126) *(127)* *(128)*

The structures have also been confirmed by independent synthesis. Since the authors were unable to isolate a cycloadduct even at −20 °C, they suggested the formation of *(127)* *via* the four-membered ring transition state *(128)*.

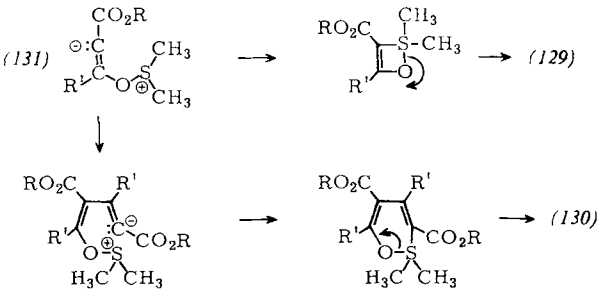
3. Addition of Sulfur Compounds

A similar transition state is required to explain the reaction of activated triple bonds with dimethyl sulfoxide. Both methyl propiolate and dimethyl acetylenedicarboxylate give the adducts *(129)* and *(130)* when heated in dimethyl sulfoxide[63].



(129) *(a)* R′ = H *(b)* R′ = CO_2R *(130)*

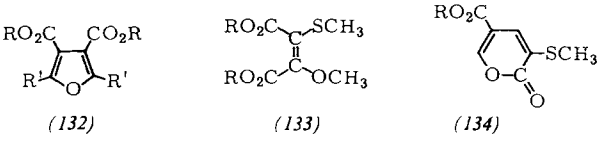
The formation of those products is explained by the assumption of a primary adduct *(131)*.



(131) *(129)* *(130)*

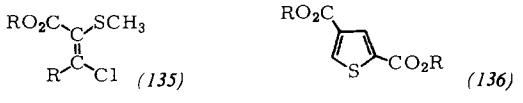
(129b) could be isolated as the main product, even at very high ester concentrations, whereas with methyl propiolate the reaction can be directed, and *(129a)* is the main product only at very high dilutions. Thus the reaction of methyl propiolate can be carried out in such a way as to obtain the 1:1 *(129a)* or the 1:2 adduct *(130a)*, as desired[27].

When heated further with methyl propiolate or dimethyl acetylenedicarboxylate, *(129a)* and *(129b)* give the furan derivatives *(132)*. When heated in the absence of the acetylene compounds, *(129b)* exhibits migration of the methyl group and formation of *(133)*. *(130b)* gives the tetraester of furantetracarboxylic acid as the main product, while *(130a)* gives the pyrone *(134)* and only very small quantities of dimethyl furandicarboxylate.



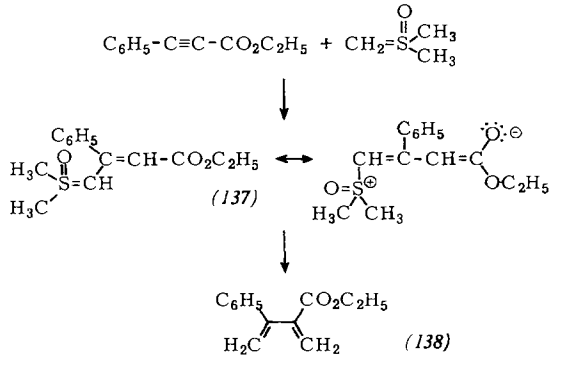
(132) *(133)* *(134)*

The compounds *(129a)* and *(129b)* react smoothly with acyl chlorides to form the thioethers *(135)*; under these conditions *(130a)* reacts surprisingly smoothly to give the dimethyl thiophenedicarboxylate *(136)*.



(135) *(136)*

The reaction of dimethylsulfoxonium methylide with acetylene compounds has also been studied by several authors[64]. Ethyl phenylpropiolate gives the crystalline ylide *(137)*.



(137) *(138)*

[60] *J. F. Arens* and *J. Cley*, Recueil Trav. chim. Pays-Bas *78*, 929 (1959).

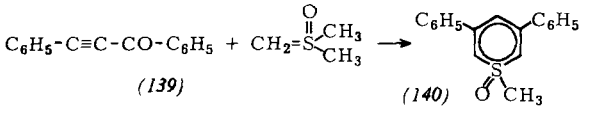
[61] *R. Huisgen* and *H. Seidel*, Tetrahedron Letters *1963*, 2023, 2191.

[62] *S.Takahashi* and *H.Kano*, J.org.Chemistry *30*, 1118 (1965).

[63] *E. Winterfeldt*, Chem. Ber. *98*, 1518 (1965).

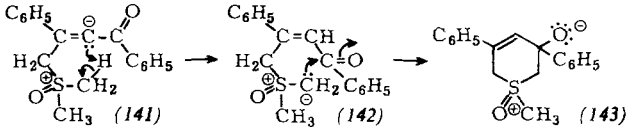
[64] a) *C. Kaiser, B. M.Trost, J. Beeson*, and *J. Weinstock*, J. org. Chemistry *30*, 3972 (1965); b) *J. Ide* and *Y.Kishida*, Tetrahedron Letters *1966*, 1787.

On treatment with triethylamine, this compound gives the interesting diene *(138)*. The same authors obtained only very unstable products in the reaction of dimethylsulfoxonium methylide with dimethyl acetylenedicarboxylate. In the reaction with the ketone *(139)*, *Hortmann* obtained the thiabenzene derivative *(140)* [65].



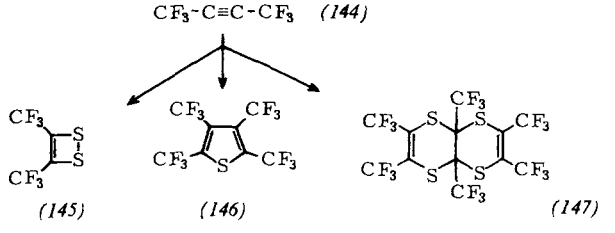
(139) *(140)*

The reaction proceeds *via (141)*, *(142)*, and *(143)*.



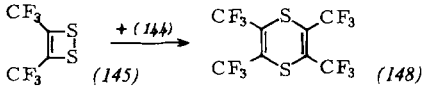
(141) *(142)* *(143)*

The action of elementary sulfur on the activated triple bond of hexafluoro-2-butyne *(144)* was studied by *Krespan* [66]. At high temperatures, the reaction yields the compounds *(145)*, *(146)*, and *(147)*.



(145) *(146)* *(147)*

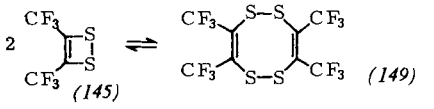
The reaction of *(144)* with sulfur vapor gives *(145)* in 80% yield. Thus this dithiete may be regarded as the primary adduct, which, because of the strained disulfide bond, smoothly adds a second mole of the acetylene compound to form *(148)*.



(145) *(148)*

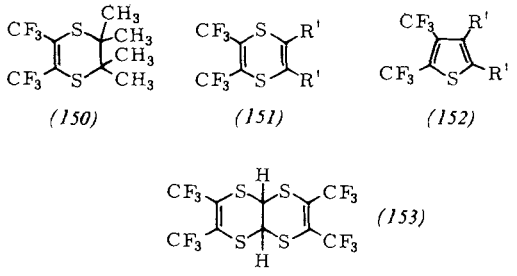
(148) may then either lose sulfur to form *(146)* or react with a second mole of *(145)* to give *(147)*. These views are strongly supported by the fact that when *(145)* and *(144)* are heated at 100 °C, they react to form *(148)*, which gives *(146)* as expected on further heating. *(146)* can be obtained as sole product by this reaction.

The ring strain in *(145)* is also shown by the smooth dimerization to form *(149)*. The equilibrium between *(145)* and *(149)* is demonstrated by the fact that *(149)* gives *(145)* when heated at 200 °C.



(145) *(149)*

In agreement with the above reactions, *(145)* reacts with 2,3-dimethyl-1,3-butadiene to form *(150)* and with acetylene at 70 °C to give *(151)* (R′ = H) while the reaction with acetylene at 125 °C yields a mixture of *(152)* and *(153)*.

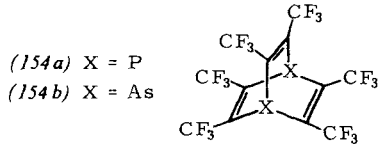


(150) *(151)* *(152)*

(153)

The reaction of *(145)* with dimethyl acetylene dicarboxylate leads only to the 1:1 adduct *(151)* (R′ = CO_2R). This compound loses sulfur when heated, and forms the thiophene derivative *(152)* (R′ = CO_2R). The acceptor groups on the double bond prevent further addition in this case.

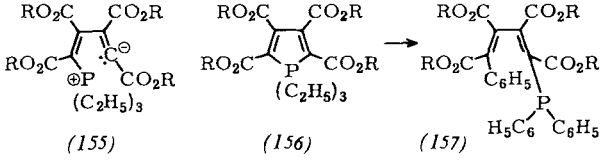
The additions described are catalysed by iodine. Under pressure, phosphorus and arsenic can also be made to react under comparable conditions to give the 1,4-diphospha- *(154a)* or 1,4-diarsabarrelene structure *(154b)* [67].



(154a) X = P
(154b) X = As

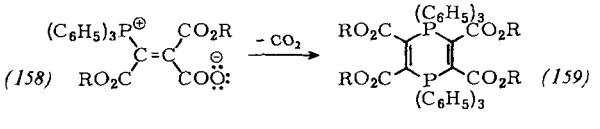
4. Addition of Phosphorus Compounds

The addition of phosphorus compounds to the activated CC triple bond has also been studied from various points of view. *Horner* and *Hoffmann* reported the reaction of triphenyl- and triethylphosphines with dimethyl acetylenedicarboxylate. They formulated a 1:1 adduct with triphenylphosphine and the 2:1 adduct *(155)* with triethylphosphine [68].



(155) *(156)* *(157)*

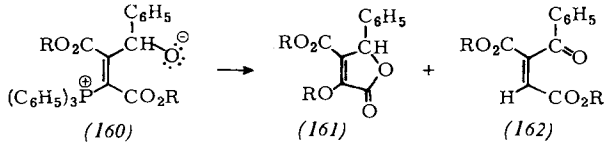
The same formulation was given by *Johnson* and *Tebby* for the 2:1 adduct with triphenylphosphine, but it can also be shown that the adduct is stabilized by formation of *(157)* when heated [69]. The same product is obtained when the reaction is carried out in boiling ether. These authors were also able to intercept the 1:1 adduct with CO_2 as the betaine *(158)*, which is readily decarboxylated to form a product that is formulated as *(159)*.



(158) *(159)*

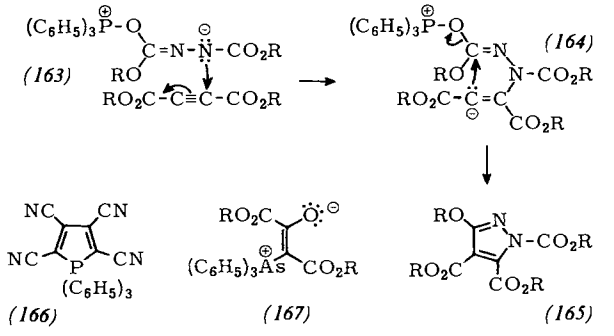
[65] *A. G. Hortmann*, J. Amer. chem. Soc. *87*, 4972 (1965).
[66] *C. G. Krespan*, J. Amer. chem. Soc. *83*, 3434, 3438 (1961).
[67] *C. G. Krespan*, J. Amer. chem. Soc. *83*, 2126 (1961).
[68] *L. Horner* and *H. Hoffmann*, Angew. Chem. *68*, 473 (1956).
[69] *A. W. Johnson* and *J. C. Tebby*, J. chem. Soc. (London) *1961*, 2126.

A similar interception reaction is possible with an excess of benzaldehyde; the stable end products *(161)* and *(162)* are obtained *via (160)* [27].



(160) *(161)* *(162)*

The reaction of triphenylphosphine with dimethyl azodicarboxylate and dimethyl acetylenedicarboxylate is also interpreted as an interception reaction, leading *via (163)* and *(164)* to the pyrazole *(165)* [70].



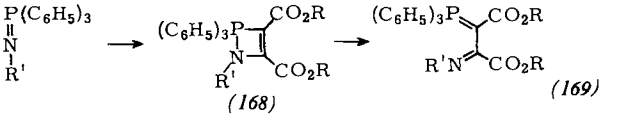
(163) *(164)* *(166)* *(167)* *(165)*

Hendrickson et al. [71] proposed the neutral structure *(156)* as the final formulation of the 2:1 adduct, since the conversion of *(156)* into *(157)* proceeds smoothly and quantitatively in acidic media, whereas an enoxide ion should be protonated under these conditions, and hence be unable to undergo rearrangement.

The product of the reaction of dicyanoacetylene and triphenylphosphine is also formulated as a phosphole *(166)* [72]. However, the adduct of dimethyl acetylenedicarboxylate and triphenylarsine, for which a similar structure was originally postulated, has been found to be the oxidation product *(167)* [71].

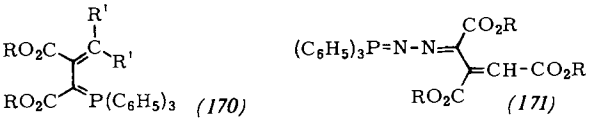
Phosphine imides react smoothly with the activated CC triple bond. The reaction proceeds *via* a four-membered ring adduct to yield the stable compound *(169)*, the structure of which has been established by X-ray analysis [73].

The unsubstituted phosphine imine, which could, in principle, enter into a Michael addition, also reacts *via* a four-membered ring [74].



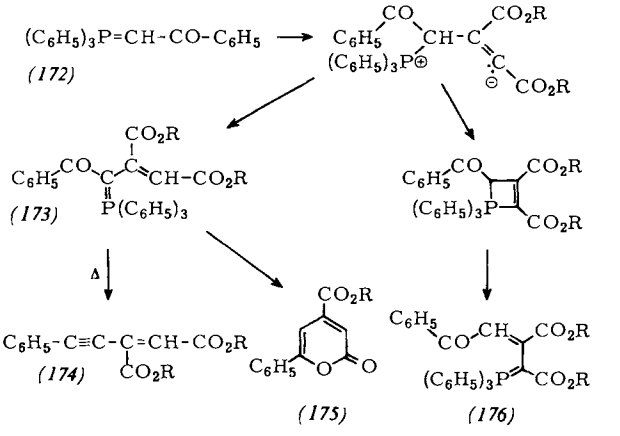
(168) *(169)*

A similar reaction of phosphoranes leads to products of the type *(170)* [75]. Phosphazines, on the other hand, react by Michael addition to give *(171)* [74].



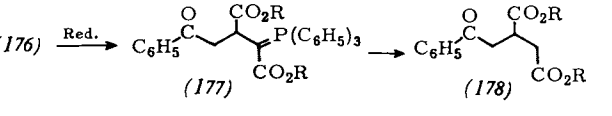
(170) *(171)*

According to *Hendrickson*, the reaction of acylphosphoranes can proceed either *via* the four-membered ring or as a Michael addition, depending on the solvent [76]. Thus *(172)* in methanol gives the Michael addition product *(173)*, the structure of which is established by pyrolysis to form *(174)* and by conversion i..to the pyrone *(175)*.



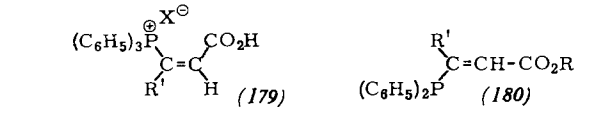
(172) *(173)* *(174)* *(175)* *(176)*

The reaction in ether, on the other hand, yields *(176)*, the structure of which was established by spectral data and by reduction to *(177)*, which forms the keto acid *(178)* on treatment with alkali.



(176) *(177)* *(178)*

According to *Hoffmann* and *Diehr*, triphenylphosphine adds to propiolic acid in acidic media to form the *trans* adduct *(179)* (R′ = H); acetylenedicarboxylic acid yields the same product on subsequent decarboxylation [77].



(179) *(180)*

The *trans* addition follows from the fact that the adduct *(179)* (R′ = C_6H_5) obtained from phenylpropiolic acid gives *trans*-cinnamic acid on hydrolysis (provided that the configuration is stable during

[70] *R. C. Cookson* and *J. M. Locke*, J. chem. Soc. (London) *1963*, 6062.

[71] *J. B. Hendrickson et al.*, Tetrahedron *19*, 707 (1963).

[72] *G.S.Reddy* and *C.D.Weis*, J. org.Chemistry *28*, 1822 (1963).

[73] *G. W. Brown*, *R. C. Cookson*, *D. R. Stevens*, *T. C. W. Mak*, and *J.Trotter*, Proc. chem. Soc. (London) *1964*, 87.

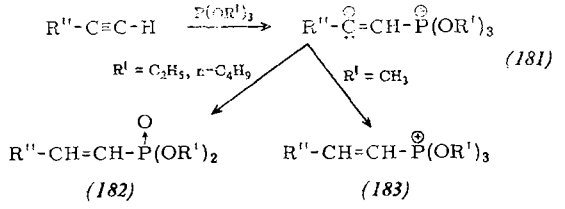
[74] *G.W.Brown*, *R.C.Cookson*, and *D.R.Stevens*, Tetrahedron Letters *1964*, 1263.

[75] *H. J. Bestmann*, Angew. Chem. *76*, 569 (1964); Angew. Chem. internat. Edit. *3*, 512 (1964).

[76] *J. B. Hendrickson*, *C. Hall*, *R. Rees*, and *J. F.Templeton*, J. org. Chemistry *30*, 3973 (1965).

[77] *H. Hoffmann* and *H. J. Diehr*, Chem. Ber. *98*, 363 (1965).

hydrolysis). The addition of diphenylphosphine was also studied in this connection; the reaction leads smoothly to the adduct of the general structure *(180)*. An interesting course is found in the addition of trialkyl phosphites. In the case of compounds with non-activated triple bonds, the primary complex *(181)* can be stabilized in various ways.

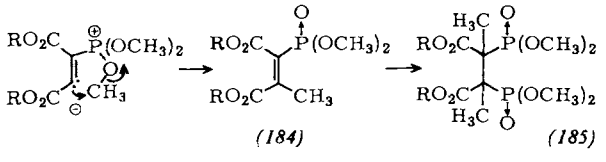


(181)

(182) *(183)*

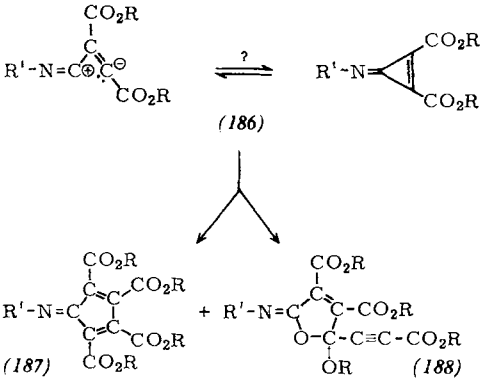
For R' = C_2H_5 and n-C_4H_9, stability is achieved by a *cis* elimination, which leads, by elimination of the corresponding olefin, to the vinylphosphonates *(182)*. This route is not possible for R' = CH_3; *(181)* is therefore protonated by a second mole of the acetylene compound to give the quasiphosphonium salt *(183)*, which then also gives *(182)* by dealkylation.

Neither of these routes is possible in the reaction of trimethyl phosphite with dimethyl acetylene dicarboxylate. Nevertheless, the two components react very vigorously, and in etheral solution the compound *(185)* is obtained in 38 % yield[78]. The most likely course for this reaction is the primary formation of the vinylphosphonate *(184)* followed by further reaction in an analogous secondary step to form *(185)*.



(184) *(185)*

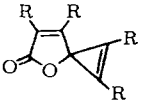
Finally, it should also be mentioned that isocyanides, as expected, react smoothly with dimethyl acetylenedicarboxylate[79]. The course of this reaction is very strongly dependent on the external parameters, and can be directed in such a way as to obtain various products. With a small excess of the ester and at low temperatures, it is possible to obtain good yields of the products *(187)* and *(188)*, the formation of which can be readily explained as proceeding *via* the primary adduct *(186)*.



(186)

(187) *(188)*

Breslow observed that a reaction similar to the formation of *(188)* takes place with a cyclopropenone derivative, which can be converted into the spirane *(189)*.



(189)

I am grateful for the industrious and imaginative cooperation of H. Preuss, H. J. Dillinger, and W. Krohn, who have attacked this problem with great enthusiasm and energy. Acknowledgment is due to the Deutsche Forschungsgemeinschaft, the Fonds der Chemischen Industrie, and the ERP-Sondervermögen for their promotion of this work. Thanks are also due to Professor F. Bohlmann for his untiring support and his constant interest.

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German version: Angew. Chem. 79, 389 (1967)
Translated by Express Translation Service, London

[78] *C. E. Griffin* and *T. D. Mitschel*, J. org. Chemistry *30*, 2829 (1965).

[79] *E. Winterfeldt* and *H. J. Dillinger*, unpublished.

Sigma-Bonded Organochromium Compounds. Hydrogen Transfer Reactions

BY H. H. ZEISS AND R. P. A. SNEEDEN [*]

The preparation and properties of two classes of organochromium compounds and their interconversion have been studied actively in recent years. These are the σ-bonded organochromium compounds in which alkyl, aryl, or aralkyl groups are covalently bonded to chromium (II or III) and the π-arenechromium complexes in which "aromatic" nuclei are covalently bonded to chromium (0 or 1). From certain reactions of the σ-bonded organochromium compounds, evidence has accumulated which shows that the chromium atom acts not only as a coordination center, but also as a hub for hydrogen transfer and H/D exchange [1,2]. σ-Organochromium compounds may act as sources of radicals and carbanions. The present paper deals with the preparation and properties of σ-bonded organochromium compounds; particular attention is given to hydrogen transfer reactions and rearrangements to bis(π-arene)chromium complexes.

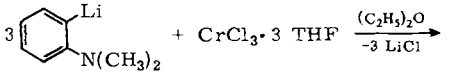
I. Preparation

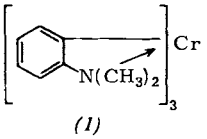
Solvated σ-bonded organochromium compounds may be prepared by the action of certain organometallic compounds on chromium halides, *e.g.*, unsolvated $CrCl_3$ or $CrCl_3 \cdot 3$ tetrahydrofuran, provided particular attention is paid to solvent, temperature, and stoichiometry of the reaction. Phenyl-lithium [3] and phenylsodium [4], for example, react with chromium trichloride according to eq. (a) and (b) to give lithium- and sodium-containing organochromium complexes of varying composition. In some cases organolithium reagents give lithium-free complexes [5], *e.g. (1)*.

$$6\ LiC_6H_5 + CrCl_3 \xrightarrow{(C_2H_5)_2O} Li_3[Cr(C_6H_5)_6] \cdot 4(C_2H_5)_2O\ [2] \quad (a)$$

$$5\ NaC_6H_5 + CrCl_3 \xrightarrow[THF]{(C_2H_5)_2O} Na_2[Cr(C_6H_5)_5S] \cdot 2S \quad (b)$$

$S = (C_2H_5)_2O$, THF [4]





(1)

However, in the reaction between triphenylaluminum and chromium(III) chloride in tetrahydrofuran only one phenyl group is introduced, giving the complex *(2)* [6].

$$Al(C_6H_5)_3 + CrCl_3 \xrightarrow{THF} C_6H_5CrCl_2 \cdot 3\ THF + (C_6H_5)_2AlCl \quad (2)$$

The most convenient and perhaps cleanest route to σ-bonded organochromium compounds is by the action of organomagnesium halides on $CrCl_3 \cdot 3THF$ in tetrahydrofuran [2,7–10,13,14] or in diethyl ether [eq. (c)]. This is a general and most versatile method for the preparation of such compounds.

$$3\ RMgX + CrCl_3 \cdot 3THF \rightarrow R_3Cr \cdot xTHF + MgXCl \cdot yTHF \quad (c)$$

R = phenyl [7]; α- and β-naphthyl [8]; ethyl [9]; mesityl [10,14b]; allyl [11,12]; vinyl [13]; benzyl [2]; *p*-tolyl [14]; *p*-F-, *p*-Cl-, *p*-Br-, *p*-C_6H_5–C_6H_4 [14a]; *m*-Cl-, *m*-CH_3–C_6H_4 [14a]; 2-thiophenyl [14a]; *o*-tolyl [14b]; methyl [9].

By varying the stoichiometric ratios of the reactants, solvated organochromium compounds of the type, $R_nCrCl_{3-n} \cdot xS$ (n = 1,2 or 3) R = *e.g.* benzyl [2,15a],

[*] Prof. Dr. H. H. Zeiss and Dr. R. P. A. Sneeden
Monsanto Research S.A.
Binzstr. 39
8045 Zürich (Switzerland)

[1] *H. H. Zeiss*, Bull. Soc. chim. France *1963*, 1500.

[2] *F. Glocking, R. P. A. Sneeden*, and *H. H. Zeiss*, J. organomet. Chemistry *2*, 109 (1964).

[3] *Fr. Hein* and *R. Weiss*, Z. anorg. allg. Chem. *295*, 145 (1958).

[4] *Fr. Hein, B. Heyn*, and *K. Schmiedeknecht*, Mber. dtsch. Akad. Wiss. Berlin *2*, 552 (1960); *Fr. Hein* and *K. Schmiedeknecht*, J. organomet. Chemistry *5*, 454 (1966); *6*, 45 (1966).

[5] *Fr. Hein* and *D. Tille*, Z. anorg. allg. Chem. *329*, 72 (1964).

[6] *E. Kurras*, Dissertation, Universität Jena, 1959.

[7] *W. Herwig* and *H. Zeiss*, J. Amer. chem. Soc. *79*, 6561 (1957).

[8] *W. Herwig, W. Metlesics*, and *H. Zeiss*, J. Amer. chem. Soc. *81*, 6203 (1959).

[9] *M. Tsutsui* and *H. Zeiss*, J. Amer. chem. Soc. *81*, 6090 (1959).

[10] *W. Metlesics* and *H. Zeiss*, J. Amer. chem. Soc. *81*, 4117 (1959).

[11] *W. Oberkirch*, Dissertation, Technische Hochschule Aachen, 1963.

[12] *E. Kurras* and *P. Klimsch*, Mber. dtsch. Akad. Wiss. Berlin *6*, 736 (1964).

[13] *H.-P. Throndsen, W. Metlesics*, and *H. Zeiss*, J. organomet. Chemistry *5*, 176 (1966).

[14] *R. P. A. Sneeden* and *H. Zeiss*, J. organomet. Chemistry *4*, 355 (1965).

[14a] *G. Stolze* and *J. Hähle*, J. organomet. Chemistry *5*, 545 (1966).

[14b] *G. Stolze*, J. organomet. Chemistry *6*, 383 (1966).

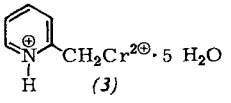
[15a] *R. P. A. Sneeden* and *H.-P. Throndsen*, Chem. Commun. *1965*, 509.

[15b,16,17] [*], phenyl [6], methyl [16], *p*-tolyl [16a], and mixed organochromium compounds RR'R''Cr·*x*S have become accessible.

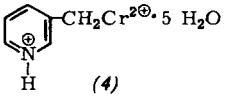
Another interesting route to organochromium species is based on the reaction of chromium(II) salts with certain organic halides [18,19] (eq. (d)). This reaction has been used to prepare the compounds *(3)–(6)* [20a–20c] as well as alkylchromium compounds [20d].

$$2\,Cr^{2+} + RCl \xrightarrow{H_2O} RCr^{2+}\cdot 5H_2O + CrCl^{2+}\cdot 5H_2O \qquad (d)$$

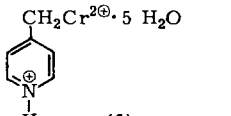
R = C_6H_5–CH_2, $CHCl_2$



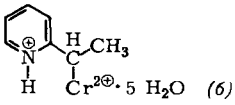
(3)



(4)



(5)



(6)

More recently this method has been adapted to the preparation of the crystalline monoorganochromium compounds $RCrCl_2$·3pyridine (R = benzyl, *o*-chlorobenzyl and *p*-chlorobenzyl) [15b].

II. Properties

The monoorganochromium dihalides $RCrCl_2$·*x*S differ markedly in thermal stability. Whereas the phenyl and *p*-tolyl derivatives may be recrystallized from tetrahydrofuran (−10 to 20 °C), the benzyl and mesityl compounds decompose rapidly in this solvent at room temperature. Solutions of $C_6H_5CH_2CrCl_2$·*x*S in tetrahydrofuran can be diluted with water and stored at −20 °C. Alternatively $C_6H_5CH_2CrCl_2$·*x*THF may be extracted quantitatively into water from ethereal suspension. Properties of the aqueous solution [15b,17], *i.e.* reducing power towards $FeCl_3$, formation of benzaldehyde on oxidation, and the visible spectrum are the same as those of a complex $CrCl_2(C_6H_5CH_2)\cdot 5H_2O$ formed directly from benzyl chloride and chromous salts [18].

The thermal decomposition of the benzyl- and mesitylcompounds as in eq. (e) involves homolysis of the carbon-chromium bond giving 1,2-diphenylethane and bimesityl, respectively, and chromium(II) chloride. It has been reported that CH_3CrCl_2·*x*S can be recrystallized from warm tetrahydrofuran [16].

$$RCrCl_2\cdot xS \xrightarrow{\Delta} R{-}R + CrCl_2\cdot xS \qquad (e)$$

R = Benzyl, mesityl

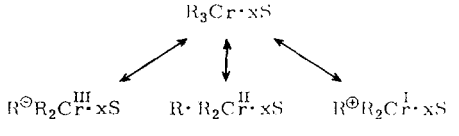
The monoorganochromium dichlorides $RCrCl_2$·*x*S react with mercuric chloride in tetrahydrofuran [eq.(f)] to give the corresponding organomercuric chloride and $CrCl_3$·3THF.

$$RCrCl_2\cdot n\text{THF} + HgCl_2 \rightarrow RHgCl + CrCl_3\cdot 3\text{THF} \qquad (f)$$

Therefore, σ-bonded organochromium compounds can be regarded as sources of carbanions or of radicals:

$$R^{\ominus}\ldots\overset{\oplus}{Cr}Cl_2\cdot xS \leftrightarrow RCrCl_2\cdot xS \leftrightarrow R^{\bullet}\ldots Cr^{\bullet}Cl_2\cdot xS$$

The triorganochromium compounds, R_3Cr·*x*S, undergo both heterolytic and homolytic carbon-chromium bond cleavage. Thus, triphenylchromium is hydrolysed to benzene and reacts with mercuric chloride to give phenylmercuric chloride [7]. Triallylchromium is converted on warming to diallylchromium(II) and presumably 1,5-hexadiene [12]. Depending on the nature of group R and of the coordination, these substances may also be regarded as sources of carbanions, of radicals, and even of carbonium ions.



III. Reactions

1. Reactions with Ketones

Organochromium compounds differ from their organomagnesium counterparts in reactions with ketones. The latter may act either as a source of alkyl or aryl groups in forming tertiary carbinols or as conventional

[15b] *R. P. A. Sneeden* and *H.-P. Throndsen*, J. organomet. Chemistry *6*, 542 (1966).

[16] *E. Kurras*, Mber. dtsch. Akad. Wiss. Berlin *5*, 378 (1963).

[16a] *J. J. Daly*, *R. P. A. Sneeden*, and *H. H. Zeiss*, J. Amer. chem. Soc. *88*, 4287 (1966).

[17] *J. K. Kochi* and *D. Buchanan*, J. Amer. chem. Soc. *87*, 853 (1965).

[*] Deuteriotoluenes [a] from the hydrolysis of benzylchromium compounds R_nCrCl_{3-n}·*x*S in D_2O at 0 C°.

n	Relative yields (%) [b]			Total yields [c]
	C_7H_8	C_7H_7D	$C_7H_6D_2$	
3	11.2	88.7	0.1	86
2	10.6	89.3	0.06	88
1	11.7	88.3	0.00	92

[a] Isolated by fractional distillation and preparative gas chromatography. Identified by mass spectrometry [37].

[b] Corrected for natural abundance isotope.

[c] The isolation of essentially pure monodeuteriotoluene in such high yields is proof of the existence of σ-bonded benzylchromium compounds.

[18] *F. A. L. Anet* and *E. Leblanc*, J. Amer. chem. Soc. *79*, 2649 (1957).

[19] *F. A. L. Anet*, Canad. J. Chem. *37*, 58 (1959).

[20a] *R. G. Coombes*, *M. D. Johnson*, *M. L. Tobe*, *N. Winterton*, and *Lai-Yong Wong*, Chem. Commun. *1965*, 251.

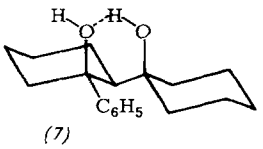
[20b] *R. G. Coombes*, *M. D. Johnson*, and *N. Winterton*, J. chem. Soc. (London) *1965*, 7029.

[20c] *R. G. Coombes* and *M. D. Johnson*, J. chem. Soc. (London) Sect. A *1966*, 177.

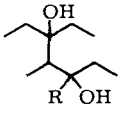
[20d] *J. K. Kochi* and *P. E. Mocaldo*, J. Amer. chem. Soc. *88*, 4094 (1966).

organic bases in effecting self-condensation of ketones [21]. Organochromium compounds, on the other hand, may serve to do both simultaneously.

Triphenylchromium reacts with cyclohexanone [22] to give 1-phenylcyclohexanol, 2-cyclohexenylcyclohexanone and 2-phenylbicyclohexyl-1',2-diol *(7)*. Similarly, triethyl- and triphenylchromium with 3-pentanone give respectively 3-ethylpentan-3-ol and 3,5-diethyl-4-methylheptane-3,5-diol *(8)*, R = C_2H_5), and 3-phenylpentan-3-ol and 5-ethyl-4-methyl-3-phenylheptane-3,5-diol *(8)*, R = C_6H_5).



(7)



(8)

The formation of 2-cyclohexenylcyclohexanone from cyclohexanone and triphenylchromium is evidence of the organochromium compound acting as a coupling center. Finally, the formation of *(8)* (R = C_6H_5) in the same reaction is evidence that triphenylchromium acts simultaneously as a coupling center [*] and a phenylating agent.

2. Reactions with Disubstituted Acetylenes and Olefins

Organochromium compounds act as coordination centers in their reactions with disubstituted acetylenes, *e.g.*, dimethyl- and diphenylacetylene [1]. In general, five main types of products are obtained:

1) Yellow, viscous polymers formed by the usual ionic polymerization of acetylenes.

2) Hexasubstituted benzenes, *e.g.*, hexamethyl- or hexaphenylbenzene, formed by trimerization of the acetylene component.

3) Tetrasubstituted cyclic products formed when two molecules of the acetylene combine with one of the groups attached to chromium with concomitant hydrogen abstraction (see Table 1).

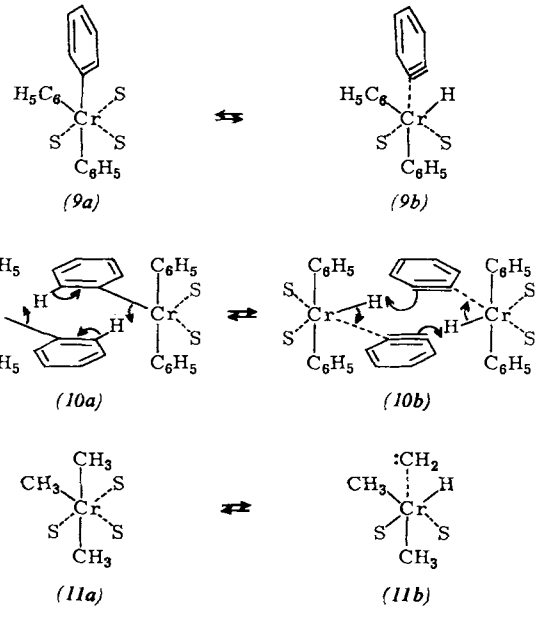
4) Compounds which are formed when one molecule of the acetylene component combines with one or two of the groups bonded to chromium. For example, trimesitylchromium and dimethylacetylene give 2-mesityl-2-butene as well as hexamethylbenzene [10]. Bicyclo[2.2.1]hepta-2,5-diene is mono and diphenylated by triphenylchromium giving *exo*-5-phenylbicyclo-[2.2.1]hept-2-ene and *exo,exo*-2,5-diphenylbicyclo-[2.2.1]heptane [23].

5) Bis(π-arene)chromium complexes formed from trimers of types 2) and 3).

The isolation of compounds of type 3) (see Table 1) provided the first evidence that organochromium compounds promote hydrogen abstraction. Although no intermediates have been isolated yet, the first step may tentatively be represented by the following equilibrium:

$$R_3Cr{\cdot}xS \rightleftharpoons R\text{-}H \,.\,.\,.\,.\,.\,.\, R_2CrH{\cdot}xS$$

The mono- and dimeric forms of the triphenylchromium complex [*(9b)*, *(10b)*, and *(11b)* respectively] have been considered as rearrangement components.



(9a) *(9b)*

(10a) *(10b)*

(11a) *(11b)*

Table 1. Products from organochromium compounds and disubstituted acetylenes.

$R_3Cr{\cdot}xS$ R	R'—C≡C—R' R'	Products Type 2)	Products Type 3)	Ref.
Phenyl	CH_3	$(CH_3)_6C_6$	1,2,3,4-tetramethylnaphthalene	[24]
Phenyl	C_6H_5	$(C_6H_5)_6C_6$	1,2,3,4-tetraphenylnaphthalene	[8]
β-Naphthyl	CH_3	$(CH_3)_6C_6$	1,2,3,4-tetramethylanthracene	[8]
			1,2,3,4-tetramethylphenanthrene	[8]
Ethyl	C_6H_5	$(C_6H_5)_6C_6$	1,2,3,4-tetraphenylbenzene	[9]
Methyl	C_6H_5	$(C_6H_5)_6C_6$	1,2,3,4-tetraphenylcyclopentadiene	[10]
Vinyl	C_6H_5	$(C_6H_5)_6C_6$	1,2,3,4-tetramethylbenzene	[13]
Allyl	CH_3	$(CH_3)_6C_6$	pentamethylbenzene	[25]

[21] *M. Kharasch* and *O. Reinmuth*: Grignard Reactions of Nonmetallic Substances. 2nd Edit., Prentice-Hall, New York 1954.

[22] *R. P. A. Sneeden, T. F. Burger*, and *H. Zeiss*, J. organomet. Chemistry *4*, 397 (1965).

[*] Evidence that the chromium atom itself acts as coupling center is provided by the facts that (i) the phenyl groups are all accounted for in the final products and (ii) no toluene can be detected in the reaction products.

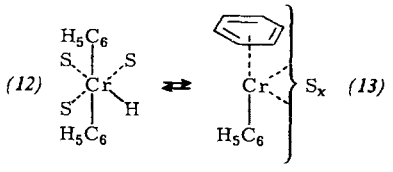
[23] *W. Metlesics, P. J. Wheatley*, and *H. Zeiss*, J. Amer. chem. Soc. *84*, 2327 (1962).

[24] *W. Herwig* and *H. Zeiss*, J. Amer. chem. Soc. *80*, 2913 (1958).

[25] *R. P. A. Sneeden* and *H. Zeiss*, unpublished.

In effect, the organochromium compound $R_3Cr \cdot xS$ can be regarded as a potential source of an aryne [*(9b)*, when R is an aryl group] or of a carbene [*(11b)* when R is an alkyl group]. In such species, rapid reaction with "two molecules of acetylene" would occur to give compounds of type 3).

This concept also implies that a σ-bonded organochromium(III) hydride *(12)* is either in equilibrium with, or can proceed to, the π-arenechromium(I) species.



3. Rearrangement

σ-Bonded arylchromium compounds undergo an unusual reaction in rearranging to π-arenechromium complexes; thus, on treatment with oxygen-free diethyl ether at 20 °C, $(C_6H_5)_3Cr \cdot 3THF$ [26] and $(p\text{-}CH_3C_6H_4)_3Cr \cdot 3THF$ [14] are converted into black intermediates which, on hydrolysis, give bis(π-arene)-chromium complexes. These complexes may be isolated as their tetraphenylborate salts, which are stable in air.

$$(p\text{-}R'\text{-}C_6H_4)_3Cr \cdot 3THF \xrightarrow[2)\ H_2O]{1)\ (C_2H_5)O} \{p\text{-}R'\text{-}C_6H_5\}_2\, Cr^{\oplus}B(C_6H_5)_4^{\ominus} \quad (14) +$$

$$R' = H, CH_3 \qquad \{p\text{-}R'\text{-}C_6H_5\}\ \{(p\text{-}R'\text{-}C_6H_4)_2\}\ Cr^{\oplus}B(C_6H_5)_4^{\ominus} \quad (15)$$

The same black intermediates can be prepared directly by the reaction of the arylmagnesium halide and $CrCl_3$ (molar ratio 3:1) in diethyl ether [14,26]. With *p*-tolylmagnesium bromide the final products are toluene and *p,p'*-dimethylbiphenyl, indicating that in this reaction, and probably in all cases involving arylchromium compounds, the "dimeric products" (both free and in the bis(π-arene)chromium complexes) arise by *para*-coupling of two aryl species within the confines of the organochromium compound.

The nature of the black intermediate [26a] and the mechanism by which σ-bonded arylchromium(III) compounds rearrange to bis(π-arene)chromium complexes remain unknown. Clearly both steric and electronic factors as well as solvent effects influence the rearrangement. Thus the early observation that solvated $(mesityl)_3Cr$ is stable and does not rearrange to a bis(π-arene) complex was taken as evidence that the two methyl groups *ortho* to the C–Cr bond impede the reaction [26b]. However, it has been shown that solvated $(o\text{-tolyl})_3Cr$, with only one methyl group *ortho* to the C–Cr bond, does rearrange to a bis(π-arene) complex. The electronic influence of substituents is illustrated by the observation that, under analogous conditions, the *ortho-*, *para-*, and *meta*-alkyl substituted compounds rearrange, whereas the *para-* and *meta*-halogen substituted compounds do not [14a,14b].

[26] *M. Tsutsui* and *H. Zeiss*, J. Amer. chem. Soc. *81*, 1367 (1959).

[26a] *H. Zeiss*: Organometallic Chemistry. Amer. chem. Soc. Monograph No. 147, Reinhold, New York 1960, p. 394.

[26b] *M. Tsutsui* and *H. Zeiss*, J. Amer. chem. Soc. *82*, 6255 (1960).

IV. Benzylchromium Compounds

1. Reactions

In pure tetrahydrofuran, the tetrahydrofuran adducts of $(CH_2C_6H_5)_3Cr$, $(C_6H_5CH_2)_2CrCl$, and $C_6H_5CH_2CrCl_2$ are readily accessible (see Section I). In pure diethyl ether, benzylmagnesium chloride and $CrCl_3 \cdot 3THF$, or $CrCl_3$, (molar ratio 1:1) react at temperatures lower than −10 °C to give monobenzylchromium dichloride which can be extracted into aqueous solution. With a reactant ratio of 3:1 and at −78 °C, the initial product is tribenzylchromium [2]. This compound is unstable in diethyl ether and at *ca.* 20 °C it rearranges to a black intermediate which, on hydrolysis, gives hydrogen, toluene, 1,2-diphenylethane, *o*-methyldiphenylmethane, and π-(*o*-methyldiphenylmethane)-π-toluenechromium(I).

Experiments have shown that when only 1,2-diphenylethane is formed (hydrolysis of THF/ether mixtures), little or no π-complex is formed. On the other hand, when *o*-methyldiphenylmethane alone, or together with 1,2-diphenylethane, is formed (hydrolysis of ethereal solutions), the bis(π arene)chromium complex is also formed. It appears, therefore, that there is a direct relationship between the formation of the bis(π-arene)chromium complex and that of *o*-methyldiphenylmethane.

Formation of *o*-methyldiphenylmethane indicates that in the original tribenzylchromium complex two benzyl groups have undergone *ortho*-coupling. This is in sharp contrast to the triaryl compounds, in which two aryl species undergo *para*-coupling (cf. Section III.3). Furthermore, in the case of tribenzylchromium, the formation of toluene and *o*-methyldiphenylmethane involves the acquisition of hydrogen by the benzyl group originally bonded to chromium. The bis(π-arene) complex can only arise by the acquisition of two hydrogen atoms by the intermediate formed in the coupling of two benzyl species within the tribenzylchromium complex. These hydrogen atoms may originate from the water used in the hydrolysis step or by internal transfer – their origin will be discussed in the following section.

2. Deuterolysis [27,28]

If the hydrogen is acquired during the simple hydrolysis of organochromium compounds or their rearrangement products, then the products of deuterolysis should be monodeuteriotoluene and monodeuterio-*o*-methyldiphenylmethane, both free and in the π-complex. However, the results of the deuterolysis experiments (Table 2 [27]; Section VI) indicate that other reactions take place besides those of simple deuterolysis. The hydrogen deuteride observed may arise from the deuterolysis of a chromium hydride

[27] *R. P. A. Sneeden, F. Glockling*, and *H. Zeiss*, J. organomet. Chemistry *6*, 149 (1966).

[28] *R. P. A. Sneeden* and *H. Zeiss*, unpublished.

Table 2. Composition [a] of toluene and *o*-methyldiphenylmethane isolated from organic products and from bis (π-arene) complex obtained in the reaction of benzylmagnesium chloride and $CrCl_3 \cdot 3THF$, ratio 3:1, −78 ° to 20 °C in diethyl ether and subsequent deuterolysis.

Experiment No.	Toluene					*o*-Methyldiphenylmethane						π-Complex	Ref.
	[b]	D_0	D_1	D_2	D_3	[b] [c]	D_0	D_1	D_2	D_3	D_4	[b]	
1 [d]	50.6	58	26	8.7	7.5	11.2	74 [e]	17 [e]	5 [e]	3 [e]	1 [e]	2.8	[27]
2	49.5	64.5	15.9	10.2	8.8	[f]						2.9	[27]
3 [g]	42.2	65.0	13.0	10.8	10.6	[f]						2.4	[27]
4 [h]	62.7	44.6	45.2	4.6	5.2	8.1	37	50	5	4	3	1.86	[28]
5	58.9	39.1	49.2	5.7	5.6	7.0	44.3	44.6	5.3	3.6	1.8		[28]
6 [i] a) Filtrate	24.7	71.8	25.5	0.8	1.9	3.2	76.2	22.6	0.7	0.5	—	0.23	[28]
b) Residue	23.9	41.6	28.2	14.0	15.0	6.2	38.0	36.2	9.9	10.1	4.9	5.7	[28]
7 [j]	59.4	97.4	2.2	0.4		10.4	97.7	1.7	0.6			4.8	[28]
From the bis-(π-arene) complex													
1	[f]	17.2	65.3	8.5	9.0	[f]	21	57	15	6	1		
4	[f]	17.0	60.3	10.0	12.2	[f]	12.9	50.1	23.3	10.4	2.8		
6b	[f]	22.3	57.5	9.6	9.8	[f]	28.0	52.2	12.0	6.7	1.0		
7	[f]	98.3	1.35	0.2		[f]	97.5	1.9	0.5	0.1			

[a] Expressed in relative percentages and corrected for natural isotopic abundance; [b] Quantity expressed in mmoles/100mmoles $H_5C_6CH_2MgCl$; [c] Representing total of 1,2-diphenylethane and *o*-methyldiphenylmethane formed; [d] In this reaction it was shown that D_2 (81 %) HD (18.2 %) and H_2 (0.2 %) were formed at the deuterolysis step; [e] 1,2-Diphenylethane content included; [f] Not measured; [g] Reaction carried out in the presence of dihydroanthracene; [h] *p*-xylene added before deuterolysis: recovered *p*-xylene was 100 % C_8H_{10}; [i] In these the crude reaction mixture was filtered, the filtrate and residue being deuterolysed separately; [j] Hydrolysis carried out with water in deuterium gas atmosphere.

intermediate. The undeuterated toluene and *o*-methyldiphenylmethane can arise only by a process of internal hydrogen transfer.

The presence of two or three deuterium atoms in the toluene and *o*-methyldiphenylmethane, both free and in the bis(π-arene) complex, indicate an H/D exchange reaction.

Experiments in the presence of anthracene and dihydroanthracene (see Table 2 and [27]), established that at no stage during the reaction were benzyl radicals released into solution. Therefore, the processes of hydrogen abstraction and hydrogen transfer all occur within the confines of an organochromium complex. In order to establish that this applies also to the H/D exchange reaction, it was first necessary to establish that the latter is promoted neither by the presence of the bis(π-arene)chromium(0) or-(I) complex, nor by colloidal chromium.

Thus it was found that when tribenzylchromium rearranges in diethyl ether solution in the presence of *p*-xylene and the reaction mixture is deuterolysed, the *p*-xylene recovered is deuterium-free (cf. Section VI). Furthermore, when a mixture of undeuterated π-(*o*-methyldiphenylmethane)-π-toluenechromium(0) and -(I) deuteroxide in benzene/D_2O is allowed to interact with D_2O/D_2, the toluene in the recovered bis(π-arene)chromium contains only traces of deuteriotoluenes (cf. Section VI).

An interpretation of these results must begin with a consideration of the behavior of tribenzylchromium. Replacement of the tetrahydrofuran in the initial tribenzylchromium complex by diethyl ether induces homolysis of the benzyl-chromium bond. The benzyl radical remains within the confines of the organochromium compound and reacts either with the solvate or with a σ-bonded benzyl group. This leads to the following considerations:

1. Hydrogen abstraction from a molecule of solvate (diethyl ether or tetrahydrofuran) gives undeuterated toluene and solvated dibenzylchromium(II). The *cis*-form of the latter can undergo *ortho*-coupling to (*o*-phenylmethylbenzyl)chromium hydride *(16)*.

2. Oxidative coupling of two benzyl groups bonded to chromium gives undeuterated 1,2-diphenylethane and benzylchromium(I) *(17)*.

$$(C_6H_5CH_2)_3Cr \cdot xS \longrightarrow C_6H_5CH_2CH_2C_6H_5 + C_6H_5CH_2Cr(I) \cdot xS \qquad (g)$$

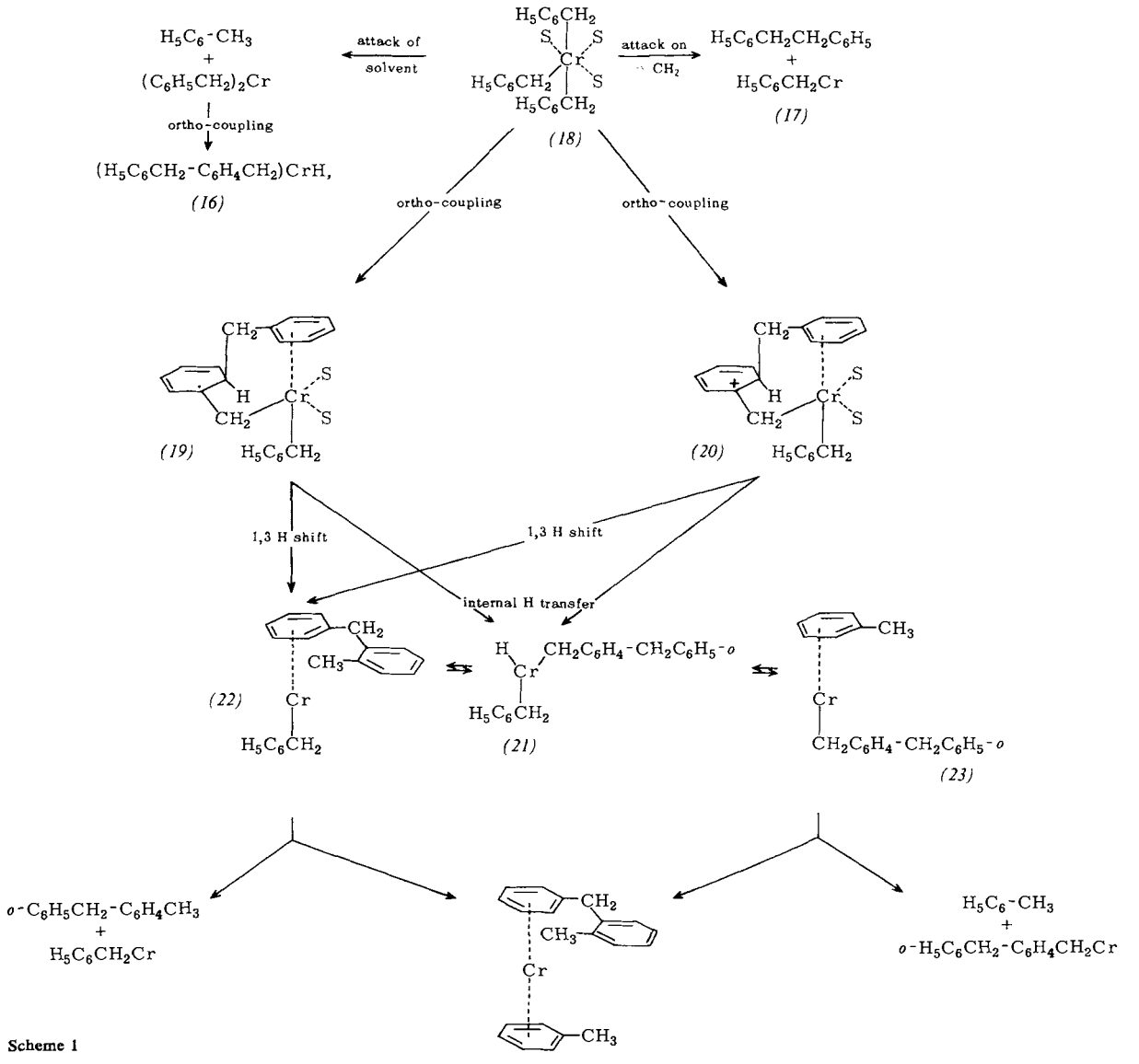
Neither of the reactions 1) or 2) leads directly to the bis(π-arene) complex, but both effectively reduce the amount of tribenzylchromium available for the ultimate formation of bis(π-arene) complex.

3. Two of the benzyl groups in tribenzylchromium *(18)* are suitably juxtaposed, for *ortho*-coupling to the radical *(19)* (see Scheme 1). This concept is supported by the recent observation that the pyridine molecules which are coordinated to chromium in $CrCl_3 \cdot 3$ pyridine are attacked by phenyl radicals, generated in solution, giving a mixture of 2-phenylpyridine (45 %), 3-phenylpyridine (19 %) and 4-phenylpyridine (36 %) [29]. Alternatively, ortho-coupling by an ionic mechanism gives the carbonium ion *(20)*. In both cases a 1,3-hydrogen shift produces undeuterated *o*-methyldiphenylmethane whereas hydrogen transfer to chromium leads to (*o*-phenylmethylbenzyl) benzylchromium hydride *(21)*.

Scheme 1 requires that some of the undeuterated toluene and *o*-methyldiphenylmethane be present in the reaction mixture before deuterolysis. This was confirmed by filtering the crude reaction mixture and deuterolysing separately the filtrate and residue. The toluene and *o*-methyldiphenylmethane found in the filtrate contain considerably more of the undeuterated species (see Table 2, reaction 6) than do those found in the residue.

The organic products, isolated after deuterolysis, always contain more toluene than the combined total of *o*-methyldiphenylmethane and 1,2-diphenylethane

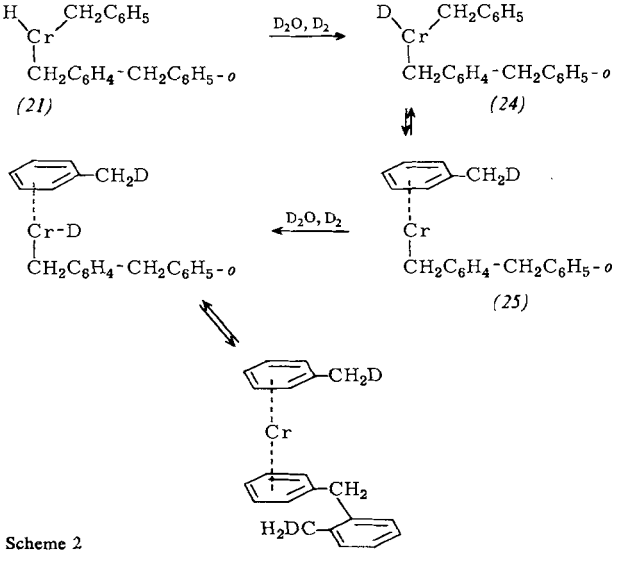
[29] *R. J. Gritter* and *A. W. Godfrey*, J. Amer. chem. Soc. *86*, 4724 (1964).



Scheme 1

(cf. Table 2). The relative isotopic compositions of the toluene and *o*-methyldiphenylmethane are similar; this implies that they are formed from similar but not necessarily the same precursors. Previous experiments on the deuterolysis of benzylchromium(III) compounds[29a] exclude organochromium(III) compounds as possible precursors. Although no experimental evidence is available, reasoning from recent theory concerning H/D exchange reactions[30,31] suggests that either an organochromium(I) compound [*e.g.*, $C_6H_5CH_2Cr \cdot xS$ *(17)*] or an organochromium(II) hydride [*e.g.*, *o*-$C_6H_5CH_2CH_2CrH$ *(16)*] is likely.

The relative deuterium contents of the toluene and *o*-methyldiphenylmethane isolated on pyrolysis of the bis(π-arene) complex are very similar, indicating that the precursor to the π-complex in which the H/D exchange occurs, must contain both future arene parts. Such an intermediate is the organochromium(III)-hydride *(21)*, which is in equilibrium with or progresses to the "tautomeric"[32] arene forms *(22)* and *(23)* (Scheme 1). Thus the hydride *(21)* reacts with D_2O to



Scheme 2

[29a] See footnote [*] p. 436.

[30] *E. Crawford* and *C. Kemball*, Trans. Faraday Soc. *58*, 2452 (1962).

[31] *J. L. Garnett* and *W. A. Sollich*, Nature (London) *201*, 902 (1964).

[32] *J. Chatt* and *J. M. Davidson*, J. chem. Soc. (London) *1965*, 843, were the first to use the term "tautomerism" for this type of system.

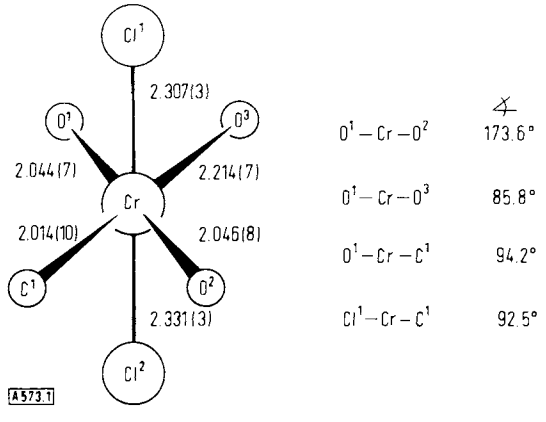
give the corresponding deuteride [Scheme 2, *(24)* and 2, *(25)*].

A series of H/D exchanges in a σ-bonded organochromium deuteride and a series of tautomeric changes account for the formation of the bis(π-arene) complexes.

V. Structure

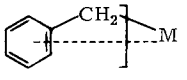
Though it had been assumed that the organic groups are directly bonded to the chromium atom on the basis of indirect evidence (*e.g.*, deuterolysis, reaction with $HgCl_2$, *etc.*) there was no direct evidence for this assumption. This has now been supplied by single crystal X-ray structure determinations of $Li_3Cr(CH_3)_6 \cdot 3$ dioxane and $(p\text{-}CH_3C_6H_4)CrCl_2 \cdot 3THF$.

The data for the first compound [33] have not been refined but they show that all six methyl groups are octahedrally disposed around the chromium atom (C–Cr bond distance ≈ 2.15 Å). The data for $(p\text{-}CH_3C_6H_4)CrCl_2 \cdot 3THF$, summarized in Fig. 1 show: i) the *p*-tolyl group is bonded to the chromium atom through one carbon atom (C–Cr bond distance 2.104 Å ± 0.010 Å); ii) the length of the chromium oxygen bond *trans* to the σ-bonded *p*-tolyl group is significantly greater than the other two (2.214 ± 0.007 Å as against 2.045 ± 0.008 Å). This trans effect could account for the selective loss of and for the replacement of one tetrahydrofuran molecule from $(C_6H_5)_3Cr \cdot 3THF$ [34] (see Section IV. 2). Reference

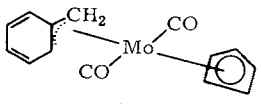


has been made earlier to the striking differences in the reactions of the benzyl- and *p*-tolyl-chromium systems. In the case of the triorgano-chromium compounds, coupling of one of the benzyl groups occurs with the *ortho* position of another, whereas in the *p*-tolyl system one of the *p*-tolyl groups couples with another to give exclusively the *para* substituted product (cf. Section IV.1). In the case of the monoorganochromium compounds, the benzyl compound is stable towards water (< 0 °), reduces $FeCl_3$, and absorbs strongly in the visible region [15b], whereas the *p*-tolyl compound is rapidly hydrolysed, does not reduce $FeCl_3$, and absorbs weakly in the visible region [16a].

It follows therefore that there are certain special features associated with the benzyl-group when bonded to metal centers. In the case of chromium it has already been suggested [2] that the benzyl group, in analogy to the allyl group, can act as a bidentate ligand (cf. *(26)*). If such a situation pertains, the reactivity of the *ortho* position (and of the *ortho* hydrogen) will be considerably enhanced. This is reflected in the recent observations [35] that the reactivity of the *ortho* carbon atom in the benzyl Grignard compound is enhanced. Furthermore, in the case of molybdenum, two benzylmolybdenum complexes have recently been prepared [36], one $(C_6H_5CH_2)Mo(CO)_3(C_5H_5)$ has been formulated as a pure σ-bonded compound, the other $(C_6H_5CH_2)Mo(CO)_2(C_5H_5)$, formed by loss of one carbon monoxide ligand, has been formulated on the basis of NMR evidence as the π-benzyl compound *(27)*.



(26)



(27)

VI. Experimental

For general reaction conditions, product isolation techniques, and preliminary results of deuterolysis see earlier publications [2, 27].

a) *Reaction of Benzylmagnesium chloride with $CrCl_3 \cdot 3THF$ (ratio 3:1) and Deuterolysis of the Complex Formed*

Ethereal benzylmagnesium chloride (300 ml, 189 mmoles) was added, over 15 min, to a briskly stirred suspension of $CrCl_3 \cdot 3THF$ (23.6 g, 63 mmoles) in diethyl ether (150 ml) at −78 °C. After 30 min at this temperature, the dark reaction mixture was allowed to warm to 20 °C (Gilman Color Test No. 1, negative). After 3 h at 20 °C, pure, oxygen-free *p*-xylene (13.4 g, 126 mmoles) was added; the reaction mixture was stirred briskly and D_2O added. The final deuterolysis mixture was filtered through a sinter disc, under nitrogen pressure, the residue being washed with ether, water, and hot acetone until the washings were colorless. The combined etheral layers were dried with Na_2SO_4 and shown by gas chromatography to contain: tetrahydrofuran (150 mmoles), toluene (119 mmoles), *p*-xylene (118 mmoles), *o*-methyldiphenylmethane and 1,2-diphenylmethane (total 15.4 mmoles, corrected for 1,2-diphenylethane in the benzyl-Grignard solution). The more volatile components were separated by fractional distillation. The pure compounds, isolated by preparative gas chromatography, were shown by mass-spectroscopy [37] to have the compositions: tetrahydrofuran, C_4H_8O, 100 %; *p*-xylene, C_8H_{10}, 100 %; toluene (see Table 2,

[33] *J. Krause*, Proceedings 9th internat. Conference on Coordination Chemistry, St. Moritz, Sept. 1966, p. 168. Helvetica Chimica Acta, Basle.

[34] *J. Hähle* and *G. Stolze*, Z. Naturforsch. *19b*, 1081 (1964).

[35] *R. A. Benkeser* and *T. E. Johnston*, J. Amer. chem. Soc. *88*, 2220 (1966).

[36] *R. B. King* and *A. Forzaglia*, J. Amer. chem. Soc. *88*, 709 (1966).

[37] We wish to thank Dr. *W. E. Koerner* and his associates of the Monsanto Company, Research Center, St. Louis, Mo., USA for determining the mass spectra.

reaction 4). The residue from the above distillation was further separated by column chromatography into 1,2-diphenylethane [m.p. and mixed m.p. 52–53 °C; δ(TMS) = 2.87 (CH_2)] and *o*-methyldiphenylmethane, [δ(TMS) = 3.91 (CH_2) and 2.18 (CH_3)]. On many columns the gas-chromatographic retention times of these two compounds are the same. NMR spectroscopy is thus the only reliable method of analysis. The isotopic composition of these compounds is given in Table 2, reaction 4. The aqueous layers were combined with the concentrated acetone extracts, filtered, and treated with $NaB(C_6H_5)_4$ (5.2 g, in H_2O 100 ml). The crude π-(*o*-methyldiphenylmethane)-π-toluenechromium(I) tetraphenylborate (2.26 g, 3.52 mmoles) was pyrolysed to give benzene and biphenyl (from the $^{\ominus}B(C_6H_5)_4$ anion), toluene, and *o*-methyldiphenylmethane. There was no trace of *p*-xylene or 1,2-diphenylethane. The isotopic composition of the toluene and *o*-methyldiphenylmethane [δ (TMS) = 3.91 (CH_2) and 2.18 (CH_3)], are given in Table 2, reaction 4.

b) *Benzylmagnesium chloride and $CrCl_3$·3THF (molar ratio 3:1), Filtration and Deuterolysis*

Ethereal benzylmagnesium chloride and $CrCl_3$·3THF, (molar ratio 3:1), were allowed to interact under the conditions described above. The reaction mixture was filtered though a sinter disc under nitrogen pressure. The residue was suspended in pure, dry, oxygen-free diethyl ether and the resulting suspension and the filtrate were deuterolysed. The products were isolated and estimated as described in the previous experiment. The distribution of toluene, 1,2-diphenylethane, and *o*-methyldiphenylmethane, and the bis-(π-arene) complex between the filtrate and the residue is given in Table 2. The isotopic composition of these products is also given in Table 2, reaction 6.

c) *(p-Tolyl)Cr(III) Cl_2·3THF*

Equimolar ratios of *p*-tolylmagnesium chloride and $CrCl_3$·3THF were allowed to react in tetrahydrofuran at −50 °C. On warming to 20 °C (3 h) the pink crystalline solid gradually dissolved, to give finally a clear green solution. This was cooled to −20 °C (24 h), and the yellow-green solid which had formed was removed by filtration under argon. Crystallization of this substance from tetrahydrofuran was carried out in a Schlenk tube, in vacuum, in the temperature range −30 ° to 20 °C. The results of elemental analysis, molecular-weight determination (found 425.2, based on measured density d_4^{20} = 1.315; calc., 430.4 [40]), and the paramagnetic nature of the compound (3.87 B.M. [38]) show it to be (*p*-tolyl)Cr(III)Cl_3·3THF. Optical data: λ_{max}(THF) 445 nm; ε_{max} 137.

d) *Attempted H/D Exchange in Bis(arene)chromium Complexes*

Crude π-(*o*-methyldiphenylmethane)-π-toluenechromium(I) hydroxide (5 mmoles) (from the benzyl Grignard compound and $CrCl_3$·3THF, ratio 3:1) was reduced in benzene (as the chromium(0) complex) with alkaline sodium dithionite [39]. The aqueous layer was replaced by D_2O (50 ml) and dry oxygen was bubbled through the system. The color passed from the benzene into the D_2O layer, indicating the formation of the chromium(I) deuteroxide. Metallic sodium was added cautiously until the color was evenly distributed between the benzene and D_2O. The apparatus was flushed with D_2, sealed, and left for 24 h at 20 °C. Dry oxygen was again bubbled through the system and the bis(π-arene) complex recovered quantitatively from the D_2O layer as its tetraphenylborate. The toluene, obtained by the pyrolysis of the crude salt, was isolated by preparative gas-chromatography and had the composition [37]: C_7H_8, 97.2; C_7H_7D, 2.6; $C_7H_6D_2$, 0.2 %.

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German version: Angew. Chem. 77, 401 (1965)

[38] Kindly determined by Drs. *G.* and *S. Olivé* of MRSA, Zürich, the value is for a tetrahydrofuran solution, and is based on a molecular weight of 430.4.

[39] *W. Herwig* and *H. Zeiss*, Liebigs Ann. Chem. *606*, 209 (1957).

[40] Kindly determined by Dr. *J. J. Daly* of MRSA Zurich, by an X-ray evaluation of the cell dimensions.

COMMUNICATIONS

Metalated Orthothioformates

By *D. Seebach* [*]

Dedicated to my tutor, Professor Rudolf Criegee, on his 65th birthday

Little is known about metalated orthothioformates [1]. By adding equimolar amounts of butyl-lithium [2] to the orthothioformates *(1a)* to *(1f)* in tetrahydrofuran at −78 °C [3,4], we obtained solutions of the lithium compounds *(2a)* to *(2f)*. Hydrolysis of the metalated compounds *(2)* with D_2O affords the deuterated orthoesters *(1a')* to *(1f')*. The compounds *(2)* are also formed conveniently from orthothiocarbonates *(3)* and butyl-lithium. (Previously, a carbon-sulfur bond cleavage of this kind had only been observed with sp-hybridized carbon [5].) Thus, the orthothioformate *(1d)* (b.p. = 74 °C/0.35 mm, n_D^{20} = 1.6180) is isolated in 70 % yield on cleavage of *(3d)* (m.p. = 32.3–32.7 °C [6]) and subsequent hydrolysis. We found the following order of decreasing thermal stability [1,7]: *(2a)* > *(2e)* ⋙ *(2d)* ~ *(2f)* > *(2c)* (cf. Table 1).

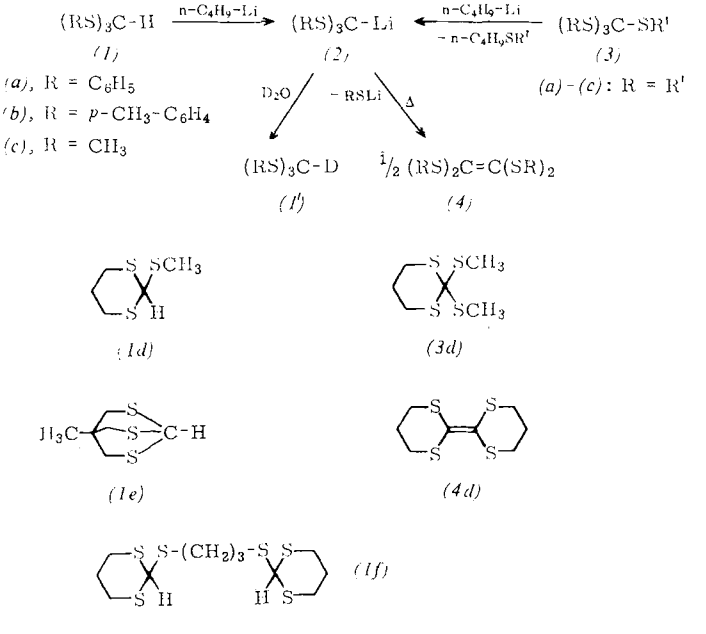


Table 1. Thermal decomposition of *(2)* to the ethylene derivatives *(4)* in tetrahydrofuran.

	(2) Conc. (mole/l)	Temp. (°C)	Time (h)	*(4)* M.p. (°C)	Yield (%)
(a)	0.2	20	24	154.5—155.0 ([1]: 153—154.5)	15
	0.2	65	12		70
(c)	0.3	−20	2	60.5—61.5 ([1]: 59—60)	80
(d)	0.1	−30	20	140.8—141.6	80
(e)	0.1	0	24	—	stable [a]
(f)	0.1	0	14	*(4d)* 140.0 — 141.0	60

[a] *(2e)* decomposes to an extent of *ca.* 60 % in 24 h at room temperature; the product of decomposition was not isolated.

With electrophiles the compounds *(2)* give good yields of products only if the reactions take place rapidly and well below the decomposition temperatures. Table 2 lists some of the products we obtained upon alkylation, hydroxyalkylation, acylation, thiolation, silylation, and oxidative dimerization. Because of its great stability and favorable stereochemistry the bicyclic *(2e)* gives the highest yields. Among the products $(RS)_3C-R^1$, the ethanes substituted by six RS-groups ($R^1 = C(SC_6H_5)_3$ and $R^1 = C(SCH_3)_3$) are of special interest, the first one being cleaved quantitatively above 150 °C (1 mm) to yield *(4a)* and diphenyldisulfide.

Table 2. Products $(RS)_3C-R^1$ of the reactions [a] of metalated orthothioformates *(2a)* [c].

Reagent	R^1 of product	Yield (%)	M.p. (°C)
CH_3I	CH_3	80—88	145.5—146.5 ([8]: 145—146)
CH_3CHICH_3	$CH(CH_3)_2$	22 (64)	119.9—120.2 (64—66)
C_6H_5CHO	$CH(OH)C_6H_5$	78 (79)	139—141 (174.6—175.4)
C_3H_7CHO	$CH(OH)C_3H_7$	75	60—63
Cyclohexanone	$(HO)C_6H_{10}$	0 [b] (77)	(174.8—175.3)
Benzophenone	$C(OH)(C_6H_5)_2$	(74)	(172.5—173.2)
Propylene oxide	$CH_2-CH(OH)CH_3$	24	90.4—91.4
$Cl-Si(CH_3)_3$	$Si(CH_3)_3$	50	101—102
$Cl-COOC_2H_5$	$COOC_2H_5$	15 (52)	85.5—86.5 (104.2—104.8)
CH_3S-SCH_3	SCH_3	80 (78)	95.2—95.8 (123.5—124.0)
$C_6H_5S-SC_6H_5$	SC_6H_5, *(3a)*	86	158.8—159.4 ([9]: 159)
$I_2/2$	$C(SC_6H_5)_3$	89	196—197 (decomposition)
$K_3Fe(CN)_6$		30	

[a] The reagent was added at −78 °C and the temperature was allowed to rise to 20 °C. — The infrared and NMR-spectra are consistent with the structures given.

[b] More than 90 % enolate formation.

[c] Figures in brackets are products of reaction with *(2e)*.

We are now investigating the use of reagents of type *(2)* for nucleophilic carboxylations (for instance, we have obtained mandelic acid by hydrolysis of the orthothiomandelic acid triphenyl ester, $R^1=CH(OH)C_6H_5$, with mercuric chloride in aqueous acetone (2 days at 20 °C, yield 60 %)).

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[*] Dr. D. Seebach
Institut für Organische Chemie der Technischen Hochschule
Richard-Willstätter-Allee
75 Karlsruhe (Germany)

[1] *A. Fröling* and *J. F. Arens*, Recueil Trav. chim. Pays-Bas *81*, 1009 (1962); *J. Hine et al.*, J. Amer. chem. Soc. *84*, 1751 (1962); *(2a)* and *(2)*, R = C_2H_5, were investigated independently under the conditions described here by *G. A. Wildschut, H. J. T. Bos, L. Brandsma*, and *J. F. Arens* (Mh. Chem., in press); I thank Prof. *Arens* for informing me accordingly.

[2] *E. J. Corey* and *D. Seebach*, Angew. Chem. *77*, 1134 (1965); Angew. Chem. internat. Edit. *4*, 1075 (1965); J. org. Chemistry *31*, 4097 (1966).

[3] *(1a)* to *(1c)* and *(1f)* were prepared under HCl-catalysis in $CHCl_3$ from orthoformates and thiols. For *(1e)* see *W. v. E. Doering* and *L. K. Levi*, J. Amer. chem. Soc. *77*, 509 (1955).

[4] *(2a)* is generated under the same conditions also with triphenylmethyl-lithium; with methylsulfinyl sodium one obtains the sodium derivative corresponding to *(2a)*.

[5] *L. Brandsma*, Recueil Trav. chim. Pays-Bas *83*, 307 (1964).

[6] From lithiumdithiane [2] and dimethyldisulfide; yield: 70 % based on unrecovered 1,3-dithiane.

[7] *D. Seebach*, Angew. Chem. *79*, 469 (1967); Angew. Chem. internat. Edit. *6*, 443 (1967).

[8] *D. S. Tarbell* and *A. H. Herz*, J. Amer. chem. Soc. *75*, 1668 (1953).

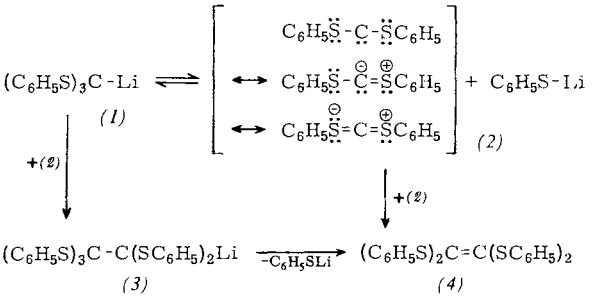
[9] *F. Arndt*, Liebigs Ann. Chem. *396*, 1 (1913).

Bis(phenylthio)carbene

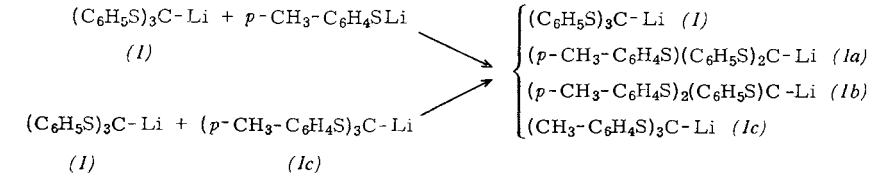
By *D. Seebach* [*]

Dedicated to my tutor, Professor Rudolf Criegee, on his 65th birthday

We have found evidence of the existence of a true equilibrium between a carbenoid (tris(phenylthio)methyl-lithium *(1)* [1]) and a carbene (bis(phenylthio)carbene *(2)*) in solution. The formation of tetrakis(phenylthio)ethylene *(4)* from the equilibrium mixture takes place either by dimerization of the carbene *(2)* or *via* the intermediate *(3)* [1]. Since the reaction is irreversible and very slow, even at room temperature, we were able to study the presumed equilibrium *(1)* ⇌ *(2)* conveniently [2]:



1. Addition of lithium thiophenolate drives the equilibrium towards *(1)*, thus decreasing the rate of formation of compound *(4)* (Table 1).



2. Addition of Li *p*-thiocresolate gives a mixture of *(1)*, *(1a)*, *(1b)*, *(1c)*, *i.e.* *p*-tolylthio groups are incorporated into the carbenoid *via (2)*; after a reaction time of 20 h at a temperature of −10 °C the mixture was hydrolysed with D_2O and H_2O and the formation of the lithium compounds *(1)* through *(1c)* proved by NMR analysis of the hydrolysates [3].

3. Under the same conditions the four products are obtained in a ratio of approximately 1:2:2:1 after mixing (1:1) solutions of *(1)* and *(1c)*.

4. Electrophiles (see Table 1) which cannot react easily with the bulky carbenoid *(1)*, but which can be attacked by the non-hindered thiophenolate without difficulty, trap C_6H_5S–Li, drive the equilibrium towards *(2)*, and increase the rate of formation of the ethylene *(4)*: three times as much *(4)* is obtained – under otherwise identical conditions – in the presence of 2 moles of propylene epoxide as in the absence of any "additive"; 1 mole of the higher substituted epoxide of cyclohexene traps thiophenolate so effectively that the yield of *(4)* becomes five times as high (Table 1). [In the first case the reaction products were, *(4)* (44 %), $(C_6H_5S)_3C-CH_2-CH(OH)CH_3$ (26 %) [1], and $C_6H_5S-CH_2-CH(OH)CH_3$ (30 %) b. p. 75 °C / 0.06 mm; $n_D^{20} = 1.5698$ [4]: b.p. 86 °C/0.35 mm; $n_D^{20} = 1.5705$). Similar results are obtained on alkylation (Table 1).]

Table 1. Yield of tetrakis(phenylthio)ethylene *(4)* from *(1)* in the presence of electrophilic reagents (0.2 M solution in tetrahydrofuran/n-hexane 10:1; 10 mmole scale; 24 h at 20 °).

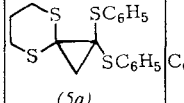
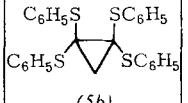
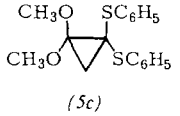
Reagent (mole/mole *(1)*)	–	C_6H_5SLi 1	Propylene oxide 2	Cyclohexene oxide 1	CH_3I 2	$(CH_3)_2CHI$ 2
(4), Yield (%)	15	5	44	74 [a]	0	45 [b]

[a] In the presence of 1 mole of lithium *trans*-2-phenylthio-cyclohexanolate-1 we obtained 25 % of *(4)* from *(1)*.

[b] 10 % of *(4)* was isolated under identical conditions when *(1)* decomposed in the presence of 1 mole of LiI.

5. Certain nucleophiles remove the weakly electrophilic carbene [5] from the equilibrium. Thus, the cyclopropanedione derivatives *(5)* are obtained (at 20 ° after several days) with 1,1-bis(methylthio)- and 1,1-dimethoxyethylene (Table 2).

Table 2. Cyclopropanes obtained by adding 1 equivalent of activated ethylenes to the equilibrium mixture.

Starting material b.p. (°C/mm); n_D^{20}	2-methylene-1,3-dithiane 80/10; 1.6064	$(C_6H_5S)_2C=CH_2$ 138/0.75; 1.6484	$(CH_3O)_2C=CH_2$
Products	 *(5a)*	 *(5b)*	 *(5c)*
Yield (%)	66	78	15
M.p. (°C)	110.2–110.9	90.0–90.7	[a]
NMR signal of cyclopropane CH_2-protons, τ (ppm), CCl_4	8.26	8.12	8.51

[a] Oil after chromatographing twice on silica gel.

Addition of 1 mole of a phosphine gives (after 5 h at room temperature) the rather inert, isolable ylides *(6)* in more than 80 % yield.

$$(C_6H_5S)_2C{=}P(n\text{-}C_4H_9)_3 \xrightarrow[48h;\ 20°C]{THF/H_2O/KOH} (C_6H_5S)_2CH_2$$

(6a)

The NMR spectrum of *(6a)* (m.p. 79–81 °C; molecular weight cryoscopically in C_6H_6: 432) shows only peaks of aromatic and aliphatic protons, ratio 10:27; that of *(6b)* (C_6H_5 instead of n-C_4H_9 in *(6a)*; m.p. 170–172 °C; molecular weight cryoscopically in C_6H_6: 502) only aromatic protons. Ultraviolet spectrum of *(6a)*: λ_{max}(dioxane) = 256.5 nm (ε = 31000), of *(6b)*: λ_{max}(dioxane) = 253.5 nm (ε = 23000), ε_{300} = 7000, ε_{340} = 2500, ε_{380} = 950. Alkaline hydrolysis of *(6a)* gives bis(phenylthio)methane, the identity of which was established by comparison with an authentic sample [1].

Although one might discuss in some cases a reaction at the bulky, nondissociated carbenoid *(1)* [6], the observations 1.–5. described here suggest that the carbene *(2)* is present in the equilibrium mixture.

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[*] Dr. D. Seebach
Institut für Organische Chemie der Technischen Hochschule
Richard-Willstätter-Allee
75 Karlsruhe (Germany)

[1] *D. Seebach*, Angew. Chem. *79*, 468 (1967); Angew. Chem. internat. Edit. *6*, 442 (1967); and lit. [1,2] cited there.

[2] From *(4)* and an excess of Li-thiophenolate no *(1)* or *(3)* could be detected by hydrolysis and NMR analysis; the reaction *(1)* → *(4)* is therefore irreversible.

[3] By blank tests we showed that no exchange takes place, under identical conditions, between Li *p*-thiocresolate and $(C_6H_5S)_3CH$, nor did we observe exchange during any of the recovery procedures.

[4] *R. C. Fuson* and *J. H. Koehneke*, J. org. Chemistry *14*, 706 (1949).

[5] Bis(alkylthio)carbenes were trapped similarly during pyrolysis of the sodium salts of tos-NH–N=C(S-alkyl)$_2$; see *U. Schöllkopf* and *E. Wiskott*, Liebigs Ann. Chem. *694*, 44 (1966); and *D. M. Lemal* and *E. H. Banitt*, Tetrahedron Letters *1964*, 245.

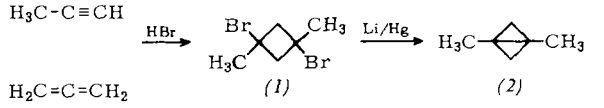
[6] Cf. *G. Köbrich*, Angew. Chem. *79*, 15 (1967); Angew. Chem. internat. Edit. *6*, 41 (1967).

Synthesis of 1,3-Dimethylbicyclo[1.1.0]butane

By *K. Griesbaum* and *P. E. Butler* [*]

Dedicated to Professor R. Criegee on the occasion of his 65th birthday

1,3-Dimethylbicyclo[1.1.0]butane *(2)* was first synthesized in an approximately 3 % overall yield [1] by the tri-n-butyltin chloride catalysed reaction of diazomethane with 1,2-dimethylcyclopropane or with the latter's precursor 2-butyne [2]. We have been able to synthesize *(2)* in high yields by means of a new two-step synthesis. Addition of hydrogen bromide to allene and/or methylacetylene leads, in a one-step reaction, to a mixture of *cis*- and *trans*-1,3-dibromo-1,3-dimethyl cyclobutane *(1)* [3]. When this mixture *(1)* is added to a suspension of 2 % lithium amalgam in dioxane and then stirred for 48 h at room temperature 1,3-dimethylbicyclo-[1.1.0]butane is produced in over 85 % yield [4]. The compound *(2)* can be isolated by fractional distillation.

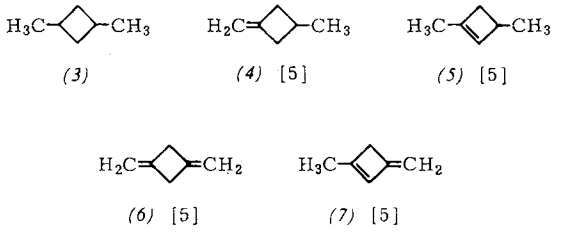


(1) *(2)*

The structural assignment of *(2)* is based on its NMR spectrum in dioxane (tetramethylsilane as internal standard, singlets at δ = 1.35 (CH_3), 1.04 (*exo*-CH_2), and 0.52 ppm (*endo*-CH_2), in the relative ratios 3:1:1, respectively) and on its time-of-flight mass spectrum (Table 1).

Analysis of the crude reaction mixture by capillary gas chromatography revealed the presence of three volatile by-

products having retention times very close to that of *(2)*. A combined analysis of the mixture by gas chromatography and time-of-flight mass spectroscopy in conjunction with an evaluation of the NMR spectra of samples in which the volatiles were substantially enriched suggested the structures *(3)* to *(7)*.



(3) *(4)* [5] *(5)* [5]

(6) [5] *(7)* [5]

Table 1. Volatile products from the debromination of 1,3-dibromo-1,3-dimethylcyclobutane with lithium amalgam.

Product	Retention time (min) [a]	Wt.-%	Molecular ion (*m/e*)	Characteristic fragment ions (*m/e*)
(3)	4.05	4.2	84 (C_6H_{12})	69 (M − CH_3); 56 (C_4H_8); 42 (C_3H_6)
(2)	4.10	87.5	82 (C_6H_{10})	81 (M − H); 67 (M − CH_3); 41 (C_3H_5)
(4) + *(5)*	4.25	5.8	82 (C_6H_{10})	81 (M − H); 67 (M − CH_3); 54 (C_4H_6)
(6) + *(7)*	4.60	2.3	80 (C_6H_8)	79 (M − H); 65 (M − CH_3); 39 (C_3H_3)

[a] Perkin-Elmer Model 226; phenylsilicone (50 %)-nitrile silicone (50 %) coated Golay column (column length 30 m).

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[*] Dr. K. Griesbaum and Dr. P. E. Butler
Enjay Polymer Laboratories
P. O. Box 45
Linden, New Jersey 07036 (U.S.A.)

[1] Based on the recovered starting material the yield was higher, *e.g.* 13 % in the reaction of diazomethane with 1,2-dimethylcyclopropene.

[2] *W. v. E. Doering* and *J. F. Coburn jr.*, Tetrahedron Letters *1965*, 991. and *J. F. Coburn jr.*, Dissertation, Yale University, 1963; Diss. Abstr. 64-7137.

[3] *K. Griesbaum*, J. Amer. chem. Soc. *86*, 2301 (1964); Angew. Chem. *76*, 782 (1964) and Angew. Chem. internat. Edit. *3*, 697 (1964); *K. Griesbaum*, *W. Naegele*, and *G. G. Wanless*, J. Amer. chem. Soc. *87*, 3151 (1965).

[4] Based on NMR analysis of the mixture before and after the reaction, using the solvent (dioxane) peak as internal standard. The result of this analysis (87 % of *(2)*) is remarkably close to that of the gas-chromatographic analysis (Table 1) which gave a value of 87.5 %.

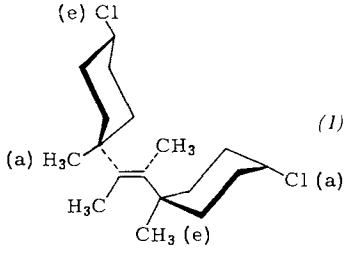
[5] The NMR spectrum of *(4)* showed a quintet for the CH_2 group at $\delta = 4.68$, downfield from TMS as internal standard. The NMR signal of the olefinic proton of *(5)* occurs at $\delta = 5.70$. The mixture of compounds *(6)* and *(7)* was identified by gas-chromatographic comparison with an authentic mixture.

Intramolecular Conformational Isomerism of the Cyclohexane Rings in Crystalline 2,3-Di-(*cis*-4-chloro-1-methylcyclohexyl)-*trans*-2-butene

By *D. Mootz* and *E. Mootz* [*]

2,3-Di-(*cis*-4-chloro-1-methylcyclohexyl)-*trans*-2-butene*(1)* [1] crystallizes from petroleum ether in a triclinic form having m.p. 97–98 °C.

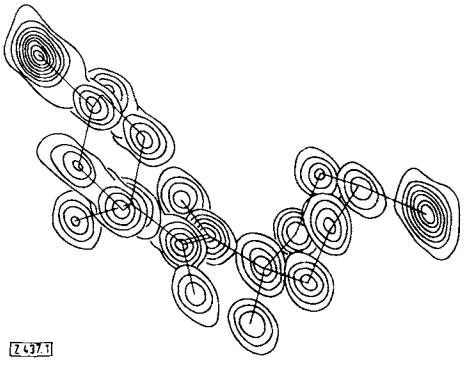
The identity of the two cyclohexane rings that one would expect from the method of preparation is confirmed by X-ray analysis in respect of configuration and substitution. However, as shown by the electron density distribution (Figure), this identity does not apply to the conformation. Both rings are in the chair form, but in one ring the chlorine atom is equatorial and the methyl group axial and in the other ring this relation is reversed. The cause of this intramolecular conformational isomerism is to be sought in an energetically more favorable packing of the molecule into the crystal lattice.



(1)

The conformation of the bonds between the rings and the butene part of the molecule can also be determined from the electron density distribution; the methyl groups attached to the rings lie on the same side of the plane of the *trans*-butene group.

1719 independent structure amplitudes were collected for the structure determination. The reflection intensities (copper radiation, integrated Weissenberg photographs) were estimated visually.



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[*] Dr. D. Mootz and Dr. E. Mootz
Institut für Molekulare Biologie, Biochemie und Biophysik,
Abteilung für Röntgenstrukturanalyse
3301 Stöckheim über Braunschweig (Germany)

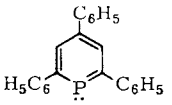
[1] We thank Professor *Inhoffen* for the substance.

Stable Anion Radicals from 2,4,6-Triphenylphosphabenzene

By *K. Dimroth* and *F. W. Steuber* [*]

2,4,6-Triphenylphosphabenzene *(1)* gives stable radicals on oxidation [1] as well as on reduction. We here report three reduction stages, which are produced by the action of metallic potassium, as a potassium mirror, or of potassium/

sodium alloy on a solution of 2,4,6-triphenylphosphabenzene in tetrahydrofuran.



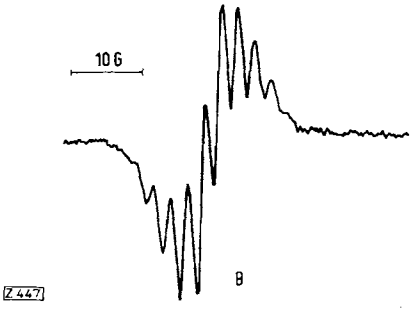
(1)

At first a solution is obtained that exhibits green fluorescence and whose ESR spectrum shows a doublet without fine structure; the phosphorus coupling constant a_P = 32.4 gauss (Fig. A).



If an equally concentrated benzene solution of the radical (a_P = 23.2 gauss) obtained by oxidation[1] is then added, the ESR signals of both radicals disappear. According to the UV spectrum, 2,4,6-triphenylphosphabenzene has been reformed.

On further action of potassium upon the radical anion (a_P = 32.4 gauss) in tetrahydrofuran the solution gradually becomes deep red and the ESR signal disappears. Further reaction with potassium then gives rise to a new signal (Fig. B).



Addition of 0.5 equivalent of a solution of unchanged 2,4,6-triphenylphosphabenzene then again gives a solution without an ESR signal, but addition of 2 equivalents leads to a solution with the above mentioned doublet in the ESR spectrum (a_P = 32.4 gauss).

Thus 2,4,6-triphenylphosphabenzene can take up three electrons stepwise. The reduction products can also release the electrons stepwise.

All three reduction stages (monoanion radical, non-radical dianion, and trianion radical) can be kept unchanged for several days if air is rigorously excluded.

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[*] Prof. Dr. K. Dimroth and Dr. F. W. Steuber
Institut für Organische Chemie der Universität
Bahnhofstr. 7
355 Marburg (Germany)

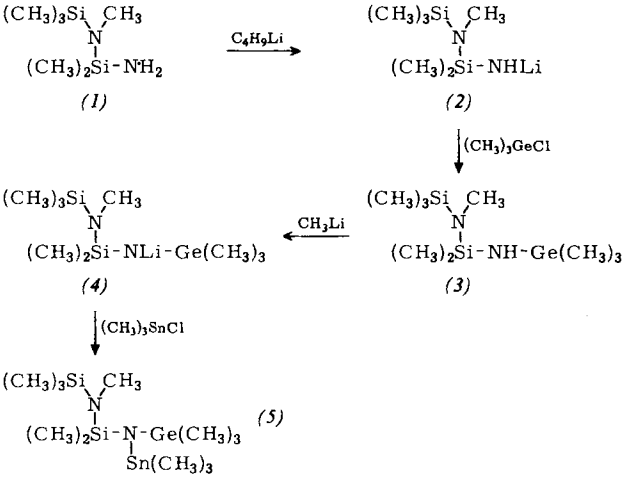
[1] *K. Dimroth, N. Greif, H. Perst,* and *F. W. Steuber,* Angew. Chem. 79, 58 (1967); Angew. Chem. internat. Edit. 6, 85 (1967).

Synthesis of a Germylsilylstannylamine

By *O. J. Scherer* and *D. Biller*[*]

As an adjunct to our studies of tri- and di-organometalylamines[1] we have achieved the first synthesis of an amine carrying the three carbon "homologues" silicon, germanium, and tin on the nitrogen atom.

On metalation with a solution of butyl-lithium in hexane at −78 °C, an ethereal solution of dimethyl[methyl(trimethylsilyl)amino]silylamine *(1)*[2] gives lithium dimethyl[methyl(trimethylsilyl)amino]silylamide *(2)*, which is readily soluble in this solvent mixture.



Treating this salt with chlorotrimethylgermane in ether at 0 °C gives a 50 % yield [calculated on *(1)*] of *N*-{dimethyl-[methyl(trimethylsilyl)amino]silyl}(trimethylgermyl)amine *(3)*. This amine is a clear, readily hydrolysable liquid of b.p. 45–47 °C/0.2 mm, and is readily soluble in proton-inactive organic solvents. Its ^{1}H–NMR spectrum (Varian A60, 60 MHz; 10 % solution in CCl_4; tetramethylsilane as internal standard) contains the expected signals with the calculated relative intensities τ = 9.95 [$(CH_3)_2Si$], 9.92 [$(CH_3)_3Si$], 9.74 (CH_3Ge), and 7.54 (CH_3N).

Further metalation of *(3)* with ethereal methyl-lithium solution at −78 °C gives lithium *N*-{dimethyl[methyl(trimethylsilyl)aminosilyl}(trimethylgermyl)amide *(4)*, which with chlorotrimethylstannane in ether at 0 °C affords *N*-{dimethyl[methyl(trimethylsilyl)aminosilyl}-*N*-(trimethylgermyl)(trimethylstannyl)amine *(5)*. The yield amounts to 60 % [calculated on *(3)*].

The amine *(5)* is a clear liquid that is readily hydrolysable and readily soluble in proton-inactive organic solvents, and can be distilled at 84–86 °C/0.2 mm without dismutation. Its composition follows from elemental analysis, molecular-weight determination, and ^{1}H–NMR spectrum (sharp signals at τ = 9.92 [$(CH_3)_3Si$ and $(CH_3)_2Si$], 9,73 (CH_3Sn), 9.69 (CH_3Ge), and 7.55 (CH_3N); $J_{117,119Sn-C-H}$ = 53.0 and 56.0 Hz; the relative intensities observed agree well with those calculated).

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[*] Dr. O. J. Scherer and Dipl.-Chem. D. Biller
Institut für Anorganische Chemie der Universität
Röntgenring 11
87 Würzburg (Germany)

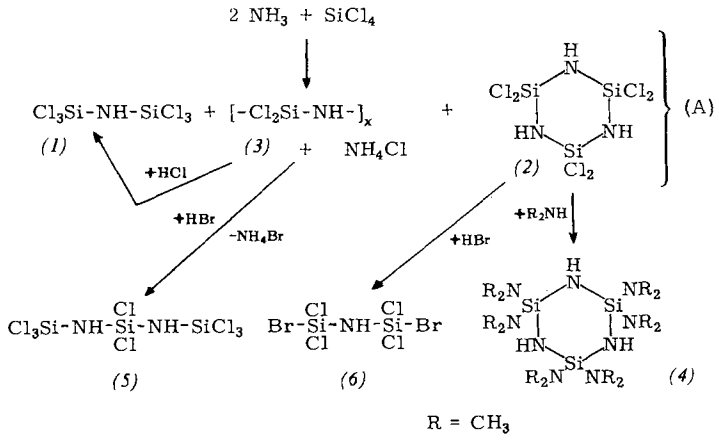
[1] *O. J. Scherer* and *M. Schmidt,* J. organometal. Chem. *1*, 496 (1964); *3*, 156 (1965).

[2] *O. J. Scherer, D. Biller,* and *M. Schmidt,* Inorg. nucl. Chem. Letters *2*, 103 (1966).

Synthesis of New Silazanes by Reaction of Silicon Tetrachloride with Ammonia [1]

By *U. Wannagat, P. Schmidt,* and *M. Schulze*[*]

If 2 mole equivalents of ammonia are passed, with stirring, into an ethereal solution of 1 mole equivalent of silicon tetrachloride at −78 °, a precipitate is formed having the approximate composition $Cl_4SiN_3H_9$ (A). It consists mainly of a mixture of hexachlorodisilazane *(1)*, oligomeric *(2)* and polymeric (–$SiCl_2$–NH–) units *(3)*, and ammonium chloride.



When (A) is heated at 80 °C/*ca.* 1 mm, the product *(1)* [2] first distils off. The oligomer *(2)* sublimes in low yield (*ca.* 3 %) onto a cold finger with the last portions of *(1)*.

Treating the residual $(Cl_2SiNH)_x/NH_4Cl$ mixture with HCl in ether leads to a further quantity of *(1)*, b.p. 174 °C, whose total yield may reach about 30 %.

Hexachlorotrisilazane *(2)* forms hexagonal platelets melting at 164 °C. The size of the ring is determined by mass spectroscopy and cryoscopy. The vibration spectra indicate a planar ring (symmetry D_{3h}) [3]. Dimethylamine converts *(2)* in high yield into hexakis(dimethylamino)cyclotrisilazane *(4)*, m.p. 94 °C, which contains the hitherto unknown Si_3N_9 skeleton. When the residue remaining after separation of *(1)* and *(2)* is treated with HBr in ether, surprisingly, octachlorotrisilazane *(5)*, b.p. 97 °C/1 mm, along with other products, is formed. Apparently the NH_4Cl present causes Cl/Br exchange in the primary products.

If the oligomeric portion of (A) is extracted with benzene and then treated with HBr in ether, 1,3-dibromotetrachlorodisilazane *(6)*, b.p. 57–58 °/2 mm, is formed.

The structures of the new compounds *(2)*, *(4)*, *(5)*, and *(6)* were proved by elemental analyses, determination of molecular weights, vibration spectra, and in some cases, NMR spectra.

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[*] Prof. Dr. U. Wannagat, Dipl.-Chem. P. Schmidt, and Dipl.-Chem. M. Schulze
Institut für Anorganische Chemie
der Technischen Hochschule
Pockelstr. 4
33 Braunschweig (Germany)

[1] Chemistry of SiN Compounds, Part 71. – Part 70: *U. Wannagat* and *F. Höfler*, Mh. Chem., in press.

[2] Hexachlorodisilazane *(1)* was first prepared, in small quantities, by heating $SiCl_4$ with NH_3 at 800 °C [*W. C. Schumb* and *L. H. Towle*, J. Amer. chem. Soc. *75*, 6085 (1953)]. It was obtained, also only in small quantities, by warming (A) (*J. Goubeau* and *G. O. Gudmunsson*, unpublished work).

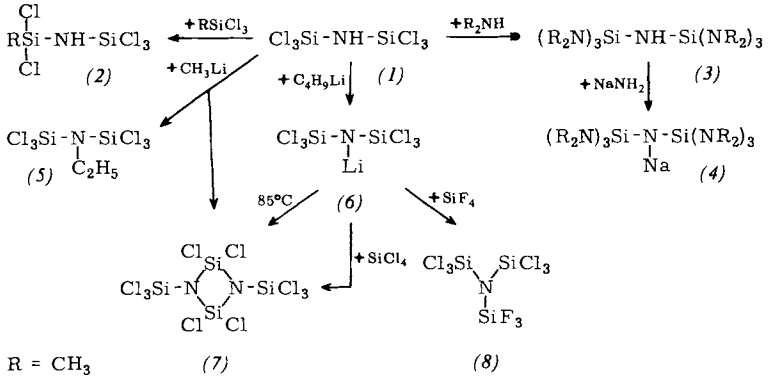
[3] *H. Bürger, M. Schulze*, and *U. Wannagat*, Inorg. nucl. Chem. Letters *3*, 43 (1967).

Reactions of Hexachlorodisilazane [1]

By *U. Wannagat, P. Schmidt*, and *M. Schulze* [*]

Reactions of hexachlorodisilazane *(1)* have not been described previously. They can occur by exchange of a $SiCl_3$ group or by replacement of a Cl or H atom.

Treating *(1)* with trichloro(methyl)silane leads to a poor yield of pentachloro(methyl)disilazane *(2)*, b.p. 56–58 °C/10 mm. Yields are better if $(Cl_2Si{-}NH)_x$ is used instead of *(1)*.



The disilazane *(1)* is converted by dimethylamine into hexakis-(dimethylamino)disilazane *(3)*, b.p. 248 °C, in high yield. This product can be metalated by sodamide in benzene, giving sodium bis[tris(dimethylamino)silyl]amide *(4)*, m.p. *ca.* 160 °C (decomp.), which can be used to build up a tris-(silyl)amine with a Si_3N_{10} skeleton.

If *(1)* is treated with methyl-lithium in ether at −78 °C, a mixture of hexachloro-*N*-ethyldisilazane *(5)*, m.p. −14 °C, b.p. 205 °C, and *(7)* is formed. However butyl-lithium in petroleum ether at −78 °C converts *(1)* into lithium bis(trichlorosilyl)amide *(6)* in high yield.

The compound *(6)* is a white solid, moderately soluble in benzene but very hygroscopic and very reactive, and, according to its ν_{as}(SiNSi) stretching frequency (1135 cm^{-1}), has the greatest valence force constant of all SiN compounds known so far. When heated to 85 °C, compound *(6)* yields, without melting, decachloro-*N,N'*-bis(silyl)cyclodisilazane *(7)* almost quantitatively.

The size of the ring can be determined by mass spectroscopy and cryoscopy. The melting point (66 °C after repeated sublimation in a vacuum) is about 20 °C lower than that of a product (m.p. 84–86 °C) that was obtained from $SiCl_4$ and N_2 in a glow discharge [2]. The latter contains a Si:N:Cl ratio of 2:1:5 and corresponds to compound *(7)* in its cryoscopically determined molecular weight.

With silicon tetrafluoride at −78 °C compound *(6)* yields smoothly bis(trichlorosilyl)trifluorosilylamine *(8)*, b.p. 42 °C/15 mm. All attempts to prepare the $(Cl_3Si)_3N$ formed in a

glow discharge[2] analogously from silicon tetrachloride failed; even under mild conditions, only *(7)* was obtained.

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[*] Prof. Dr. U. Wannagat, Dipl.-Chem. P. Schmidt, and Dipl.-Chem. M. Schulze
Institut für Anorganische Chemie der Technischen Hochschule
Pockelstr. 4
33 Braunschweig (Germany)

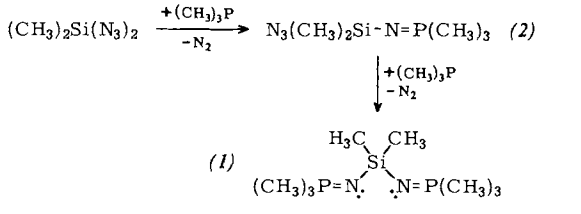
[1] Chemistry of SiN Compounds, Part 72. – Part 71: *U. Wannagat, P. Schmidt,* and *M. Schultze,* Angew. Chem. *79*, 409 (1967); Angew. Chem. internat. Edit. *6*, 446 (1967).

[2] *A. Pflugmacher* and *H. Dahmen,* Z. anorg. allg. Chem. *290*, 184 (1957); *A. Pflugmacher* and *H. Ernst,* unpublished; *H. Ernst,* Dissertation, Technische Hochschule Aachen, 1958.

Coordination Compounds with Stationary and Oscillating Acceptors

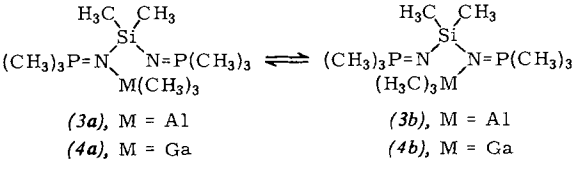
By *H. Schmidbaur* and *W. Wolfsberger*[*]

If an acceptor molecule A with one free coordination position is confronted with a donor molecule containing two spatially proximate donor centers B[1], then the acceptor A may not form a bond to only one of the two donor positions B but may interact with both the basic centers alternately[2]. Bis-(trimethylphosphoranylideneamino)dimethyl silane *(1)* has now been found to be a bidentate ligand for which this phenomenon can be observed. The silane *(1)* is obtained from dimethylsilylene diazide and trimethylphosphine *via* the intermediate dimethyl(trimethylphosphoranylideneamino)silyl azide *(2)*. It forms stable 1:1 complexes *(3)* and *(4)* with trimethylaluminum and trimethylgallium, respectively.



The ^{1}H–NMR spectra of solutions of *(3)* and *(4)* in methylene dichloride or benzene at room temperature show only one signal each for the protons of the methyl groups attached to the silicon and to the metal atoms, and one doublet for the H_3C–P groups. When the temperature is lowered the $(CH_3)_3P$ doublet becomes broader and eventually splits to two doublets (see Table)[3].

Since the singlet nature of the $(CH_3)_2Si$ and $(CH_3)_3M$ signals is retained at all temperatures, this pheonomenon can be explained only by assuming a temperature-dependent exchange process in the sense *(3a/b)* and *(4a/b)*. The phenomenon is fully reversible and can be repeated *ad infinitum*. The activation energy of the interchange of positions can be estimated from the alteration in line widths and from the splitting temperatures as being 13.4 and 12.8 kcal/mole for *(3)* and *(4)*, respectively, in CH_2Cl_2. The values are solvent-dependent and are somewhat higher for benzene solutions[4].



(3a), M = Al *(3b)*, M = Al
(4a), M = Ga *(4b)*, M = Ga

It remains to decide whether the interchange of position of the metal atoms requires intermediate complete dissociation of the donor from the acceptor (within the solvent cage) or whether it can occur through a transition state containing pentacoordinated metal.

In contrast to *(3)* and *(4)*, the complex with trimethylindium *(5)* at temperatures down to –70 °C gives a temperature-independent NMR spectrum with one $(CH_3)_3P$ doublet only. Thus for this compound a fixed structure with a pentacoordinated metal atom or an extremely rapid exchange of positions can be considered. In the latter case the activation energy for the "jump" must be less than 8 to 9 kcal/mole. "Stationary" 1:1 complexes with tetracoordinated metal atoms are obtained from *(1)* and dimethylzinc or dimethylcadmium.

Preparation of (1):

$(CH_3)_3P$ (16.5 g) is added slowly from a cooled dropping funnel to $(CH_3)_2Si(N_3)_2$ (26.5 g) at room temperature. Reaction ensues immediately with evolution of nitrogen. Fractional distillation of the reaction mixture gives *(2)* (yield 33.3 g; 94 %). 33.2 g of this intermediate reacts with a further 16.5 g of $(CH_3)_3P$ in an autoclave at 110–130 °C to give *(1)*, which is purified by distillation (yield 40.1 g; 96 %).

		(1)	*(2)*	*(3)*	*(4)*	*(5)*
	M.p. (°C)	24–25	–	93–95	80–82	74–
	B.p. (°C/mm)	77–78/0.3	40/0.3	–	–	–
	Yield (%)	90.3	93.6	96.9	97.9	98.3
NMR [a] 30 °C	δ CH_3Si	+3.7	–4.4 [b]	–10.2	–5.0	–5.(
	δ CH_3M	–	–	+58.5	+37.5	+31
	δ CH_3P	–86.4	–87.7 [b]	–97.0	–93.0	–93
	$J(^1H–C–^{31}P)$	12.75	12.9 [b]	13.0	12.9	12.8
NMR [a] –60 °C	δ CH_3P [c]	–	–	–88	–86	–93
	$J(^1H–C–^{31}P)$ [c]	–	–	13.3	13.0	12.7
	δ CH_3P [d]	–	–	–108	–102	–93
	$J(^1H–C–^{31}P)$[d]	–	–	12.8	12.75	12.7

[a] In CH_2Cl_2 with tetramethylsilane as external standard. All values are in Hz at 60 MHz.

[b] In CCl_4 with tetramethylsilane as internal standard.

[c] Signal of the free phosphoranylideneamino group.

[d] Signal of the coordinately-bound phosphoranylideneamino group.

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[*] Prof. Dr. H. Schmidbaur and Dipl.-Chem. W. Wolfsberger
Institut für Anorganische Chemie der Universität
Röntgenring 11
87 Würzburg (Germany)

[1] In this connection compare *Sisler et al.*, Inorg. Chem. *2* 1251 (1963); *5*, 527 (1966); *Thiele et al.*, Z. anorg. allg. Chem. *345*, 194 (1966); *349*, 33 (1967); *348*, 179 (1967); *K. W. Morse* and *R. W. Parry*, J. Amer. chem. Soc. *89*, 172 (1967).

[2] The unsymmetrical hydrogen bridge bond may, with reservations, be considered a model case.

[3] We thank the NMR-Abteilung des Anorganisch-chemischen Laboratoriums, Technische Hochschule, München, for the low-temperature NMR measurements.

[4] These views are also in agreement with the fact that the doublets appearing at low temperature have different coupling constants, that with the large coupling being assigned to the coordinately bound and that with the lower coupling constant to the free phosphoranylideneamino group [5]. Only the doublet with the larger *J* value shows the expected Al or Ga quadrupole broadening of the signal.

[5] *H. Schmidbaur* and *W. Wolfsberger*, Angew. Chem. *78*, 306 (1966); Angew. Chem. internat. Edit. *5*, 312 (1966); Chem. Ber. *100*, 1000 (1967).

Trimethyl(methylene)phosphorane

By *H. Schmidbaur* and *W. Tronich*[*]

Trialkyl(alkylene)phosphoranes cannot be obtained by any of the synthetic procedures available for phosphorylides. Their properties are thus substantially unknown[1].

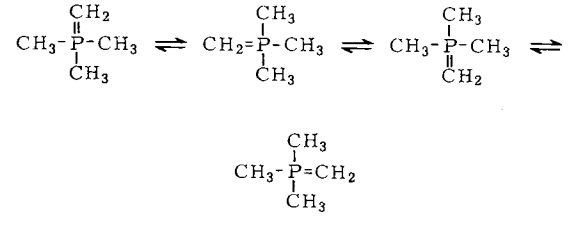
We have now synthesized pure trimethyl(methylene)phosphorane, which *Wittig* and *Rieber* had obtained as etheral solution as early as 1949 but were unable to isolate[2].

Our synthetic principle utilizes the notable readiness of formation of organosiloxanes to promote formation of the ylide. When trimethyl(trimethylsilylmethylene)phosphorane[3] is treated with silanols or alcohols such as trimethylsilanol or methanol, compound *(1)* is formed, even at 0 °C, in more than 90 % yield. The only by-products are hexamethyldisiloxane and methoxytrimethylsilane, respectively, which can readily be removed by distillation.

$$\begin{array}{l} \qquad\qquad + (CH_3)_3SiOH \qquad\qquad + (CHi_3(_3SiOSi(CH_3)_3 \\ (CH_3)_3Si{-}CH{=}P(CH_3)_3 \;\rightarrow\; (CH_3)_3P{=}CH_2 \\ \qquad\qquad + CH_3OH \qquad\quad (1) \qquad + (CH_3)_3SiOCH_3 \end{array}$$

Compound *(1)* can be distilled without decomposition at atmospheric pressure (b.p. 118–120 °C). It solidifies to colorless crystals (m.p. 14–15 °C) when cooled. *(1)* was shown cryoscopically to be monomeric in benzene solution. Decomposition with brown coloration occurs almost instantaneously on contact with oxygen or moisture.

The ^1H–NMR spectrum[4] of the pure compound *(1)* at room temperature shows well resolved doublets for the methyl and methylene protons (relative areas 9:2) at $\delta = -73$ Hz (CH_3P), $J(^1H{-}C{-}^{31}P) = 12.6$ Hz, and at $\delta = +45$ Hz (CH_2P), $J(^1H{-}C{-}^{31}P) = 6.9$ Hz. However, when the temperature is raised the signals become broader, resolution of the doublet becomes poor, and finally (> 100 °C) the two resonance signals merge to a singlet. This phenomenon may be reproduced repeatedly and can be interpreted only as the result of rapid proton exchange in *(1)*, whereby all 11 protons, and thus all four carbon atoms, are equilibrated at elevated temperatures:



On addition of a proton active species (*e.g.* a trace of methanol) the NMR equivalence of the methyl and methylene groups is brought about at room temperature by proton catalysis.

With hydrogen halides, compound *(1)* forms tetramethylphosphonium halides; with methyl iodide, ethyltrimethylphosphonium iodide is formed. On its addition to trimethylaluminum the zwitterionic compound *(2)* (m.p. 62 °C, b.p. 130–134 °C/1 mm) results; *(2)* is an isostere of bis(trimethylsilyl)methylene[5].

$$(1) + Al(CH_3)_3 \;\rightarrow\; \underset{(2)}{(CH_3)_3\overset{\oplus}{P}CH_2\overset{\ominus}{Al}(CH_3)_3}$$

Trimethylbis(trimethylsilyl)methylenephosphorane *(4)*[3] and *(1)* comproportionate to trimethyl(trimethylsilylmethylene)-phosphorane at 100 °C:

$$(CH_3)_3P{=}CH_2 + \underset{(4)}{[(CH_3)_3Si]_2C{=}P(CH_3)_3} \;\rightarrow\; 2\,(CH_3)_3Si{-}CH{=}P(CH_3)_3$$

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[*] Prof. Dr. H. Schmidbaur and Dipl.-Chem. W. Tronich
Institut für Anorganische Chemie der Universität
Röntgenring 11
87 Würzburg (Germany)

[1] *W. A. Johnson*: Ylid Chemistry. Academic Press, New York 1966; *L. Horner*, Fortschr. chem. Forsch. *7*, 1 (1966).

[2] *G. Wittig* and *M. Rieber*, Liebigs Ann. Chem. *562*, 177 (1949).

[3] *H. Schmidbaur* and *W. Tronich*, Chem. Ber. *100*, 1032 (1967); *N. E. Miller*, J. Amer. chem. Soc. *87*, 390 (1965); Inorg. Chem. *4*, 1458 (1965).

[4] All values are at 60 MHz, referred to tetramethylsilane as external standard; negative δ values for lower field strengths; 20 °C.

[5] *H. Schmidbaur*, Chem. Ber. *97*, 270 (1964) and further literature cited there.

Trimethylphosphine Imide: Synthesis and Reactions with Organometallic Compounds

By *H. Schmidbaur* and *G. Jonas* [*]

The few known methods for the preparation of triorganophosphine imides can be used only with difficulty[2], if at all[1], for the synthesis of trimethylphosphine imide *(2)*. Attempts to prepare other alkylmethylphosphine imides also met with serious difficulties[3].

We have now found that $(CH_3)_3P{=}NH$ *(2)* can be obtained in high yield by starting from trimethylphosphine and hydrogen azide; the reaction proceeding *via* the intermediate trimethylphosphine imidium azide *(1)*[4]. The imide *(2)* is formed, with sodium azide, on reaction of the azide *(1)* with sodium in liquid ammonia at −78 °C:

$$(CH_3)_3P + 2\,HN_3 \;\rightarrow\; N_2 + \underset{(1)}{[(CH_3)_3PNH_2]N_3}$$

$$[(CH_3)_3PNH_2]N_3 + Na \;\rightarrow\; {}^1/_2\,H_2 + NaN_3 + \underset{(2)}{(CH_3)_3P{=}NH}$$

(2) is separated easily from NaN_3 by extraction with anhydrous benzene and can be purified (m.p. 59–60 °C) by sublimation (from 45 °C/1mm) or distillation (70 °C/1mm). It has the simple molecular weight in benzene (cryoscopy). The imide *(2)* is converted by an alkyl-lithium, in ether or in a hydrocarbon solvent, into lithium trimethylphosphine imide *(3)*, with loss of alkane:

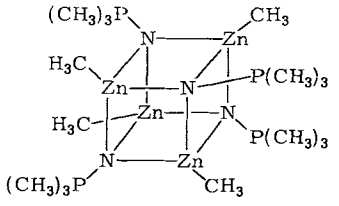
$$(CH_3)_3P{=}NH + LiCH_3 \;\rightarrow\; CH_4 + \underset{(3)}{(CH_3)_3P{=}NLi}$$

This derivative is an involatile compound, very sparingly soluble in ether or benzene and, like its homologues of the type R_3PNLi[5], an extremely reactive component for the synthesis of new derivatives of trimethylphosphine imide.

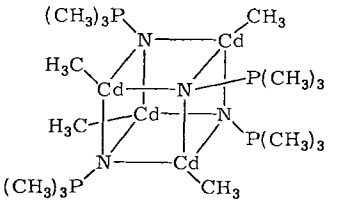
On treatment of *(2)* with dimethylzinc or dimethylcadmium in diethyl ether, methane is evolved and the organometallic derivative *(4)* or *(5)*, respectively, is formed:

$$\begin{array}{l} 4\,(CH_3)_2Zn + \qquad\qquad + [CH_3Zn{-}N{=}P(CH_3)_3]_4 \\ \qquad\qquad 4\,(CH_3)_3P{=}NH \;\rightarrow\; 4\,CH_4 \qquad (4) \\ 4\,(CH_3)_2Cd + \qquad\qquad + [CH_3Cd{-}N{=}P(CH_3)_3]_4 \\ \qquad\qquad\qquad\qquad\qquad\qquad (5) \end{array}$$

Determination of molecular weights and IR and NMR spectroscopic studies indicate a tetrameric cubanite structure for the inorganic skeleton of compounds *(4)* and *(5)*. This structure is confirmed by comparison of the X-ray diagrams of the homologous ethyl compounds with those of the isosteric methylzinc and methylcadmium triethylsilanolates for which the cubanite structure has meanwhile been proved[6, 7]. Compounds *(4)* and *(5)* decompose without melting at temperatures considerably above 200 °C; they can be sublimed in a high vacuum above 240 °C and 180 °C, respectively (with partial decomposition).



(4)

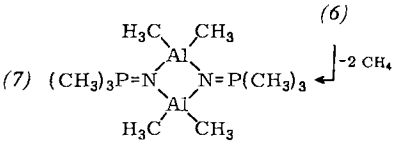


(5)

Trimethylaluminum and the imide *(2)* give first trimethylphosphine imidium trimethylaluminate *(6)* [which can be isolated; m.p. 44–46 °C (decomp.)] and then, on warming, form methane and dimeric trimethyl(dimethylalumino)phosphine imide *(7)*, which was recently prepared by two other methods[8]:

$$2\ (CH_3)_3P{=}NH + [Al(CH_3)_3]_2 \rightarrow 2\ (CH_3)_3P{=}\overset{\oplus}{N}H\text{-}\overset{\ominus}{Al}(CH_3)_3$$

(6)



(7)

The lithium imide *(3)* reacts with trimethyltin chloride with loss of LiCl, yielding trimethyltin trimethylphosphine imide[5], and with dimethylarsenic chloride to yield dimethylarsenic(III) trimethylphosphine imide *(8)*, b.p. 96–99 °C/12 mm, which is quaternized at the arsenic atom by methyl iodide, yielding *(9)*.

$$(CH_3)_3P{=}N\text{-}As(CH_3)_2 + CH_3I \rightarrow [(CH_3)_3P\cdots N\cdots As(CH_3)_3]^+I^-$$

(8) *(9)*

Compounds *(2)–(9)* are of interest because of their isoelectronic relationship to siloxane and silazane derivatives.

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[*] Prof. Dr. H. Schmidbaur and Dipl.-Chem. G. Jonas
Institut für Anorganische Chemie der Universität
Röntgenring 11
87 Würzburg (Germany)

[1] *L. Birkofer, A. Ritter*, and *S. M. Kim*, Chem. Ber. *96*, 2750, 3099 (1963); *L. Birkofer* and *S. M. Kim*, *ibid. 97*, 2100 (1964), and our own unpublished work.

[2] *R. Appel* and *A. Hauss*, Chem. Ber. *93*, 405 (1960); *95*, 2225 (1962).

[3] *T. W. Rave* and *H. R. Hays*, J. org. Chemistry *31*, 2894 (1966), and literature cited there.

[4] *H. Staudinger* and *E. Hauser*, Helv. chim. Acta *4*, 869 (1921).

[5] *H. Schmidbaur* and *G. Jonas*, Chem. Ber. *100*, 1120 (1967).

[6] *F. Schindler, H. Schmidbaur*, and *U. Krüger*, Angew. Chem. *77*, 865 (1965); Angew. Chem. internat. Edit. *4*, 876 (1965), and X-ray studies by *E. Hellner* and *G. Dittmar*, Marburg.

[7] *H. Schmidbaur* and *G. Jonas*, unpublished work.

[8] *H. Schmidbaur, W. Wolfsberger*, and *H. Kröner*, Chem. Ber. *100*, 1023 (1967); *H. Schmidbaur* and *W. Wolfsberger*, unpublished.

Low-Melting Nematic Phases for Determination of NMR Spectra of Orientated Molecules

By *H. Spiesecke* and *J. Bellion-Jourdan*[*]

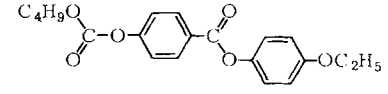
Measurement of the highly resolved nuclear magnetic resonance spectra of samples dissolved in the nematic phase of liquid crystals offers the possibility of determining the relative atomic distances, bond angles, anisotropy of chemical shift, sign of the scalar coupling constants, and intermolecular reactions of host and guest molecules[1].

The relatively high melting point (70 to 80 °C) of liquid crystals has hitherto, however, posed experimental difficulties. For instance, the orientation of the guest molecule in the nematic host substance – and thus the width of the NMR lines – is strongly temperature-dependent, which requires that the temperature around the sample be kept constant[2] (± *ca.* 0.1 °C). Further, at the temperatures necessary for transition into isotropic melts (>120 °C) low-boiling substances must be kept under too high a pressure. The spectra of simple gases, which would be most interesting on theoretical grounds, have therefore not been investigated experimentally because of these disadvantages.

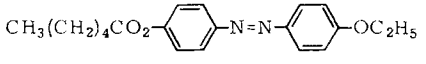
Components, 80:20 (mole-%)	M.p. (°C)	Clearing point (°C)
(1):*(2)*	41	108
(1):*(3)*	48	114
(1):*(4)*	39	91
(1):*(5)*	29	78
(1):*(6)*	44	114

If, however, eutectic mixtures of liquid crystals (see Table) are used, the melting point can be lowered to 30 to 40 °C. Samples prepared in such host substances can be equilibrated in the usual thermostats and studied in the usual NMR sample head at 34 °C.

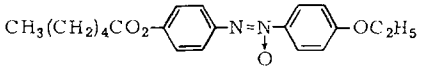
The following are suitable components for the eutectics[3]:



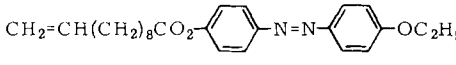
(1)



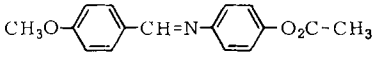
(2)



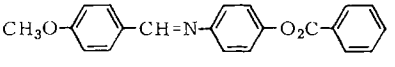
(3)



(4)



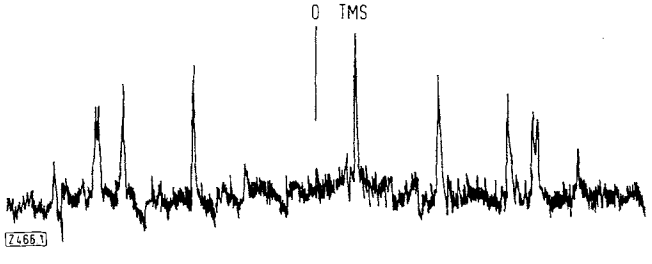
(5)



(6)

Except for the Schiff bases *(5)* and *(6)* all these compounds are relatively indifferent chemically, so that even reactive gases such as $H^{13}CN$, ethylene, and acetylene can be studied.

The 60 MHz spectrum of 20 mole-% of allene in a mixture of 60 mole-% of *(1)* and 20 mole-% of *(2)* (see Figure) may



serve as example (internal standard: tetramethylsilane). The rather high viscosity of the melt at 34 °C has no apparent disturbing effect on the line width (6 Hz for all lines). The

symmetrical spectrum contains five pairs of lines (distances from the centre: 901, 1414, 1591, 1613, 1922 Hz; TMS at 276 Hz).

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[*] Dr. H. Spiesecke and Mlle. J. Bellion-Jourdan
Euratom Research Center, Magnetic Resonance
Ispra (Italy)

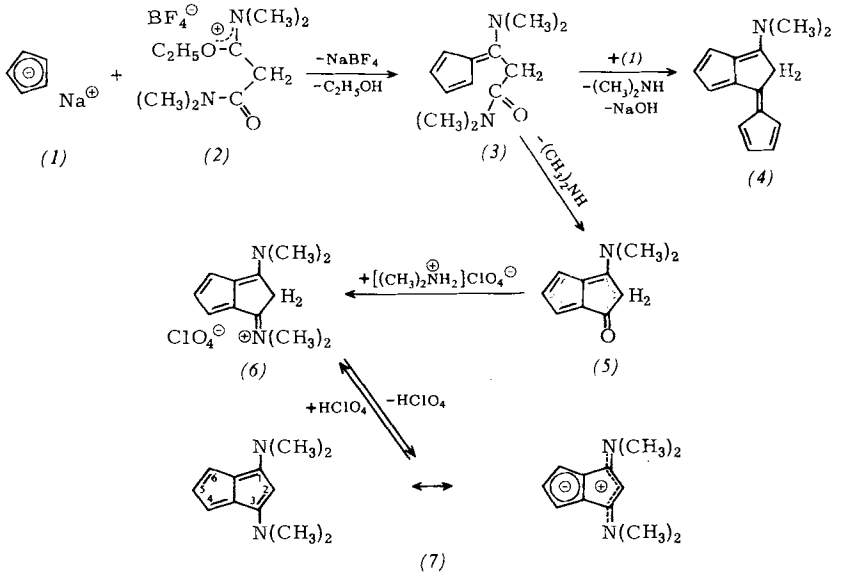
[1] *A. Saupe* and *G. Englert*, Physic. Rev. Letters *11*, 462 (1963).
[2] *A. Saupe*, Z. Naturforsch. *20a*, 572 (1965).
[3] *E. Schroeter*, Dissertation, Universität Halle, 1927.

1,3-Bis(dimethylamino)pentalene

By *K. Hafner*, *K. F. Bangert*, and *V. Orfanos* [*]

Hitherto it has not been possible to synthesize pentalene or its simple derivatives[1]. Like fulvene, pentalene should be stabilized by electron donors in the 1- or 3-position[2]. Synthesis of the thermally stable 1,3-bis(dimethylamino)-pentalene *(7)* has now confirmed this hypothesis.

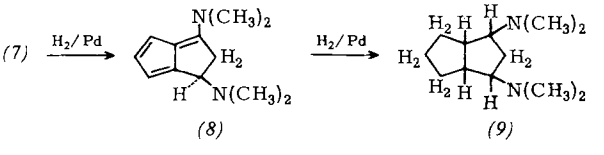
Cyclopentadienylsodium *(1)* in tetrahydrofuran reacts at 20 °C with the complex *(2)* (a yellow, viscous oil) obtained from tetra-*N*-methylmalonodiamide and triethyloxonium tetrafluoroborate, yielding the fulvene derivative *(3)* {yield 44 %; yellow leaflets of m.p. 135 °C; λ_{max} = 339 mμ (log ε = 4.45) in CH_3OH; $\nu_{C=O}$ = 1650 cm^{-1} (in $CHCl_3$); NMR spectrum (in $CDCl_3$): multiplet centered at τ = 3.75 (4 ring protons), singlets at τ = 6.30 (CH_2), 6.80 [$N(CH_3)_2$], and 7.05 as well as 7.15 [$N(CH_3)_2$]}. A by-product is compound *(4)*, which is separated from *(3)* by chromatography (neutral Al_2O_3 of activity III; eluent, ether/ethyl acetate) and forms red needles, decomposing above 140 °C (yield 2 %; λ_{max} = 219 mμ (log ε = 4.14), 285 (4.36), 399 (4.18), 455 (4.40) in CH_3OH; NMR spectrum in [D_6]dimethyl sulfoxide); multiplet centered at τ = 3.65 (7 ring protons), singlets at τ = 5.80 (CH_2) and 6.65 as well as 6.72 [$N(CH_3)_2$].



In boiling xylene (5 h) compound *(3)* loses dimethylamine, forming 3-(dimethylamino)-1(2*H*)pentalenone *(5)* in 63 % yield. This forms yellow needles of m.p. 225 °C and has λ_{max} = 247 mμ (log ε = 4.43), 371 (4.29) in CH_3OH, $\nu_{C=O}$ = 1675 cm^{-1} (in nujol), and an NMR spectrum (in [D_5]-pyridine)[3] with multiplets centered at τ = 3.13 (H-4, H-6) and 3.52 (H-5), and singlets at τ = 6.58 (CH_2) and 6.91 as well as 7.03 [$N(CH_2)_2$]. With dimethylammonium perchlorate in CH_2Cl_2/CH_3OH (3:1 v/v), compound *(5)* affords the immonium perchlorate *(6)* (yield 95 %) as yellow needles (from CH_3CN), decomp. > 150 °C, λ_{max} = 253 mμ (log ε = 4.47), 260 (4.48), 359 (4.11), 3.97 (4.30) in CH_3CN, NMR spectrum (in [D_6]dimethyl sulfoxide) 3 singlets at τ = 3.04 (3 olefinic ring protons), 5.43 (CH_2), and 6.50 [2 $N(CH_3)_2$].

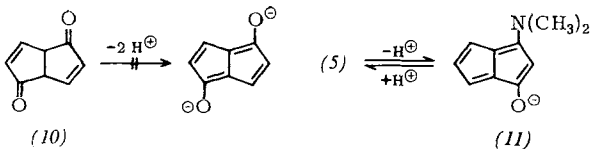
Deprotonation of *(6)* by a strong base (*e.g.* isopropylmagnesium chloride) in ether leads to compound *(7)*, which is purified by sublimation in a high vacuum at 110 °C, or by recrystallization from acetone. This compound is obtained in 88 % yield as dark blue crystals of m.p. 163 °C (decomp.). Its UV spectrum [λ_{max} = 236 mμ (log ε = 4.21), 329 (4.42), 384 (4.04), 618 (2.56) in CH_2Cl_2] resembles that of hexaphenylpentalene[1] and agrees satisfactorily with the results of an SCF–CI calculation[4]. The NMR spectrum (in [D_6]-acetone) proves the structure of *(7)*, showing, besides the A_2B system of the unsubstituted five-membered ring [doublet centered at τ = 4.31 (H-4, H-6), triplet centered at τ = 4.66 (H-5, J_{AB} = 3.4 Hz)], a singlet for the protons of two equivalent dimethylamino groups at τ = 6.92, as well as a singlet shifted to high field (τ = 7.20) for the proton on C-2 (β-position of the quasidouble enamine system).

Compound *(7)* is stable towards atmospheric oxygen for several hours at 20 °C and dissolves in polar aprotic solvents to give deep blue solutions. It reacts with protic acids as an enamine, with protonation on C-2, regenerating *(6)*. Catalytic hydrogenation (20 °C, 760 mm, H/Pd) leads to absorption of one mol. equivalent of H_2 and formation of *(8)*, which is also obtained by reduction of *(6)* with $NaBH_4$ in H_2O and forms yellowish leaflets of m.p. 72 °C, λ_{max} = 319 mμ (log ε = 4.39) in n-hexane; its NMR spectrum (in $CDCl_3$)



has 3 multiplets centered at τ = 3.39 (H-5), 3.89 (H-4, H-6), 5.82 (H-1), singlets at τ = 6.76 and 6.81 [$N(CH_3)_2$ on C-3], a multiplet centered at τ = 6.92 (CH_2), and a singlet at τ = 7.72 [$N(CH_3)_2$ on C-1]. Further hydrogenation of *(8)*, which requires three moles of H_2, affords *(9)* as a colorless oil.

Whereas 1,4-pentalenedione *(10)* is not enolized in the presence of strong bases[5], compound *(5)* is readily converted by potassium t-butoxide in t-butyl alcohol into the blue enolate *(11)*, whose UV spectrum resembles as that of *(7)*. Hydrolysis of *(11)* regenerates *(5)*.



(10) (5) (11)

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[*] Prof. Dr. K. Hafner, Dr. K. F. Bangert, and
Dipl.-Chem. V. Orfanos
Institut für Organische Chemie der Technischen Hochschule
Schlossgartenstr. 2
61 Darmstadt (Germany)

[1] *E. D. Bergmann* in *D. Ginsburg*: Non Benzenoid Aromatic Compounds. Interscience, New York 1959, p. 141; the simplest recorded bicyclic pentalene derivatives are hexaphenylpentalene [*E. LeGoff*, J. Amer. chem. Soc. *84*, 3975 (1962)] and the pentalene dianion [*T. J. Katz* and *M. Rosenberger*, J. Amer. chem. Soc. *84*, 865 (1962); *86*, 249 (1964)].

[2] *K. Hafner, K. H. Häfner, C. König, M. Kreuder, G. Ploss, G. Schulz, E. Sturm*, and *K. H. Vöpel*, Angew. Chem. *75*, 35 (1963); Angew. Chem. internat. Edit. *2*, 123 (1963); *K. Hafner*, Angew. Chem. *75*, 1041 (1963); Angew. Chem. internat. Edit. *3*, 165 (1964).

[3] We thank Dr. *U. Scheidegger*, Varian AG., Zürich, for measurement of this spectrum (100 MHz).

[4] We thank *U. Müller-Westerhoff* for the quantum-chemical calculation for *(7)*.

[5] *H. J. Dauben, S. H. K. Jiang*, and *V. R. Ben*, Hua Hsueh Hsueh Pao *23*, 411 (1957); Chem. Abstr. *52*, 16309h (1958).

1,5-Cyclooctadienenickel Bromide and Iodide

By *L. Porri, G. Vitulli*, and *M. C. Gallazzi*[*]

We have prepared two new nickel complexes, namely, 1,5-cyclooctadienenickel bromide, $C_8H_{12}NiBr$, and iodide, $C_8H_{12}NiI$. A π-allylnickel halide is treated with 1,5-cyclooctadiene (20- to 30-fold excess) in n-heptane in the presence of norbornene (slight excess) at room temperature. The complex separates as well-formed crystals two to three hours after the beginning of the reaction, the yield being *ca.* 75 % after 15 hours.

The complex $C_8H_{12}NiI$ can also be obtained (about 80 % yield) directly by heating a solution of π-allylnickel iodide in 1,5-cyclooctadiene to *ca.* 80 °C and then slowly cooling the mixture. The less stable bromide could not be obtained in this way.

The two cyclooctadienenickel halides are very sensitive to air. They dissolve slightly (*ca.* 1.5 wt.-%) in cyclooctadiene and these solutions are stable in absence of oxygen. Both compounds dissolve in benzene, tetrahydrofuran, or ethanol; these solutions, however, decompose rapidly, even under nitrogen, with formation of metallic nickel, nickel halide, and 1,5-cyclooctadiene, but they are stable if small amounts (2–3 %) of free cyclooctadiene are added.

There is no band at 1667 or 1486 cm^{-1} in the IR spectrum of either compound, which indicates that both double bonds of the cyclooctadiene are coordinated to the nickel atom.

The magnetic moments of the solid complexes could not be determined because of the low stability. However, reaction with triphenylphosphine in benzene at room temperature gave the known[1] complexes $(C_6H_5P)_3NiX$, whose magnetic moments (*ca.* 1.9 B.M. for the bromide, *ca.* 1.98 B.M. for the iodide) correspond to an unpaired electron; the presence of nickel(I) in these complexes is thus indicated.

The $(C_8H_{12})NiX$ complexes react readily, even at room temperature, with benzonitrile, acrylonitrile, quinones, or esters of unsaturated carboxylic acids, with formation of new complexes in which the cyclooctadiene is replaced by another ligand. The $(C_8H_{12})NiX$ complexes catalyse polymerisation of butadiene, allene, or acetylene to linear polymers[2].

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[*] Dr. L. Porri, Dr. G. Vitulli, and Dr. M. C. Gallazzi
Istituto di Chimica Industriale del Politecnico
Piazza Leonardo da Vinci 32
Milano (Italy)

[1] *L. Porri, M. C. Gallazzi*, and *G. Vitulli*, Chem. Commun., *1967*, 228.

[2] *L. Porri, M. C. Gallazzi*, and *G. Vitulli*, Polymer Letters, in press.

Radical Formation on Heating of Trityl-aluminum or -boron Compounds

By *H. Hoberg* and *E. Ziegler*[*]

Trityl-aluminum and -boron derivatives are accessible from the corresponding chlorides and triphenylmethylsodium in ether[**]:

$$X_2MCl + (C_6H_5)_3CNa \rightarrow X_2M{-}C(C_6H_5)_3 + NaCl$$

M = Al or B; X = Cl, alkyl, or phenyl

Diphenyltritylaluminum, $(C_6H_5)_2Al{-}C(C_6H_5)_3$, m.p. 205 °C (decomp.), can also be obtained by the action of diphenyldiazomethane on triphenylaluminum in anisole at 20 °C:

$$(C_6H_5)_2CN_2 + (C_6H_5)_3Al \rightarrow (C_6H_5)_2Al{-}C(C_6H_5)_3 + N_2$$

Like the central C–C bond of hexaphenylethane, the $M{-}C_{(trityl)}$ bond of trityl-aluminum and -boron compounds readily undergoes homolysis. For colorless diphenyltritylaluminum, this homolysis, which occurs at 130 °C in the solid state, is demonstrated by an intense yellow coloration and by development of the ESR signal of triphenylmethyl. Also, on pyrolysis in an aliphatic or aromatic hydrocarbon, aluminum separates after several hours' heating at 130 °C; deposition of aluminum is observed only above 240 °C for trialkylaluminums[1].

$$3\ X_2Al{-}C(C_6H_5)_3 \rightarrow [3\ X_2Al\bullet] + (C_6H_5)_3C\bullet \quad ([3\ X_2Al\bullet] \rightarrow 2\ AlX_3 + Al)$$

The aluminum radical can be trapped by a primary or secondary amine, the separation of aluminum being thus prevented.

$$R_2Al{-}C(C_6H_5)_3 + R^1_2NH \rightarrow R_2Al{-}NR^1_2 + (C_6H_5)_3CH$$

If pyrolysis is effected in the presence of pyridine bases[2], colored solutions containing radicals with Al–N bonds are formed whose ESR spectra (20 °C) are no longer identical with that of triphenylmethyl [the trityl radical reacts with the solvent at the reaction temperature (130 °C), yielding $(C_6H_5)_3CH$]. The hyperfine structure of these spectra is so little developed that the number and type of the nuclei (H, N, Al) concerned in the splitting cannot be determined. On pyrolysis of tritylaluminum dichloride in pyridine a deep blue solution is obtained whose ESR spectrum shows a hyperfine structure of 57 lines; the same spectrum develops on dehalogenation of $AlCl_3$ with sodium or on cathodic reduction in pyridine[3].

Pyrolysis of dialkyltritylboron in quinoline or isoquinoline also affords colored solutions containing radicals with B–N bonds. The ESR spectra show resolution into 10 equidistant HFS lines, with a relative separation of 4.10 or 4.17 gauss, that is interpreted as due to coupling of the electrons with

three equivalent ^{11}B nuclei[4]. Pyrolysis of diethyltritylboron in the presence of pyridine leads to a radical whose ESR signal, unlike that of the radical produced by dehalogenation[4], shows distinct 1:1 splitting of *ca.* 12.6 gauss. Homolytic fission of trityl-aluminum and -boron compounds can also be induced by photolysis, even at room temperature[5]; on irradiation of tritylaluminum dichloride in the presence of pyridine the 57-line hyperfine structure is again observed in the ESR spectrum.

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[*] Dr. H. Hoberg and Dr. E. Ziegler
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1
433 Mülheim/Ruhr (Germany)

[**] This method was used by *G. Benedikt* (1963) to prepare diphenyltritylboron (m.p. 99–101 °C, yellow) and by *H. Lehmkuhl* (1964) to prepare diethyltritylaluminum (m.p. 114–115 °C) [personal communication 1967].

[1] *K. Ziegler, K. Nagel,* and *W. Pfohl,* Liebigs Ann. Chem. *629,* 210 (1960).

[2] *R. Köster, G. Benedikt,* and *H. W. Schrötter,* Angew. Chem. *76,* 649 (1964); Angew. Chem. internat. Edit. *3,* 514 (1964).

[3] *E. Ziegler, G. Fuchs,* and *H. Lehmkuhl,* Z. anorg. allg. Chem., in press.

[4] *R. Köster, H. Bellut,* and *E. Ziegler,* Angew. Chem. *79,* 241 (1967); Angew. Chem. internat. Edit. *6,* 255 (1967).

[5] High-pressure Hg lamp Philips HPK 125 W.

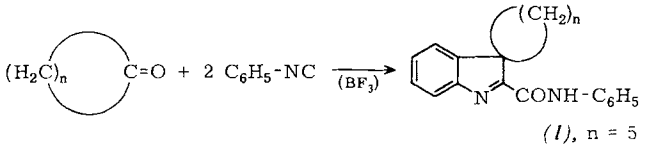
A New Indolenine Synthesis

By *B. Zeeh*[*]

Müller and *Zeeh*[1] recently reported the formation of *t*-butylamides of cycloalkenylglyoxylic acids on treatment of cycloaliphatic ketones with t-butyl isocyanide. A Lewis acid such as boron trifluoride is required as catalyst.

Surprisingly this reaction takes a different course with aromatic isocyanides: the indolenine skeleton can be built in one step from phenyl isocyanide and cycloaliphatic ketones.

When a mixture of cyclohexanone and phenyl isocyanide is allowed to react in the presence of boron trifluoride for 1 h at 0 °C, subsequent chromatography (aluminum oxide, petroleum ether/benzene eluant) leads to isolation of spiro-[indolenine-3,1′-cyclohexane]-2-carboxanilide *(1)* in 40 % yield [m.p. 148–149 °C; λ_{max} = 228 (ε = 14600), 315 nm (12200) in ethanol].



(1), n = 5
(2), n = 6

Spiro[indolenine - 3,1′ - cycloheptane]-2-carboxanilide *(2)* (yield 30 %; m.p. 94–95 °C) is obtained analogously from cycloheptanone.

The IR spectra (in KBr) of *(1)* and *(2)* show characteristic bands at 3360 (NH), 1698 (C=N), 1680, 1603, and 1530 cm^{-1} (CO–NH). In the NMR spectra (in $CDCl_3$) signals are observed for 9 aromatic protons and respectively 10 or 12 aliphatic protons as multiplets, as well as the NH signal (τ = 0.53) as a singlet. Important structural indications are also provided by the mass spectrum (base peak: M–$CONHC_6H_5$).

The C=N double bond in *(1)* and *(2)* can be reduced either with $LiAlH_4$ or catalytically with platinum/hydrogen. The hydrogenation products [m.p. 132–133 °C from *(1)*; m.p. 152–153 °C from *(2)*] arise in almost quantitative yield. Their NMR spectra show the newly formed –NH–CH group as two doublets between τ = 5.7 and 6.0 (J = 5 Hz). The proton attached to the nitrogen undergoes exchange in D_2O, the doublet being thereby converted into a singlet (τ = 5.98).

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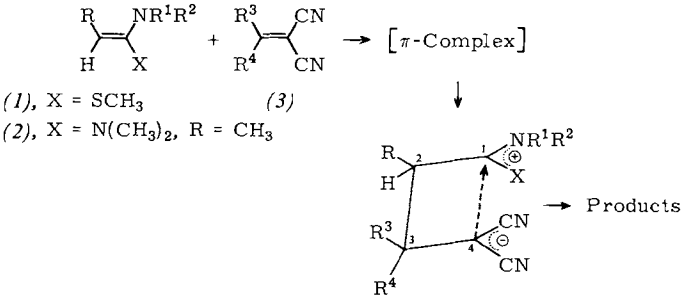
[*] Dr. B. Zeeh
Chemisches Institut der Universität
Wilhelmstr. 33
74 Tübingen (Germany)

[1] *E. Müller* and *B. Zeeh,* Tetrahedron Letters *1965,* 3951; Liebigs Ann. Chem. *696,* 72 (1966).

Stable 1,4-Dipolar Compounds from Ketene Acetals and Methylenemalononitriles[1]

By *R. Gompper, W. Elser,* and *H.-J. Müller*[*]

Reaction of electron-rich with electron-deficient olefins gives 1:1 and 1:2 or 2:1 cyclo adducts (four- or six-membered rings), mechanistic alternatives being a synchronous and a two-stage process[2]. On treating ketene *S,N*-acetals *(1)* and ketene aminals *(2)* with methylenemalononitriles *(3)* we have been able to isolate the 1,4-dipolar compounds *(4)* and *(5)* for the first time, and to investigate their properties.



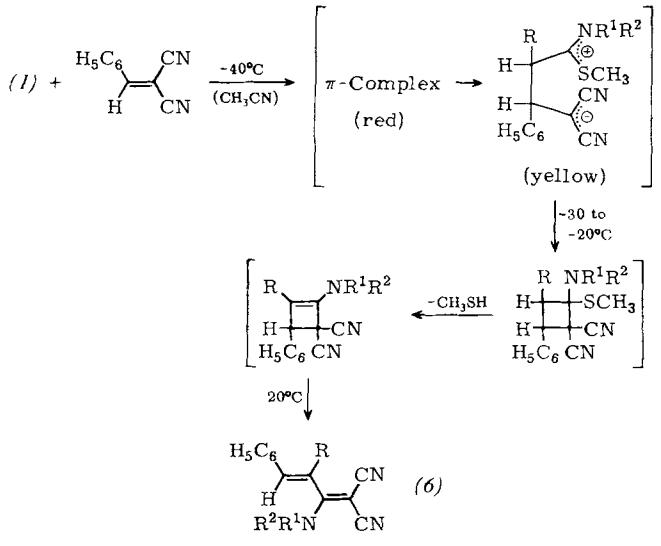
(1), X = SCH_3 *(3)*
(2), X = $N(CH_3)_2$, R = CH_3

(4), X = SCH_3
(5), X = $N(CH_3)_2$, R = CH_3

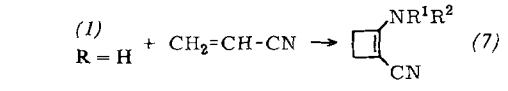
R = H, CH_3, C_2H_5, n-C_3H_7, or C_6H_5
$R^1 + R^2 = (CH_2)_{2-4}$
R^3 = C_6H_5, *p*-O_2N–C_6H_4, CF_3, or CN
R^4 = H, CF_3, or CN

On treatment of solutions of tetracyanoethylene in acetonitrile at *ca.* –50 °C with *(1)* or *(2)* there is immediate deep blue coloration (formation of π-complexes). When the temperature is raised to –20 to 10 °C, the blue color vanishes and yellow compounds crystallize which can be filtered off at room temperature and purified by washing with ether. Elemental analyses indicate that they are 1:1 adducts. Their structure as 1,4-dipolar compounds *(4)* and *(5)*, $R^3 = R^4$ = CN, follows from the IR spectra (in Hostaflon oil; νC≡N 2110, 2170 cm^{-1}; νC=N 1580–1610 cm^{-1}) and from the NMR spectra (in liquid SO_2)[**]. Particular stability is exhibited by the orange-red and the yellow 1,4-dipolar compounds resulting from *(1)* and *p*-nitrobenzylidene- and hexafluoroisopropylidenemalononitrile, respectively. In contrast to other 1,4-dipolar compounds, which can be preserved only at –20 to –40 °C, these compounds can be kept for a considerable time at room temperature; some of them begin to decompose only at 60 to 80 °C.

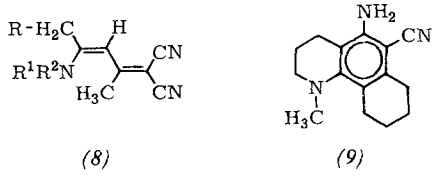
The yellow, crystalline 1,4-dipolar compounds formed from *(1)* and benzylidenemalononitrile are so unstable that, with one exception [*(4)*, R = CH_3, $R^1 + R^2 = (CH_2)_4$, $R^3 = C_6H_5$, R^4 = H], they react further to give butadiene derivatives *(6)* when attempts are made to isolate them.



We were not able to identify a 1,4-dipolar compound after reaction of *(1)* with acrylonitrile; the cyclobutene derivatives *(7)* were isolated.



Reaction of isopropylidenemalononitrile *(3)*, $R^3 = R^4 = CH_3$, with *(1)* does not give a 1,4-dipolar compound, but because of the activated methyl groups affords the butadiene de-



(8) *(9)*

rivatives *(8)*. Cyclohexylidenemalononitrile and *(1)*, R = CH_3, $R^1 + R^2 = (CH_2)_3$, afford the octahydrobenzo[*h*]-quinoline *(9)*, m.p. 119–120 °, in an analogous fashion.

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[*] Prof. Dr. R. Gompper, Dr. W. Elser, and
Dipl.-Chem. H.-J. Müller
Institut für Organische Chemie der Universität
Karlstr. 23
8 München 2 (Germany)

[**] An intramolecular charge transfer would explain the color.

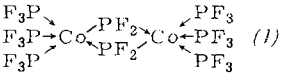
[1] We thank the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for supporting this investigation.

[2] Cf., for example, *J. K. Williams, D. W. Wiley*, and *B. C. McKusick*, J. Amer. chem. Soc. *84*, 2210 (1962); *R. Huisgen, L. Feiler*, and *G. Binsch*, Angew. Chem. *76*, 892 (1964); Angew. Chem. internat. Edit. *3*, 753 (1964); *St. Proskow, H. E. Simmons*, and *T. L. Cairns*, J. Amer. chem. Soc. *88*, 5254 (1966).

PF_2 Bridges in Metal Complexes [1]

By *Th. Kruck* and *W. Lang* [*]

In a search for polynuclear metal complexes containing PF_n bridging groups ($n = 1$ to 3), we have established formation of the first trifluorophosphinemetal complex with PF_2 bridges by studying the cobalt(II) iodide/PF_3 (pressure) system, which has already been investigated extensively [2]. Bis(μ-difluorophosphino)hexakis(trifluorophosphine)dicobalt *(1)* was isolated and characterized; it is diamagnetic, has the noble-gas configuration, and is the first representative of a series of type $[(PF_3)_nM(PF_2)]_2$ that is to be expected especially with transition metals of odd atomic number.



It is formed in about 30 % yield, along with another binuclear complex, on reaction of anhydrous CoI_2 and Cu powder (molar ratio 1:10) with trifluorophosphine under 400 atm at temperatures above 170 °C (15 h). The oily, deep red liquid solidifies at 25 °C and can be distilled at *ca.* 50 °C/10^{-3} mm. It is soluble in polar and non-polar organic solvents and is stable for some days towards atmospheric oxygen. The thermal stability is noteworthy, for in a sealed tube the compound decomposes, with discoloration, only at temperatures above 200 °C.

The IR spectrum of the substance in pentane solution contains P–F stretching vibrations at 909 (m, sh), 901 (vs), 858 (w,sh), and 855 cm^{-1} (s) [3], *i.e.* in the region that has up to now been regarded as characteristic of terminal PF_3 groups. Although this does not establish the presence of PF_2 bridges, their existence has been proved, in particular, by mass spectroscopy and NMR studies [4].

The mass spectrum (Atlas-CH-4, 15–70 eV) indicates a molecular weight of 784 which, together with the analytical data (Co:P:F = 2:7.95:22.4), proves the molecular formula $Co_2P_8F_{22}$. Further, it was found that on excitation by electrons of not too high an energy, six PF_3 groups are lost stepwise, with formation of the ions $[(PF_3)_{6-n}Co_2(PF_2)_2]^{\oplus}$ ($n = 0$ to 6). The high relative intensity of a peak at 256 mass units also shows the notable stability of the $Co_2(PF_2)_2$ group.

In the ^{19}F–NMR spectrum (Spectrospin-KIS-2, 60 MHz, pure substance at 26 °C, CCl_3F as external standard) two groups of signals appear; one of these ($\delta = +13.2$ ppm) lies in a region characteristic of terminal PF_3 groups of trifluorophosphine-metal complexes, but the other is shifted by a further 33.8 ppm to higher field strengths. On account of their position and intensity the signals of the second group are assigned to F atoms of two PF_2 bridges. Studies of the hyperfine structure are in agreement with this, for they show that all the ^{19}F signals of the bridge fluorine atoms are split into septets owing to coupling with the P nuclei of the six terminal PF_3 ligands. The coupling constant $^3J_{P-F}$, (28 Hz) is of the order of magnitude found also for other systems; furthermore, the spectrum affords coupling constants $^1J_{P-F}$ for the terminal PF_3 groups of *ca.* 1330 Hz and for the PF_2 bridges of *ca.* 1230 Hz.

All these results indicate a molecule of structure *(1)* with an almost planar arrangement of the four-membered $Co(PF_2)_2Co$ ring. No certain information can yet be given about the position of the PF_3 ligands, but the low number of the P–F stretching frequencies indicates a high symmetry for the overall structure.

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[*] Prof. Dr. Th. Kruck and Dr. W. Lang
Institut für Anorganische Chemie der Universität
Zülpicherstr. 47
5 Köln (Germany)

[1] Part XVIII of Trifluorophosphine-Metal Complexes. – Part XVII: *Th. Kruck* and *A. Engelmann*, Angew. Chem. *78*, 820 (1966); Angew. Chem. internat. Edit. *5*, 836 (1966).

[2] *Th. Kruck, W. Lang*, and *A. Engelmann*, Angew. Chem. *77*, 132 (1965); Angew. Chem. internat. Edit. *4*, 148 (1965); Z. anorg. allg. Chem. *343*, 181 (1966).

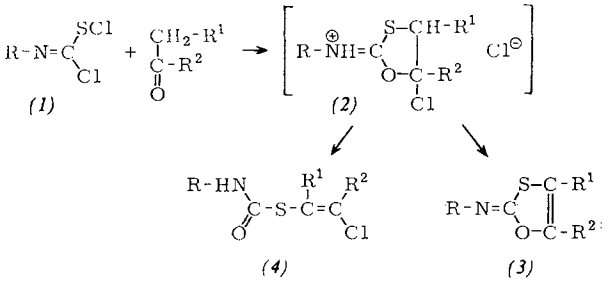
[3] m = medium, vs = very strong, w = weak, s = strong, sh = shoulder.

[4] We thank *H. Glinka* for measurement of the mass spectrum, and *P. Junkes* for the ^{19}F–NMR investigations.

2-Imino-1,3-oxathioles [1]

By *G. Ottmann* and *H. Hooks jr.* [*]

N-Substituted *S*-chloroisothiocarbamoyl chlorides *(1)*, which are obtained by careful chlorination of isothiocyanates [3], react with aryl alkyl ketones to form derivatives of the unknown class of 2-imino-1,3-oxathioles *(3)*. In the case of

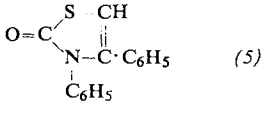


(1) *(2)* *(4)* *(3)*

R	R^1	R^2	*(3)* M.p. (°C)	*(3)* Yield [5] (%)	*(3)* Hydrochloride m.p. (°C)
C_6H_5	H	C_6H_5	137–138	52	210–212
C_6H_5	CH_3	C_6H_5	143–144	48	188–189
C_6H_5	H	p-$CH_3OC_6H_4$	159–160	59	193–194
C_6H_5	H	3.4-Cl_2-C_6H_3	169.5–170.5	40	192–194
C_4H_9	H	C_6H_5	60.5–61	64	143.5–144.5
C_4H_9	CH_3	C_6H_5	31.5–32	34	153–154

N-aryl substituted *S*-chloroisothiocarbamoyl chlorides the reaction proceeds directly, with hydrogen chloride elimination, to the hydrochlorides of *(3)*, not permitting isolation of a stable reaction intermediate [4]. In some instances, the reaction is accompanied by formation of substantial amounts of *S*-(2-chlorovinyl)thiocarbamates, *e.g.* *N*-phenyl-*S*-[2-chloro-2-(4-methoxyphenyl)vinyl] thiocarbamate *(4)* from *(1)* (R = C_6H_5) and 4-methoxyacetophenone. The simultaneous formation of *(3)* and *(4)* can be explained by elimination of hydrogen chloride from the hypothetical intermediate *(2)*. In the case of *(3)*, a simple β-elimination with a rupture of the C–Cl bond occurs, while HCl-formation and cleavage of the C(4)-O bond accounts for the formation of *(4)*.

The hydrochlorides of *(3)* are readily converted to the free bases by triethylamine under anhydrous conditions, or simply with water. Treatment of the hydrochlorides of *(3)* with alcohols, however, affects structural rearrangement and affords, besides sulfur-free by-products (mainly aniline hydrochloride), 1,3-thiazolin-2-ones, *e.g.* 3,4-diphenyl-1,3-thiazolin-2-one *(5)*, m.p. 121.5–123 °C from 5-phenyl-2-phenylimino-1,3-oxathiole hydrochloride and methanol.



(5)

The structures of compounds *(3)* are supported by elemental analysis, NMR, IR, and mass spectroscopy. The structure of *(4)* is evidenced by hydrolytic degradation to 2-chloro-2-(4-methoxyphenyl)vinylmercaptane *(6)*, m.p. 87.5-88 °C

$HSCH{=}C(Cl)C_6H_4OCH_3$

(6)

Experimental:

103 g of *S*-chloro-*N*-phenylisothiocarbamoyl chloride is added dropwise to a stirred solution of 75 g of acetophenone in 150 ml of ether at 40–45 °C. The reaction is accompanied by heavy HCl-evolution. The reaction mixture is stirred overnight, and the precipitate is then separated, washed with ether/pentane, and dried. Yield: 80 g (55 %) of 5-phenyl-2-phenylimino-1,3-oxathiole hydrochloride.

a) A solution of 17 g of triethylamine in 75 ml of ether is added to a stirred slurry of 47 g of the hydrochloride in 1000 ml ether over a period of 45 min at 10–15 °C. After 4 h at room temperature, the solid is separated and extracted with ether in a Soxhlet apparatus. 5-Phenyl-2-phenylimino-1,3-oxathiole is recovered from both ether solutions and recrystallized from methanol. Yield: 37 g (90 %).

b) 11 g of the above hydrochloride is added to 100 ml of water (~60 °C) in several portions with vigorous agitation. The precipitate of 5-phenyl-2-phenylimino-1,3-oxathiole is recrystallized from methanol.

c) 22 g of the above hydrochloride is mixed with 50 ml of methanol and slowly heated. At about 50 °C an exothermic reaction ensues and a clear solution is formed. The methanol is evaporated and the oily portion of the residue separated from aniline hydrochloride by extraction with ether. The ether was removed, and the remaining oil allowed to crystallize over several days. The crystals (8.5 g) are freed from contaminating oil and recrystallized from methanol and then from cyclohexane yielding 3.2 g of pure 3,4-diphenyl-1,3-thiazolin-2-one *(5)*.

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[*] Dr. G. Ottmann and H. Hooks jr.
Olin Mathieson Chemical Corporation Research Center
275 Winchester Avenue
New Haven, Conn. 06504 (U.S.A.)

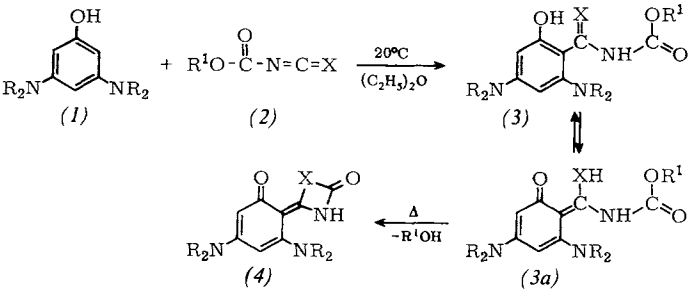
[1] Chlorination of Isothiocyanates, Part VI. – Part V: [2].
[2] *G. Ottmann* and *H. Hooks jr.*, J. heterocyclic Chem., in press.
[3] *G. Ottmann* and *H. Hooks jr.*, J. org. Chemistry *31*, 838 (1966).
[4] In contrast, a reaction intermediate of the empirical formula $[C_{14}H_{19}ClNOS]^{\oplus}Cl^{\ominus}$ was isolated from the reaction of *N*-butyl-*S*-chloroisothiocarbamoyl chloride with propiophenone and converted stepwise to *(3)* (R=n-C_4H_9, $R^1 = CH_3$, $R^2 = C_6H_5$).
[5] Yields are based on the amount of starting material *(1)*.

Reaction of Isocyanato- and Isothiocyanatoformates with Activated Phenols [1]

By *F. Effenberger* and *R. Niess* [*]

3,5-Bis(dialkylamino)phenols *(1)* [2], which are accessible from phloroglucinol and secondary amines, contain positive electromeric substituents in *meta*-position to one another, the effect of which is markedly displayed in an increased reactivity of the ring-carbon atoms towards electrophilic reagents.

Thus they react with isocyanatoformates *(2)*, X = O, and isothiocyanatoformates *(2)*, X = S, even at room temperature with exclusive *C*-acylation that yields the compounds *(3)* and *(3a)*, respectively. Acylation in the *para*-position could not be detected by ^1H–NMR spectroscopy.



(1) *(2)* *(3)* *(4)* *(3a)*

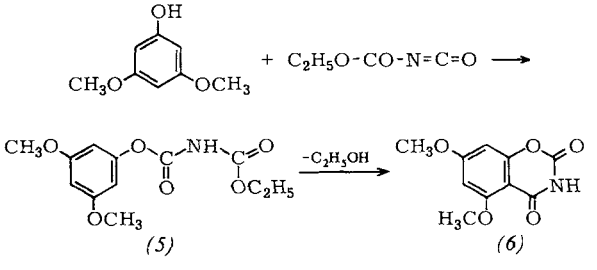
The compounds *(1)* and *(2)* were dissolved in anhydrous ether and mixed in the molar ratio 1:1 at 20 °C. After 2h at this temperature, the solution was cooled to −20 °C and after *ca.* 12h the crystals that had separated were collected by filtration.

R, R–N–	R¹	X	(3a) Yield (%)	(3a) M.p. (°C)	(4) Yield (%)	(4) M.p.
Piperidino-	CH_3	O	77.5	156–157	94	247–248
Piperidino-	C_2H_5	O	80	155–157	84.5	247–248
Piperidino-	C_2H_5	S	87	*ca.* 148	87	220–221
Dimethylamino-	CH_3	O	100	125–127	80	223–224
Dimethylamino-	C_2H_5	S	87.5	110–111	100	221–223

Whereas the aminophenols *(1)* are in the benzenoid form, spectroscopic results indicate that the acylation products have the tautomeric quinonemethide structure *(3a)*. According to the results of *Gompper et al.*[3] quinonemethides with ω,ω-hetero-substituents are relatively stable. It is possible that hydrogen bridges contribute further to the stabilization of *(3a)*.

Heating the acylation products *(3a)* above their melting points causes intramolecular removal of alcohol and formation of 1,3-oxazetidin-2-ones *(4)*, X = O, and 1,3-thiazetidin-2-ones *(4)*, X = S, whose structures are proved by elemental analysis, molecular-weight determination, and ^{1}H–NMR and UV spectra.

In contrast to the behavior of the bis(dialkylamino)phenols *(1)*, reaction of the less activated phloroglucinol dimethyl ether with *(2)*, X = O, R′ = C_2H_5, causes exclusive *O*-acylation with formation of the urethane *(5)*, which, when heated above the melting point, also loses alcohol and gives the benzoxazine derivative *(6)*.



Other phenols also react similarly to yield benzoxazines *(6)*.

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[*] Doz. Dr. F. Effenberger and Dr. R. Niess
Institut für organische Chemie der Technischen Hochschule
Azenbergstr. 14
7 Stuttgart-N (Germany)

[1] We thank the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for support of this work.

[2] *F. Effenberger* and *R. Niess*, Angew. Chem. 1967, in press; Angew. Chem. internat. Edit. 1967, in press.

[3] *R. Gompper*, *R. R. Schmidt*, and *E. Kutter*, Liebigs Ann. Chem. *684*, 37 (1965); *R. Gompper* and *E. Kutter*, Chem. Ber. *98*, 1365 (1965); *R. Gompper* and *R. R. Schmidt*, *ibid.* *98*, 1385 (1965).

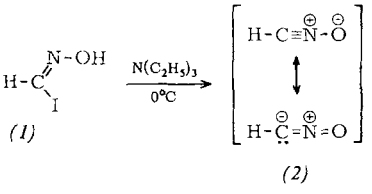
1,3-Dipolar Cycloadditions of Fulminic Acid

By *R. Huisgen* and *M. Christl*[*]

Quilico et al.[1,2] described cycloadditions of fulminic acid *(2)*, which was liberated from sodium fulminate by 20 % sulfuric acid or from formohydroximoyl iodide *(1)* by a base.

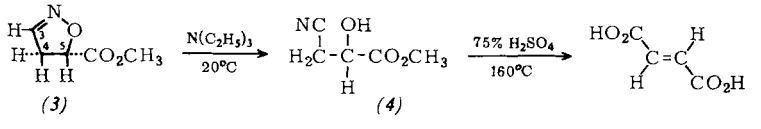
The rapid polymerization of *(2)* is responsible for the low yields of adducts. For instance, with acetylene only 3 % of isoxazole was obtained but 20 % of isoxazole-3-aldoxime (the adduct of dimeric fulminic acid)[1].

We converted mercuric fulminate into pure crystalline formohydroximoyl iodide *(1)* in 60 % yield with HI/KI without the detour through the sodium salt[3]. The fulminic acid is liberated by adding one equivalent of triethylamine dropwise and slowly to an ice-cooled, stirred solution of *(1)* in an excess of the dipolarophile (sometimes after dilution with ether). The low stationary concentration of *(2)* provides optimal conditions for the formation of 2-isoxazolines or isoxazoles from olefinic or acetylenic dipolarophiles, respectively.



(1) *(2)*

Methyl acrylate gives a 90 % yield of methyl 2-isoxazoline-5-carboxylate *(3)*, which is purified by high-vacuum distillation (b.p. 70–80 °C/0.001 mm) [NMR ($CDCl_3$): τ = 2.72 (H-3,t), J_{34} = 1.7 Hz; τ = 6.67 (H-4, q), J_{45} = 9.1 Hz; τ = 5.00 (H-5, t); τ = 6.20 (OCH_3,s)]. An excess of triethylamine converts *(3)* quantitatively into methyl 3-cyano-2-hydroxypropionate *(4)* [NMR ($CDCl_3$): τ = 5.48 (H-2, t), J_{23} = 5.5 Hz; τ = 6.12 (OCH_3, s); τ = 6.37 (OH, s, broad); τ = 7.12 (H-3, d): IR (film), 2248 (C≡N), 3400 cm^{-1} (OH)].

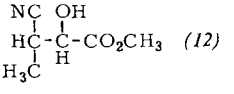


(3) *(4)*

Methyl crotonate and *(2)* afford the adducts *(5)* and *(6)* in the proportions 62:38 (yield 36 %) and the 2:1 adducts *(7)* and *(8)* in the proportions 45:55 (31 % yield). Thus cycloaddition of *(2)* to give *(5)* and *(6)* is in competition with dimerization of *(2)* to hydroxyiminoacetonitrile oxide which combines with the dipolarophile to give *(7)* and *(8)*. Benzonitrile oxide and methyl crotonate provide *(9)* and *(10)* in the proportions 34:66[4].



(5), R = H *(6)*, R = H
(7), R = -CH=NOH *(8)*, R = -CH=NOH
(9), R = C_6H_5 *(10)*, R = C_6H_5



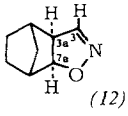
(12)

The adducts *(5)* and *(6)* can be separated by thin-layer chromatography (with benzene on silica gel PF_{254} + 366). NMR spectra indicate the structures. Ring opening of *(5)* to give *(11)*, catalysed by triethylamine, occurs even in the cold. NMR spectrum of *(11)* ($CDCl_3$): τ = 5.74 (H-2, d), J_{23} = 3.5 Hz; τ = 6.81 (H-3, octuplet); τ = 8.67 (4-CH_3, d), J_{34} = 7.3 Hz; τ = 6.11 (OCH_3,s); τ = 6.28 (OH, s, broad). IR (film): 2270 (C≡N), 3400 cm^{-1} (OH). The 2:1 adducts *(7)* and *(8)*, which distil only at 120–150 °C (bath)/0.001 mm, were analysed in admixture by NMR spectroscopy.

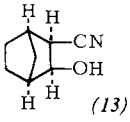
Methyl cinnamate affords analogously 1:1 (23 % yield) and 2:1 adducts (33 % yield). The 1:1 adducts contain the 4- and

5-carboxylic esters in the proportions 76:24 (70:30 on addition of benzonitrile oxide to cinnamic ester[4]).

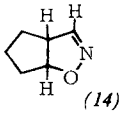
By virtue of the angular strain of its double bond, norbornene reacts with *(2)* to give 76 % of the adduct *(12)*, b.p. 65–75 °C/0.001 mm [NMR ($CDCl_3$): τ = 3.08 (H-3, d), J_{33a} = 1 Hz; τ = 6.85 (H-3a, q), J_{3a7a} = 8.2 Hz; τ = 5.61 (H-7a, d). The absence of coupling of H-3a and H-7a with the bridgehead hydrogen proves the *exo*-addition. Triethylamine converts *(12)* into the nitrile *(13)* [m.p. 35–38 °C; IR: 2270 (C≡N), 3450 cm^{-1} (OH)] in 93 % yield, but only after boiling for 12 h.



(12)

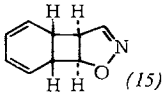


(13)

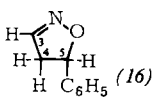


(14)

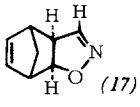
Cyclopentene and *(2)* give *(14)* in 8 % yield (b.p. 95–110 °C (bath)/10 mm). The adduct *(15)* of cyclooctatetraene, also isolated in 8 % yield, is derived from the bicyclo[4.2.0]-octadiene skeleton, as is shown by the ratio of vinyl-H to



(15)



(16)



(17)

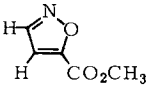
tertiary-5-Phenyl-2-isoxazoline *(16)* (b.p. 90–100 °C/0.001 mm) is formed in 70 % yield by cycloaddition of *(2)* to styrene. Its NMR spectrum ($CDCl_3$) proves the structure: τ = 2.91 (H-3, to J_{34} = 1.7 Hz; the CH_2 group on C-4 provides the expected 16-line signal (J_{gem} = −17.6 Hz). Ring opening to give the hydroxynitrile occurs only in boiling triethylamine.

The norbornadiene adduct *(17)*, which is isolated by distillation (b.p. 60–65 °C/0.001 mm) in 41 % yield and whose structure is proved by NMR and IR spectra, undergoes a retro-Diels-Alder reaction at 140–160 °C, which leads to cyclopentadiene and isoxazole (90 % yield). NMR spectrum of *(18)* ($CDCl_3$): τ = 1.66 (H-3, d), τ = 3.59 (H-4, t), and τ = 1.49 (H-5, d) with J_{34} = J_{45} = 1.5 Hz.

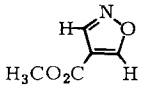


(18) R = H

(19) R = C_6H_5



(20)



(21)

Reaction of *(2)* with phenylacetylene gives a 51 % yield of 5-phenylisoxazole *(19)*. NMR ($CDCl_3$): τ = 1.72 (H-3, d) and τ = 3.52 (H-4, d) with J_{34} = 1.9 Hz.

Methyl propiolate adds fulminic acid in both directions. A 84:16 mixture of *(20)*, m.p. 47–50 °C[5], and *(21)* is obtained in 50 % yield. NMR spectrum of *(20)* ($CDCl_3$): τ = 1.47 and 2.93 (H-3 and H-4, d) with J_{34} = 1.8 Hz, τ = 5.98 (OCH_3,s). NMR spectrum of *(21)* ($CDCl_3$): τ = 1.30 (H-3, s), τ = 0.85 (H-5, s), and τ = 6.09 (OCH_3, s). Benzonitrile oxide reacts with methylpropiolate, giving the 5- and the 4-carboxylic ester in the ratio 72:28[4].

These cycloadditions are incompatible with the classical carboxime formula but agree with the formonitrile oxide structure of fulminic acid, thus supporting a recent assignment[6] based on IR spectroscopy.

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[*] Prof. R. Huisgen and Dipl.-Chem. M. Christl
Institut für Organische Chemie der Universität
Karlstr. 23
8 München 2 (Germany)

[1] *A. Quilico* and *G. Stagno d'Alcontres*, Gazz. chim. ital. *79*, 654, 703 (1949).

[2] *G. Stagno d'Alcontres* and *G. Fenech*, Gazz. chim. ital. *82*, 175 (1952).

[3] *A. Quilico* and *L. Panizzi*, Gazz. chim. ital. *72*, 155 (1942).

[4] *R. Sustmann*, Dissertation, Universität München, 1965.

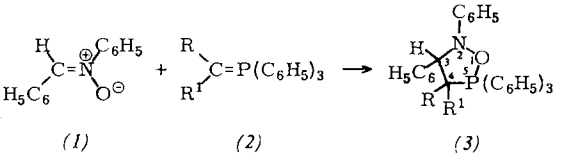
[5] Synthesis by another method: *A. Quilico* and *L. Panizzi*, Gazz. chim. ital. *72*, 458 (1942); M.p. 49–50 °C.

[6] *W. Beck* and *K. Feldl*, Angew. Chem. *78*, 746 (1966); Angew. Chem. internat. Edit. *5*, 525 (1966).

1,3-Cycloadditions of Nitrones to Methylenephosphoranes

By *J. Wulff* and *R. Huisgen*[*]

It has recently been shown that methylenephosphoranes are dipolarophiles and combine with nitrile oxides to give five-membered cycloadducts[1,2]. We have chosen azomethine oxides (nitrones) for further investigations since they represent a class of 1,3-dipoles that contain no double bond in their sextet structure[3].



(1) *(2)* *(3)*

(a), R = R^1 = H

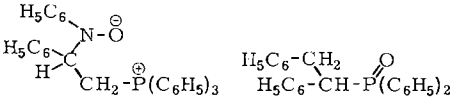
(b), R = R^1 = D

(c), R = C_6H_5, R^1 = H

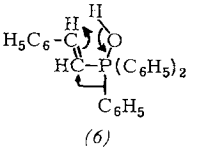
(d), R = R^1 = CH_3

If one equivalent each of *C,N*-diphenylnitrone *(1)* and methylenetriphenylphosphorane *(2a)* are mixed in ether at 20 °C, the colorless, crystalline 1,2,5-oxazaphosphole derivative *(3a)* precipitates in 93 % yield (decomp. 136–137 °C); C, H, and N analyses and osmometric determination of the molecular weight give correct values for *(3a)* as well as for the other new compounds prepared. NMR spectrum ($CDCl_3$) of *(3a)*: H-4 and H-4′ as octuplets at τ = 6.36 and 6.93 with $J_{44'}$ = −16.3, J_{34} = 8.5, J_{45} = 12.0, $J_{34'}$ = 7.0, and $J_{4'5}$ = 12.4 Hz. The similarity of the couplings of H-3 (J_{35} = 8.1 Hz) leads to a quadruplet at τ = 5.30. The ^{31}P signal at +58.6 ppm ($CDCl_3$, 85 % phosphoric acid as external standard) indicates quinquecovalent phosphorus; if the phosphonium zwitterion *(4)* were present instead of the isomeric *(3a)*, then a large negative chemical shift would be observed[4].

The ^1H–NMR spectrum could be interpreted only by comparison with that of the 4,4-dideuterio compound *(3b)*. The compound *(2b)* is obtained from (trideuteriomethyl)-triphenylphosphonium bromide by reaction with sodamide in benzene[5] without D-exchange. NMR spectrum ($CDCl_3$) of *(3b)*: H-3 as broad doublet at τ = 5.32 with J_{35} = 8.1 Hz.



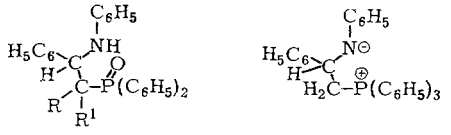
(4) *(5)*



(6)

Hydrolysis of *(3a)* in dioxane / water (5:1 v/v) at 100 °C gives (1,2-diphenylethyl)diphenylphosphine oxide *(5)* (yield 81 %) identified by comparison with an authentic specimen[6]. The *N*-phenylhydroxylamine that is also expected can be isolated

as *C,N*-diphenylnitrone if the hydrolysis is conducted in the presence of benzaldehyde. The reaction route leading to *(5)* [*(6)* is conceivable as intermediate] is as far from clear, as is the formation of *(5)* from a methyltriphenylphosphonium salt and benzaldehyde in the presence of sodium ethoxide in ethanol [7].



(7) *(8)*

(a), R = R^1 = H

(c), R = C_6H_5, R^1 = H

(d), R = R^1 = CH_3

Thermolysis of *(3a)* in boiling xylene, which occurs with formal loss of benzyne and formation of *(7a)* in 38 % yield, is also not understood; m.p. 204–205 °C; IR spectrum (KBr): 3320 (NH) and 1182 cm^{-1} (P=O). In an independent synthesis of *(7a)* (91 % yield), the zwitterion obtained from *(2a)* and *N*-benzylideneaniline in ether is hydrolysed.

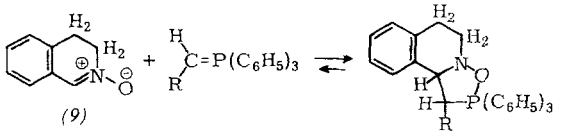
Slow reaction of benzylidenetriphenylphosphorane *(2c)* with *(1)* in benzene at 60 °C for 24 h gives the cycloadduct *(3c)* in 39 % yield, (decomp. 146–147 °C). NMR spectrum ($CDCl_3$): τ = 5.13 (H-3, t) with $J_{34} = J_{35}$ = 6.5 Hz, and τ = 5.67 (H-4, q) with J_{45} = 10.0 Hz; the ^{31}P signal ($CDCl_3$) is at +57.9 ppm. Thermolysis of *(3c)* in xylene gives the phosphine oxide *(7c)* in 24 % yield, m.p. 228–229 °C; IR spectrum (KBr): 3360 (NH) and 1178 cm^{-1} (P=O).

Isopropylidenetriphenylphosphorane *(2d)* also adds *(1)* in ether at 20 °C. The adduct *(3d)* (yield 22 %, decomp. 142 to 143 °C), is isolated along with 15 % of triphenylphosphine. NMR spectrum ($CDCl_3$) of *(3d)*: τ = 9.09 (4-CH_3, d) with J_{45} = 21 Hz, τ = 8.37 (4'-CH_3) with $J_{4'5}$ = 18 Hz, and τ = 5.01 (H-3, s); ^{31}P signal ($CDCl_3$) + 46.3 ppm. Hydrolysis of *(3d)* in boiling dioxane/water (10:3 v/v), or pyrolysis in a high vacuum at 150 °C, leads to the same product *(7d)*. (2-Anilino-1,1-dimethylphenethyl)diphenylphosphine oxide melts at 217–219 °C and is identical with a product which was obtained from *(2d)* and *N*-benzylideneaniline with subsequent hydrolysis. NMR spectrum ($CDCl_3$) of *(7d)*: τ = 8.69 (CH_3, d) with *J* = 14 Hz, τ = 8.89 (CH_3, d) with *J* = 16 Hz, τ = 5.84 (tertiary H, d, broad) with *J* = 7.0 Hz, IR band (KBr) at 3320 cm^{-1} (NH).

N-Methyl-*C*-phenylnitrone reacts more slowly than *(1)* with methylenetriphenylphosphorane *(2a)* in ether. The resulting cycloadduct (analogous to *(3a)*, N–CH_3 instead of N–C_6H_5) melts at 134–135 °C; ^{31}P signal ($CDCl_3$): + 60.3 ppm. Hydrolysis with dioxane/water gives the same phosphine oxide *(5)* (yield 43 %) as is formed from *(3a)*.

1,3-Dipolar cycloaddition of 3,4-dihydroisoquinoline *N*-oxide *(9)* to ethyl crotonate at 100 °C is 43 times faster than that of *C,N*-diphenylnitrone *(1)* [8]. The nitrone *(9)*, however, combines more slowly with *(2a)* than does *(1)*; after a week in benzene at room temperature *(10a)* (73 % yield, m.p. 146–147 °C, ^{31}P signal ($CDCl_3$): +56.4 ppm) is isolated.

Hydrolysis of *(10a)* in boiling dioxane/water is accompanied by fragmentation to starting materials, yielding, alongside *(9)*, 78 % of methyldiphenylphosphine oxide which is a



(9) *(10)*

(a), R = H

(b), R = C_6H_5

known hydrolysis product of *(2a)*. If *(10a)* is heated in the presence of benzaldehyde in anhydrous ethanol, (1,2-diphenylethyl)diphenylphosphine oxide *(5)* is formed in 48 % yield by the route described by *Trippett* and *Walker* [7] *i.e. via (2a)*.

The *N*-oxide *(9)* can be recovered to the extent of 70 % after being boiled for three days with benzylidenetriphenylphosphorane *(2c)* in benzene. 81 % of the *(9)* consumed appears as the colorless cycloadduct *(10b)*, decomp. 150–152 °C; NMR spectrum ($CDCl_3$), τ = 5.24 and 5.80 (2 tertiary H, q); the ABX spectrum shows the *J* values 5.4, 15.0, and 15.5 Hz; ^{31}P signal ($CDCl_3$): +50.9 ppm.

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[*] Dipl.-Chem. J. Wulff and Prof. R. Huisgen
Institut für Organische Chemie der Universität
Karlstr. 23
8 München 2 (Germany)

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[2] *H. J. Bestmann* and *H. Kunstmann*, Angew. Chem. *78*, 1059 (1966); Angew. Chem. internat. Edit. *5*, 1039 (1966).

[3] For classification of 1,3-dipoles see *R. Huisgen*, Angew. Chem. *75*, 604 (1963); Angew. Chem. internat. Edit. *2*, 565 (1963).

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[5] *G. Wittig* and *H. Pommer*, German Pat. 1003730 (BASF); Chem. Abstr. *53*, 16063 (1959).

[6] *L. Horner* and *P. Beck*, Chem. Ber. *93*, 1371 (1960).

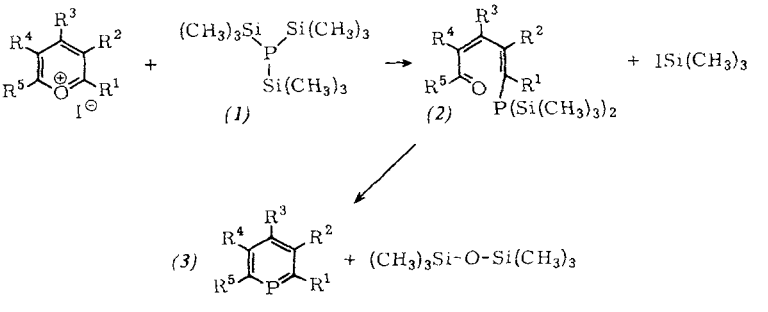
[7] *S. Trippett* and *D. J. Walker*, Chem. Commun. *1965*, 106.

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A New Synthesis of Phosphabenzene Derivatives

By *G. Märkl*, *F. Lieb*, and *A. Merz* [*]

It is usually impossible to isolate the phosphonium salts that are formed from silylphosphines and alkyl halides since they readily decompose into alkylphosphines and halosilanes [1]. Thus the reaction of tris(trimethylsilyl)phosphine [2] *(1)* with pyrylium iodides (fluoroborates and perchlorates cannot be used because of the low nucleophilicity of the anions) gives iodotrimethylsilane and the bis(trimethylsilyl)phosphine *(2)* [3]; however, the latter is not isolated but cyclizes with separation of hexamethyldisiloxane and formation of the substituted phosphabenzene *(3)*.



$R^1 = R^5$	R^2	R^3	R^4	(3), M.p. (°C)	(3), Yield (%)	(3), λ_{max} (ε) in CH_3CH_2OH
C_6H_5	H	C_6H_5	H	172–173	45.0	278 (41000) [4]
C_6H_5	C_6H_5	C_6H_5	H	209–210	41.0	270 (28000)
C_6H_5	C_6H_5	C_6H_5	C_6H_5	253–254	50.6	258 (32700)
						283 (25400) [a]
p-CH_3–C_6H_4	H	C_6H_5	H	133–134	62.5	283 (40700)
C_6H_5	H	p-CH_3O–C_6H_4	H	106	35.2	283 (36200)
p-CH_3O–C_6H_4	H	C_6H_5	H	136–137	44.7	292 (40200)
p-CH_3O–C_6H_4	H	p-CH_3O–C_6H_4	H	105–106	36.5	299 (46600)

[a] Shoulder.

In contrast with the synthesis of 2,4,6-triphenylphosphabenzene[4] from the pyrylium salt and tris(hydroxymethyl)-phosphine in boiling pyridine, no basic solvent is needed in this case. Water is not formed as a reaction product. Yields of the phosphabenzene derivatives are higher than in the tris(hydroxymethyl)phosphine synthesis in all cases.

2,4,6-Triphenylphosphabenzene:

2,4,6-Triphenylpyrylium iodide (1.1 g, 2.5 mmoles) in anhydrous acetonitrile (15 ml) is treated with tris(trimethylsilyl)phosphine (0.7 g, 2.8 mmoles) and boiled under reflux in an atmosphere of pure nitrogen for 20 h. After removal of the solvent by vacuum distillation, chromatographic separation of the reaction mixture with benzene on Al_2O_3 gives 365 mg of product, m.p. 172–173 °C after one recrystallization from chloroform/ethanol (1:3 v/v).

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[*] Priv.-Doz. Dr. G. Märkl, F. Lieb, and A. Merz
Institut für Organische Chemie der Universität
Röntgenring 11
87 Würzburg (Germany)

[1] *G. Fritz, G. Becker*, and *G. Poppenburg*, Angew. Chem. *78*, 80 (1966); Angew. Chem. internat. Edit. *5*, 53 (1966).

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[3] Note added in proof: *(1)* reacts at room temperature with 2,4,6-triphenylpyryliumfluoroborate/lithium bromide in acetonitrile to give 2,4,6-triphenylphosphabenzene (yield 39%; at boiling temperature 62%). The phosphine corresponding to the intermediate *(2)* may be isolated from the reaction products of $(C_6H_5)_2P$–$Si(CH_3)_3$ and the 2,4,6-triphenylpyrylium salt.

[4] *G. Märkl*, Angew. Chem. *78*, 907 (1966); Angew. Chem. internat. Edit. *5*, 846 (1966).

CONFERENCE REPORTS

Macromolecular Colloquium

This colloquium was held on March 9th–11th, 1967, at the Institut für Makromolekulare Chemie der Universität Freiburg (Germany).

From the lectures:

Secondary and Tertiary Structure of Transfer Ribonucleic Acid

By F. *Cramer*[*]

Transfer ribonucleic acids, which bring the amino acids into the genetically determined positions prior to incorporation, are the shortest definite nucleic acids known, since they contain only 70 to 80 nucleotide units. The sequences of four transfer ribonucleic acids have been established so far. In order to understand the function of the molecule, it is necessary to know its secondary and tertiary structure.

It was found earlier that monoperoxyphthalic acid oxidizes adenine units in nucleic acid only when these are not situated in base-paired regions.

Transfer ribonucleic acid is oxidized by monoperoxyphthalic acid at pH = 7. The course of reaction can be followed either by the change in the absorption spectrum as a result of the oxidation or by degradation of the nucleic acid and determination of the AMP 1-*N*-oxide units.

[*] Prof. Dr. F. Cramer
Max-Planck-Institut für experimentelle Medizin,
Abteilung Chemie
Hermann-Rein-Str. 3
34 Göttingen (Germany)

It is possible in this way to determine the number of non-base-paired A residues per molecule of RNA. The linear relationship between the oxidizability and the thermal hyperchromicity confirms that the A residues in transfer RNA are protected against oxidation as a result of the secondary structure (Watson-Crick base pairing). In this way, the thermal hyperchromicity can be calibrated with the aid of a chemical reaction. If the distribution of the A residues is assumed to be statistical, the number of base pairs in RNA can be calculated from hyperchromicity. It is found that the total s-RNA from yeast and *Coli* have 28 and 23 base pairs per molecule, respectively, at 20 °C. Of the 28 base pairs in yeast s-RNA, five disappear at 40 °C. These five base pairs are assigned to a tertiary structure (additional folding).

Dynamic Investigations on Oligo- and Polynucleotides

By *M. Eigen*, *G. Maass*, and *D. Pörschke*[*] (delivered by *G. Maass*)

It is known from the work of *Watson*, *Crick*, *Nirenberg*, *Khorana*, and many others that the program for the synthesis of proteins is contained in the sequence of the purine and pyrimidine bases A, G, T, and C in the double helix of the deoxyribonucleic acid (DNA) in the cell. The reading of the code is based on the complementarity between these

[*] Prof. Dr. M. Eigen, Dr. G. Maass, and
Dipl.-Chem. D. Pörschke
Max-Planck-Institut für Physikalische Chemie
Bunsenstr. 10
34 Göttingen (Germany)

nucleo bases. This complementarity depends on the specific hydrogen-bonding interaction between the bases. The main reason for the stability of the double helix of nucleic acid, apart from the hydrogen bonding, is the "stacking" interaction of the planar base pairs in the direction of the axis of the helix. To obtain an understanding of the elementary processes involved in the formation of the double helix and the nature of the complementary interaction in smaller code units (*e.g.* the codon–anticodon interaction), we studied the dynamic behaviour of synthetic polynucleotides and oligonucleotides of various chain lengths (from the trimer to the nonamer). The adenylic acid double helix was used as the model system.

The measurement of hypochromicity as a function of temperature gave results that agree with a statistical-thermodynamic theory developed by *Applequist* and *Damle* for the helix-coil transition of short-chain adenylic acids. The slopes of the melting curves at the T_m value and the dependence of the T_m value on the concentration gave reaction enthalpies of -7 to -8 kcal per mole of base pair.

Using the temperature jump relaxation method [1], it is shown that the helix-coil transition of oligoadenylic acids proceeds as a second-order reaction. The recombination rate constants for the helix formation are about 3×10^6 l mole^{-1} sec^{-1}, and are largely independent of the chain length. The dissociation rate constants are independent of the chain length for a constant melting range, but increase with increasing helix-coil transition. The results are discussed in relation to the denaturation kinetics of highly polymeric DNA and non-specific transfer RNA. The elementary steps in the helix-coil transition of adenylic acids, *i.e.* the formation and dissolution of base pairs, take 10^{-6} to 10^{-7} sec.

Quaternary Structure and Activity of Enzymes (Alcohol Dehydrogenase, Glutamic Dehydrogenase, Catalase)

By *H. Sund* [*]

The ageing of yeast alcohol dehydrogenase, which is accompanied by a decrease in the number of free SH groups (mainly as result of oxidation to disulfide groups) and in the enzyme activity as well as by partial dissociation into the polypeptide chains, does not affect all molecules to the same extent. In addition to fully active molecules (molecular weight 157000) and inactive polypeptide chains (molecular weight 40000), there are also inactive, or largely inactive, molecules that have not yet dissociated into polypeptide chains. These can be reactivated by incubation in the presence of mercaptoethanol and zinc ions. Even after dissociation into the polypeptide chains, a considerable degree of reactivation, with concurrent reassociation, has been accomplished by incubation at 0 °C in the presence of mercaptoethanol; the turnover number rises from 2500 to 28000 min^{-1} when the S_7 component (molecular weight 157000) is increased from 15 % to 85 % [2].

Glutamic dehydrogenase from ox liver dissociates into enzymatically active sub-units at low protein concentrations. To determine the size of these sub-units, the sedimentation coefficient was studied at protein concentrations down to 25 µg/ml. Extrapolation gave $s^0_{20,w} = 13.3$ S, corresponding to a minimum molecular weight of 260000 for the sub-unit. In the associated state (molecular weight 2×10^6), glutamic dehydrogenase probably contains eight sub-units [3].

To determine whether the structural information for the conformation of glutamic dehydrogenase is contained in the primary structure, the reactivation following the action of dodecyl sulfate was studied. In the presence of dodecyl sulfate, inactive sub-units ($s^0_{20,w}$ values of 5.8 S and 7.6 S), which probably consist of two and three polypeptide chains, are formed as well as the inactive polypeptide chains having a molecular weight of 50000. Substantial reactivation is possible after dissociation into the $S_{7.6}$ component. The extent of reactivation depends on the incubation time and on the protein concentration [4].

After succinylation and at pH = 12.5, ox-liver catalase (molecular weight 250000) dissociates under the influence of 5M guanidine hydrochloride (in the presence of mercaptoethanol) or sodium dodecyl sulfate to give four sub-units of equal size and having a molecular weight of 63000. In the absence of mercaptoethanol, denaturation by guanidine hydrochloride or urea, or incubation at pH = 3, leads to dissociation into two sub-units of molecular weight 125000. The four sub-units are held together in the native catalase molecule by non-covalent bonds. Electron micrographs show the catalase molecule as a flat parallelepiped having an edge length of about 80 Å and an altitude of about 35 Å; a symmetrical division into four is clearly discernible. It is assumed that each sub-unit having a molecular weight of 63000 contains an active center [5].

Synthesis of Polyarabinonucleotides with Esters of Polyphosphoric Acid

By *G. Schramm* [*]

A new type of polynucleotide has been obtained by polycondensation of uridylic acid with the aid of phenyl polyphosphate. Polyarabinonucleotides are formed with inversion of the 2′-hydroxyl group, poly-*O*^{2}-2′-cyclourydilic acid occurring as an intermediate. The polyarabinonucleotides are resistant to ribonuclease, and are only slowly hydrolysed by acid and alkali. This permits their separation from polyuridylic acid. Degradation with bacterial monophosphatase and snake-venom diesterase gave 9-β-D-arabinosyluracil. This substance ("spongouridine") has been isolated from sponges. In polyspongouridylic acid, the nucleotides are joined by 3′–5′ bonds, as in the natural nucleic acids. The condensation products were separated chromatographically according to their chain lengths, fractions containing up to 17 units being obtained. The polyarabinonucleotides are intermediate between RNA and DNA. Competitive inhibition of the degradation of DNA by deoxyribonuclease and RNA by ribonuclease was observed. Polyspongouridylic acid stimulates the adaptation of phenylalanine transfer RNA to ribosomes in the same manner as polyuridylic acid.

Synthesis of Insulin by the Merrifield Method [6]

By *H. Zahn, T. Okuda,* and *Y. Shimonishi* [**]
(delivered by *H. Zahn*)

Marglin and *Merrifield* [7] recently reported the syntheses of the A and B chains of ox insulin on chloromethylated polystyrene [8]. In co-operation with these authors, we have car-

[1] *M. Eigen* and *D. Pörschke*, J. molecular Biol., in preparation.

[*] Doz. Dr. H. Sund
Chemisches Laboratorium der Universität
Albertstr. 21
78 Freiburg/Br. (Germany)

[2] *M. Bühner* and *H. Sund*, unpublished.

[3] *H. Reckert, H. Sund,* and *G. Träxler*, unpublished.

[4] *M. Minssen* and *H. Sund*, unpublished.

[5] *H. Sund, K. Weber,* and *E. Möbbert*, Europ. J. Biochem., in press.

[*] Prof. Dr. G. Schramm
Max-Planck-Institut für Virusforschung
Spemannstr. 35
74 Tübingen (Germany)

[**] Prof. Dr. H. Zahn, Dr. T. Okuda, and Dr. Y. Shimonishi
Deutsches Wollforschungsinstitut
an der Technischen Hochschule
Veltmanplatz
51 Aachen (Germany)

[6] Cf. also 8th European Peptide Symposium Noordwijk, Sept. 1966.

[7] *A. Marglin* and *R. B. Merrifield*, J. Amer. chem. Soc. *88*, 5051 (1966).

[8] *R. B. Merrifield*, J. Amer. chem. Soc. *85*, 2149 (1963).

ried out similar work since October 1965 which has culminated in the synthesis of insulin chains in larger quantities than before[9]. Syntheses carried out included that of the A chain of human insulin and of the B chain of the ox (sheep) insulin. A new method used was the formation of peptide linkages on the amino group of threonine with the aid of *p*-nitrophenyl esters; in this method there is no need to protect the hydroxyl group of the threonine. The yields of analytically pure and partially protected chains, based on the C-terminal amino acid in the resin, were 23–34%. (This value includes the synthesis of the peptide chain, cleavage from the resin, double reprecipitation, and final purification by gel filtration.)

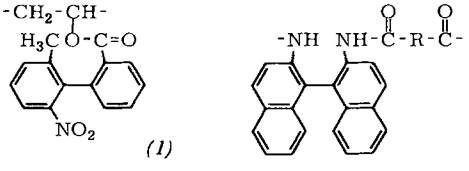
The partially protected insulin chains were converted into the *S*-sulfonates by reduction with sodium in liquid ammonia and oxidative sulfitolysis. The yields of electrophoretically homogeneous Bunte salts after purification by gel filtration and ion-exchange chromatography were about 10 to 15%, based on the protected chains. Combination of the synthetic human A chain with isolated ox B chain gave half-synthetic pig insulin in a yield of 1–2%. We obtained half-synthetic ox insulin with an insulin content of 1–3% from isolated ox A chain and synthetic ox B chain. Crystals were obtained from this preparation.

Though the Merrifield synthesis has increased the yields of protected insulin chains by several powers of ten, the preparation of crystalline insulin from the protected chains is still associated with extremely large losses.

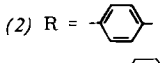
Polymers with Atropisomeric Biphenyl Structural Units

By *R. C. Schulz* and *R. H. Jung*[*]
(delivered by *R. C. Schulz*)

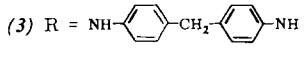
In the course of investigations on optically active polymers, we have prepared polymers containing the units *(1)*–*(6)*; they contain atropisomeric biphenyl or binaphthyl groups either as substituents along the main chain or as components thereof.



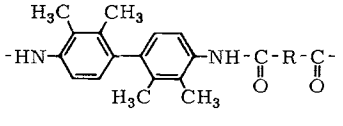
(1)



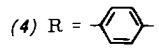
(2) R =



(3) R =



(4) R =



(5) R = $-(CH_2)_8-$

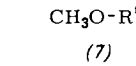
(6) R = $-(CH_2)_3-O-(CH_2)_3-$

[9] *H. Zahn, H. Bremer,* and *R. Zabel,* Z. Naturforsch. *20b,* 653 (1965); *J. Meienhofer* and *E. Schnabel, ibid. 20b,* 661 (1965); *H. Zahn, W. Danho,* and *B. Gutte, ibid. 21b,* 763 (1966); *H. Zahn,* Excerpta Medica Int. Congress Ser. *112,* 317 (1965).

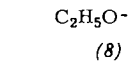
[*] Prof. Dr. R. C. Schulz and Dipl.-Chem. R. H. Jung
Organisch-Chemisches Institut der Universität
Johann-Joachim-Becher-Weg 18
65 Mainz (Germany)

The polymers *(1)* and *(2)* are soluble *e.g.* in γ-butyrolactone, dimethylformamide, or tetrahydrofuran; *(4)* is soluble only in hexafluoroisopropanol, and *(5)* is also soluble in hexafluoroacetone sesquihydrate and hexamethyltriamidophosphoric acid. Only oligomers of *(3)* and *(6)* have so far been isolated. *(1)* softens at about 160 °C and *(5)* at 260 °C, while *(2)* and *(4)* do not soften below 300 °C.

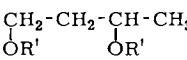
The polymers *(1)*, *(2)*, and *(5)* have been obtained in optically active forms. The compounds *(7)*–*(12)* were used as model substances for the optical measurements.



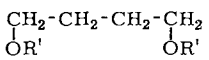
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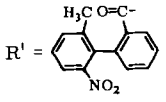
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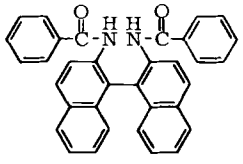


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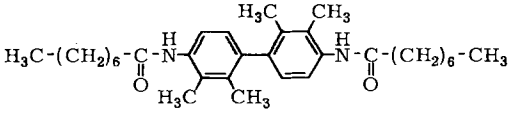


(10)





(11)



(12)

Compound	M.p.	$[M]_{578}$	1st extreme value		2nd extreme value	
			λ (mμ)	[α]	λ (mμ)	[α]
(7)	43	+176.3	380	+960	323	−2470
(8)	75–76	+154.9	380	—	320	—
(10)	165–166	+372.4	380	+880	324	−2400
(11)	190	+328.1 [a]	346	−786	305	+8650

[a] In tetrahydrofuran, $c = 0.5$; all others in dioxane, $c = 1$.

The polymers agree with the corresponding models in their rotatory dispersion and in their circular dichroism; however, on racemization considerable differences become apparent, which are due to the polymer structure.

Synthesis of Polyamides in the Fine-Grain Form from Diphenyl Esters and Diamines

By *W. Wolfes*[*]

Solutions of Diphenyl esters of dicarboxylic acids in aromatic hydrocarbons can be made to react with solutions of primary aliphatic diamines at low temperatures. The resulting polyamides precipitate out as fine powders. Polyamides having higher molecular weights are obtained by further condensation in suspension at higher temperatures (but below the melting point of the polyamide). The weight ratio of suspending medium to polyamide powder is about 4:1.

[*] Dr. W. Wolfes
Dynamit-Nobel AG.
521 Troisdorf (Germany)

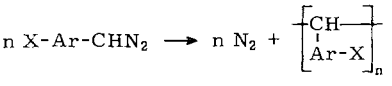
The condensation plant consists of a steam-heated stirring reactor fitted with a distillation column, a centrifuge, a wash tower, and drying apparatus; all solvents and washing agents are recycled. The phenol liberated during the condensation is used again for the production of the diphenyl ester. The average molecular weight of the polyamide depends mainly on the condensation temperature. The particle size depends on the stirring speed, the reaction temperature, and the solvent or suspending medium. The condensation process described permits the incorporation of divided fillers such as glass fibers, copper powder, or graphite, in a very uniform distribution.

The process is suitable for the production of polyamides of aromatic dicarboxylic acids that have a high melting point and do not swell appreciably.

Polymers and Copolymers of Diazoalkanes

By *G. Smets*[*]

When aryldiazoalkanes are unsubstituted or carry substituents which are unreactive towards the diazoalkane function, polymerization can proceed with nitrogen evolution and formation of polyarylidenes.



Such a type of polymerization of diazoalkane can be achieved by a pseudo-cationic mechanism (*Bawn*), or catalytically on colloidal metal surfaces (*Nasini*).

It was found that several polyarylidene polymers are formed by decomposition of aryldiazoalkanes in the presence of an alcohol, either in an homogeneous benzene-alcohol solution, or in heterogeneous systems by alkaline thermal decomposition of N-tosylbenzalhydrazones in water-benzene-methanol. The presence of an alcohol is indispensable for polymer production although its structure is of secondary importance. The yield of polymer is always high (80 to 95 %). The degree of polymerization varies with the nature of the aryl group and of the substituent. The overall activation energy of polymerization of phenyldiazomethane is equal to 5.5 kcal/mol.

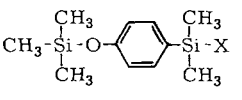
The fact that no polymerization takes place in the presence of peroxides, the failure of phenyldiazomethane to copolymerize with vinyl monomers, and the role of the alcohol are indicative of a reaction mechanism that involves the formation of an aryldiazoalkane methanol molecular complex (see reaction scheme) and which is based upon the low reactivity of diazoalkanes towards alcohol in the absence of any acid hydrogen. Copolymerization experiments were carried out in order to elucidate the nature of the reaction mechanism. The copolymerization parameters have been determined for the system phenyl-(M_1) and *p*-chlorophenyl-(M_2)-diazomethane (r_1 = 1.2; r_2 = 0.3) and the system phenyl-(M_1) and *p*-bromophenyl(M_2)-diazomethane (r_1 = 0.85 and r_2 = 0.4). These values are different from those for the corresponding ionic and radical polymerization of substituted styrenes. These copolymerization experiments agree therefore with the reaction mechanism through molecular complexes as suggested for the homopolymerization.

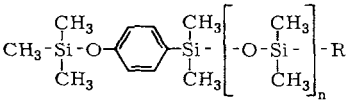
[*] Prof. Dr. G. Smets
Laboratoire de Chimie Macromoléculaire
98, rue de Namur
Louvain (Belgium)

Synthesis and Reactions of Siloxane-Substituted Phenols

By *G. Greber* and *D. Lohmann*[*] (delivered by *G. Greber*)

We synthesized the chlorosilane *(1)*, the phenol group of which is protected by a trimethylsilyl residue, by the Wurtz-Fittig reaction of *p*-chlorophenoxytrimethylsilane, dimethyldichlorosilane, and sodium, and by the reaction of the Grignard compound of *p*-bromophenoxytrimethylsilane with dimethyldichlorosilane. On hydrolysis with aqueous ammonia, *(1)* is converted into the silanol *(2)* without loss of the protecting group.



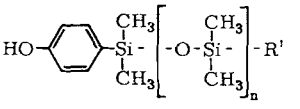


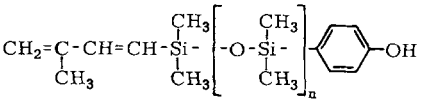
(1), X = Cl
(2), X = OH

(3), R = CH_3, n = 1–3
(4), R = Cl, *n* = 1–3
(5), R = H, *n* = 0–2
(6), R = C_6H_4–O–Si$(CH_3)_3$, *n* = 1–3

The reactions of the silanol *(2)* with trimethylchlorosilane or 1-chloropolysiloxanes lead to the siloxane-substituted phenols *(3)*, which are still protected. With an excess of dimethyldichlorosilane or ω,ω′-dichloropolysiloxanes, on the other hand, they give polysiloxanes *(4)* having a protected phenol group and a Cl–Si end-group ,which can be reduced to an H–Si group (in *(5)*) by $LiAlH_4$. Polysiloxanes having two protected phenol end-groups *(6)* are formed on condensation of the silanol *(2)* with *(1)* or with dimethyldichlorosilane or ω,ω′-dichloropolysiloxanes in a molar ratio of 2:1.

Siloxane-modified polymers can be obtained from the bisphenols *(8)* by reaction with bifunctional components.





(7), R′ = CH_3, *n* = 1–3
(8), R′ = C_6H_4OH, *n* = 1–3

(9), *n* = 1, 2

The compounds *(5)* containing H–Si groups add *e.g.* to the triple bond in isopropenylacetylene with H_2PtCl_6 as catalyst. Removal of the trimethylsilyl protecting groups yields *trans*-isoprene derivatives containing a *p*-hydroxyphenylsiloxane residue *(9)*, which copolymerize with a readiness similar to that of isoprene, and copolymerize *e.g.* with styrene to form products containing lateral free phenol groups.

The Mechanism of Formation of Polyesters from Cyclic Anhydrides and Cyclic Ethers with Cationic Initiators

By *K.-H. Reichert*, *J. Habermeier*, and *K. Hamann*[**] (delivered by *K. Hamann*)

Earlier investigations on the cationically initiated formation of polyester and poly(ester ethers) from cyclic ethers and dicarboxylic anhydrides[10] showed that the content of ether

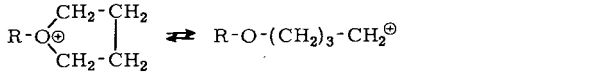
[*] Priv.-Doz. Dr. G. Greber and Dipl.-Chem. D. Lohmann
Institut für Makromolekulare Chemie der Universität
Stefan-Meier-Str. 31
78 Freiburg/Br. (Germany)

[**] Dr. K.-H. Reichert, Dipl.-Chem. J. Habermeier, and
Prof. Dr. K. Hamann
Forschungsinstitut für Pigmente und Lacke e.V.
Wiederholstr. 10
7 Stuttgart (Germany)

[10] *J. Habermeier*, *K.-H. Reichert* and *K. Hamann*, J. Polymer Sci. *C*, in press; *A. Hilt*, *K.-H. Reichert*, and *K. Hamann*, Makromolekulare Chem. *101*, 246 (1967).

groups in the resulting polymer is strongly dependent on the reaction conditions, and particularly on the nature and concentration of the initiator.

The assumption that the reaction may be regarded essentially as a copolymerization with a coupled polymerization–depolymerization equilibrium of the ring ether was confirmed by comparative kinetic studies on the polymer formation and on model reactions. The rate of formation of the polymers is independent of the concentration of the monomers up to yields of about 60 wt-%. It is therefore concluded that the ring cleavage of the initially formed cyclic oxonium ion determines the rate of the overall reaction.



Model experiments on the rate of the acylation of n-butyl ether with succinic anhydride, the establishment of the polymerization–depolymerization equilibrium of polytetrahydrofuran by depolymerisation, and the rate of formation of polyesters or poly(ester ethers) from polytetrahydrofuran and succinic anhydride showed that under the normal copolymerization conditions, very little direct acylation of ether groups in the polymer chain is to be expected, whereas the ether content of the resulting polymers is certainly strongly influenced by the polymerization–depolymerization equilibrium of the corresponding polyether. The kinetic studies were carried out with two types of initiators having different effects on the course of the reaction. Whereas the copolymers of tetrahydrofuran and succinic anhydride obtained with $CH_3CO^{\oplus}SbCl_6^{\ominus}$ have a constant ether content over the entire range of yields, $C_4H_8\overset{\oplus}{O}-\overset{\ominus}{P}F_5$ leads to a decrease in the ether content as the reaction progresses. This is in agreement with the results of depolymerization of polytetrahydrofuran, according to which $CH_3CO^{\oplus}SbCl_6^{\ominus}$ causes faster equilibrium than $C_4H_8\overset{\oplus}{O}-\overset{\ominus}{P}F_5$.

Further experiments showed that the course of the copolymerization of cyclic ethers with dicarboxylic anhydrides under comparable conditions depends on the reactants. Thus the polymer yields and the ether contents indicate that the reactivity of a number of dicarboxylic anhydrides toward tetrahydrofuran decreases in the order: succinic anhydride > *cis*-hexahydrophthalic anhydride > maleic anhydride > phthalic anhydride. The reactivity of cyclic ethers toward succinic anhydride decreases in the order: tetrahydrofuran > 3-methyltetrahydrofuran > 2-methyltetrahydrofuran > oxepane > 1,4-dioxane > tetrahydropyran. The order of the cyclic ethers can be qualitatively explained by the combined effects of ring strain and the basicity of the ether oxygen.

Isoprene and Organolithium Compounds in Hydrocarbons and Ethers

By *H. Sinn, F. Bandermann, K. Trukenbrod*, and *G. Dobratz* [*] (delivered by *H. Sinn*)

Butyl-lithium and isoprene react in diethyl ether to form isoprenyl-lithium. Spectroscopic investigation of the reaction showed that the reactivity of butyl-lithium toward isoprene is about 1000 times as high as that of isoprenyl-lithium toward isoprene. Whereas isoprenyl-lithium is monomeric in ether, butyl-lithium is present in associates of approximately three molecules. These degrees of association were also found in the metalation of triphenylmethane with butyl-lithium and isoprenyl-lithium. In hydrocarbons, on the other hand, the two organometallic compounds are associated to approximately the same extent, and the reactivity of butyl-lithium towards isoprene is smaller by a factor of 250 than that of isoprenyl-lithium.

Since isoprenes from various sources differ in the content of polar impurities (in the ppm-range) even after careful purification, extremely reproducible time-conversion curves are obtained with isoprenyl-lithium. but not with butyl-lithium. This follows quantitatively from the above reactivity ratios, and can be experimentally confirmed by the addition of appropriate quantities of ether to very pure isoprene. As a result of these additions, the initiating reaction becomes faster than the propogation reaction.

Calculations for real reactors show that isothermal reactions are impossible owing to the finite rate of heat transfer (except with programmed temperature control). The temperature fluctuations are of the order of a few tenths of a degree. The calculation is carried out by means of the three differential equations:

$$-\frac{dV}{dt} = \frac{V-K_1}{K_1}(K_2 n_{LiBu} + K_3)$$

$$-\frac{V dn_{LiBu}}{dt} + \frac{n_{LiBu} dV}{dt} = K_4 (V-K_1) n_{LiBu}$$

$$\frac{dT}{dt} = \frac{1}{V}\left(K_5 \frac{dV}{dt} - K_6 T + K_7\right)$$

V = volume, n = number of moles, T = temperature, t = time, K = experimental constants.

It is interesting to note that with equations of this degree of complexity, the differences in the course of the time-conversion curves obtained by means of digital and analogue computers are greater than the experimental error.

The system involved in these studies are characterized by their conductivity and dielectric constant as functions of concentration and reaction time. The maximum ion concentrations are around 10^{-9} g-equiv./l. Their concentration-dependence cannot be correlated with the kinetic findings.

A Novel Method of Determing Reactivity Ratios in Copolymerization

By *V. Jaacks* [*]

The copolymerization of two monomers M_1 and M_2 is carried out with a sufficiently large excess of one of the monomers *e.g.* M_1, so that the copolymer contains only a few isolated M_2 units. The composition of this polymer is then determined almost entirely by the parameter $r_1 (= k_{11}/k_{12})$, and is independent of r_2. The copolymerization proceeds in accordance with the equation

$$\log [M_1]_0/[M_1]_t = r_1 \log [M_2]_0/[M_2]_t \quad (1)$$

A graph of $\log [M_2]_0/[M_2]_t$ against $\log [M_1]_0/[M_1]_t$ at various conversions gives a straight line whose gradient is equal to r_1. ($[M]_0$ and $[M]_t$ = concentrations of a comonomer at the beginning and at the end of copolymerization, respectively.)

The advantage of this method is that equation (1) is valid up to high conversions, provided that the excess of M_1 remains large enough. It is therefore no longer necessary to isolate and analyse the copolymer after small conversions in order to determine the consumption of the two monomers (it is well known that this involves analytical difficulties is many cases). The high monomer conversions can instead be measured

[*] Prof. Dr. H. Sinn, Dr. H. Bandermann,
Dipl.-Chem. K. Trukenbrod, and cand. chem. G. Dobratz
Chemisches Staatsinstitut, Lehrstuhl für Angewandte Chemie
Papendamm 6b
2 Hamburg 13 (Germany)

[*] Dr. V. Jaacks
Organisch-Chemisches Institut der Universität
Johann-Joachim-Becher-Weg 18–20
65 Mainz (Germany)

relatively accurately by gas-chromatographic determination of the monomers in the copolymerization mixture. This determination could not be carried out with sufficient accuracy in the usual method for the determination of reactivity ratios, which is restricted to low conversions.

The method described was first used for the copolymerization of trioxane (M_1) and styrene (M_2) ($r_1 = 0.025$, $r_2 \sim 10$, at 30 °C in methylene dichloride with $SnCl_4$). The determination of the relative reactivities of this pair of comonomers by the usual *Mayo-Lewis* method had been unsuccessful because of side reactions. The principle described above can also be applied to ter- and quaterpolymerizations. Quaterpolymerizations in which an excess of one monomer is present at any time will give three reactivity ratios for each monomer present in excess.

The Frequency Distribution of the Chemical Composition in Binary Copolymers

By *G. Markert*[*]

Mayo's copolymerization equation is valid for any mixing ratio of a pair of monomers (defined by the mole fraction), irrespective of copolymers that have already been formed. Thus the change in the chemical composition of the copolymers formed at any time with increasing conversion follows a single curve, irrespective of the initial mixing ratio of the monomers, which determines only the position of the zero point on the curve (the distance on the ordinate between the zero point and the end of the curve always corresponds to 100 % conversion).

However, such a "general conversion curve" is unsuitable in practice for a representation of the copolymerization process. The frequency distribution of the chemical composition is more readily accessible to generalization. From the general frequency curve (for a given pair of paremeters r) based on the frequency minimum, together with the copolymerization curve, it is possible to read off directly the frequency distribution in a copolymer of any overall composition. This type of plot is suitable for pairs of monomers with and without azeotropes.

Influence of the Anomalous Chain-Growth Reaction on the Copolymerization Kinetics

By *B. Erussalimskii, S. Lyubetskii, A. Goldenberg*, and *F. Duntov*[**] (delivered by *B. Erussalimskii*)

Some copolymers of ethylene are characterized by an appreciable content of anomalous sequences, $-CH_2CHX-CH_2CH_2-CHXCH_2-$[11]. A kinetic scheme that takes into account the formation and the reactions of the anomalously growing chains leads to a modified Mayo equation[12] the parameters of which can be determined in various ways. The calculated values agree satisfactorily with those found by measurement.

The existence of the anomalous growth reaction may be regarded as one of the reasons for the dependence of the φ factor (cross-termination constant) on the monomer ratio.

[*] Dr. G. Markert
Röhm & Haas GmbH.
Mainzer Str. 42
61 Darmstadt (Germany)

[**] Dr. B. Erussalimskii, Dr. S. Lyubetskii, Dr. A. Goldenberg, and Dr. F. Duntov
Institut Vysokomolekulyarnikh Soedinenii AN SSSR
Leningrad (USSR)

[11] *B. Erussalimsky, N. Tumarkin, F. Duntov, S. Lyubetzky*, and *A. Goldenberg*, Makromolekulare Chem., in press.

[12] *S. Lyubetzkii, B. Erussalimskii*, and *A. Goldenberg*, Doklady Akad. Nauk SSSR, *172*, 1372 (1967); Internat. Symposium on Macromolecular Chem. Tokyo, 1966, Preprint. 1. 1. 10.

Attempts to Characterize the Catalytically Active Center in Homogeneous Ziegler-Natta Polymerization

By *G. Henrici-Olivé* and *S. Olivé*[*] (delivered by *G. Henrici-Olivé*)

Magnetic measurements (susceptibility, ESR) and determination of the rate of polymerization were combined in order to obtain information about the valence and ligands of the titanium ion in the active species of a Ziegler-Natta catalyst. The system dicyclopentadienyltitanium dichloride–ethylaluminum dichloride in toluene was used as the catalyst, with ethylene as the monomer.

A linear relationship was found between the rate of polymerization and the concentration of Ti(IV) that had not been reduced. It was also found that at least two Ti(IV)–Al compounds containing bridge bonds must be the source of the Ti(III) compounds whose ESR spectra were observed. Only one of the complexes proves to be catalytically active.

Isolation and Characterization of Cyclic Oligomers of Formaldehyde

By *K. Burg* and *H. D. Hermann*[**]

During product recovery from residues from the polymerization of trioxane, higher oligomers of formaldehyde could be isolated as well as trioxane and tetroxane. The pentamer was isolated with the aid of preparative gas chromatography, while zone melting could be used for the isolation of a ring containing 15 formaldehyde units. The acid-catalysed pyrolysis of polytrioxane also leads to higher cyclic oligomers of formaldehyde. Pyrolytic gas-chromatographic investigations indicated formation of pentoxane, and probably also of hexoxane.

The cyclic acetals isolated were characterized on the basis of their polymerizability, their melting points, and their IR, NMR, and mass spectra.

The Efficiency of Gel Permeation Chromatography

By *G. Meyerhoff*[***]

Gel permeation chromatography (GPC) has recently developed into a very important aid for the determination of the molecular weight distributions of polymers. This method gives the relationship between the polymer concentration and the elution volume V_e. The molecular weight distribution is found by conversion of V_e into the molecular weight M by means of a suitable function.

The transformation function is obtained empirically; a function of the form $\log M = A - BV_e$ can often be used for suitable column combinations. These and other calibration functions are used to find theoretical elution curves for polymers having the well-known Schulz distribution; deviations in behavior from the GPC curves are also determined.

Rather surprisingly, almost perfect agreement is found between the theoretical and recorded curves for a single GPC column provided that the column is suitable for the molecular weight range under investigation. On the other hand, the recorded

[*] Dr. G. Henrici-Olivé and Dr. S. Olivé
Monsanto Research A.S.
Binzstr. 39
Zürich (Switzerland)

[**] Dr. K. Burg and Dr. H. D. Hermann
Farbwerke Hoechst AG.
6230 Frankfurt/M.-Höchst (Germany)

[***] Prof. G. Meyerhoff
Institut für Physikalische Chemie der Universität
Saarstr. 21
65 Mainz (Germany)

elution curves for the more efficient combinations of columns in groups of two or four correspond to a molecular weight distribution that is too narrow. This means that the separating efficiency is too high for a mixture of two polymers having very different average molecular weights. Analysis of this result is made difficult by the fact that the type of polystyrene gel and the elution velocity strongly influence the separation process.

The Influence of the Order in Polymer Solutions on Light Scattering

By *W. Burchard*[*]

For macromolecules that form a random coil in solution, plots of $c/i(\Theta)$ against $\sin^2 \Theta/2$ normally give straight lines (Θ = scattering angle, $i(\Theta)$ = scattering intensity).

On the other hand, solutions of polyvinyl carbanilate (PVCarb) in diethyl ketone shows an upward deflection of the curve at small angles. This means that the value of the shape factor $P(\Theta)$ at $\Theta = 0$ is not 1, but may be as much as 60 % lower.

This behavior shows that the angle-dependence is due not only to internal intereferences on one macromolecule, but also to external interferences on neighboring molecules.

The light-scattering measurements on PVCarb are evaluated by means of the equation given by *Zernicke* and *Prins*[13].

$$P'(\Theta) = P(\Theta) \left\{ 1 - 4\pi \frac{N}{X} \int_0^\infty [1-\rho(r,c)] r^2 \frac{\sin sr}{sr} \, dr \right\} \approx P(\Theta)$$

$$[1 + b\, c\, \bar{r}^{2\,3/2} \frac{N_L}{M} \Phi(\Theta)]^{-1}$$

$P'(\Theta)$ is the shape factor perturbed by external interference, $P(\Theta)$ the true shape factor, $\Phi^2(\Theta)$ the shape factor of a spherically symmetrical particle, $\rho(r,c)$ the probability of finding a macromolecule at distance r, M the molecular weight of the macromolecule, c the concentration, N_L the Loschmidt number, and b a constant, N the number of particles, V the volume, $\bar{r}^2$ the mean square radius.

A Guinier plot of $[P(0)/P'(\Theta)] - 1$ for PVCarb gives straight lines, the gradients of which are used to find the average distance to which two PVCarb molecules can approach each other. These results indicate strongly hindered penetration of the PVCarb coils in diethyl ketone. This hindrance is assumed to be due to a very firm and extensive solvation sheath.

Association of Macromolecules

By *H.-G. Elias, H. Dietschy, J. Gerber*, and *H. Lys*[**]

Association is a reversible combination of similar molecules. The limiting cases are open association ($2\,M_I \rightleftarrows M_{II}$, $M_{II} + M_I \rightleftarrows M_{III}$, *etc.*) and closed association ($N\,M_I \rightleftarrows M_N$). Equations for the relationship between the apparent molecular weight of unassociated molecules, the association equilibrium constants, multiplicity N, and concentration c for theta solutions have been derived for the two extreme cases. It is not possible to give closed equations that are valid for all solvents. The determination of the molecular weight of the unassociated molecules is difficult, particularly in the case of association in good solvents (2nd virial coefficient positive). Open association is exhibited by polyethylene glycols in benzene and carbon tetrachloride, and by "amorphous" polypropylene, *e.g.* in benzene, toluene, and cyclohexane. The association of polypropylene is probably due to desolvation. For ether-soluble polypropylene in CCl_4, association increases with the content of isotactic triads. Poly-γ-benzyl-L-glutamate obeys the laws of closed association in many theta solvents.

Electron-Microscope and X-Ray Investigations on the Structure of Drawn High Polymers

By *E. W. Fischer, H. Goddar*, and *G. F. Schmidt*[*] (delivered by *E. W. Fischer*)

The mechanical properties of drawn, partially crystalline high polymers depend largely on the mutual arrangement of the crystallites and on the conformation of the chains in the disordered regions. These two structural characteristics were studied for samples of polyethylene, polyoxymethylene, and polyethylene terephthalate by means of the electron microscope and with the aid of small-angle X-ray scattering, and compared with various models that have been proposed for the structure of the drawn polymers.

In the case of polyethylene, it is well known that the long period observed in X-ray studies is identical with the distance between lamellar crystallites in the direction of the fiber. However, the results reported here show that not only the positions of the reflections, but also the intensity distribution in the small-angle X-ray diagram can be explained with the aid of the structures observed by electron microscopy. For example, the investigations on cold drawn polyethylene showed that the four-point diagrams obtained with many high polymers are due to the oblique position of the lamellar crystallites with respect to the fiber direction.

To obtain further information on the structure of the disordered regions, the change in the small-angle intensity as a result of the infiltration of iodine into these regions was studied. It was concluded from these measurements that the difference in density between crystallites and disordered regions is caused by folding of some chains. Even in the case of oblique crystal layers (four-point diagram), chain folding must be assumed to occur on the boundary surfaces of the crystallites. It could be shown by this method that the difference in density between the amorphous and crystalline regions increases by a factor of 5 when the drawn sample is annealed. This is because the defects created in the crystallites during drawing diffuse out of the crystallites on heating, and take up an arrangement in layers transverse to the axis of the fiber.

The Influence of Chain Rigidity on the Crystallization Process in Macromolecules

By *H. Bittiger* and *E. Husemann*[**] (delivered by *H. Bittiger*)

The molecular mechanism of the crystallization process in polymers, *i.e.* the transition of the molecular coils into ordered solids, was investigated by electron microscopy for cellulosetricarbanilate and polyethylene. The influence of the proper-

[*] Dr. W. Burchard
Institut für makromolekulare Chemie der Universität
Stefan-Meier-Str. 31
78 Freiburg/Br. (Germany)

[13] *F. Zernicke* and *J. A. Prins*, Z. Physik *41*, 184 (1927).

[**] Prof. Dr. H.-G. Elias, Dr. H. Dietschy,
Dipl.-Ing. Chem. J. Gerber, and Dr. H. Lys
Technisch-Chemisches Laboratorium der ETH
Universitätsstr. 6
CH –8006 Zürich (Switzerland)

[*] Prof. Dr. E. W. Fischer, Dipl.-Physiker H. Goddar, and
Dr. G. F. Schmidt
Institut für Physikalische Chemie der Universität
Saarstr. 21
65 Mainz (Germany)

[**] Dr. H. Bittiger and Prof. Dr. E. Husemann
Institut für Makromolekulare Chemie der Universität
Stefan-Meier-Str. 31
78 Freiburg/Br. (Germany)

ties of the molecules (molecular weight, chain rigidity, extension of the coils, chain diameter) on the crystallization behavior (formation of nuclei, monocrystals, and fibrils, *etc.*) was compared for polymer-homologous series of the very rigid cellulosetricarbanilate and of the flexible polyethylene, in order to determine the reason for the folding of chain molecules.

In the case of the very rigid cellulosetricarbanilate, it was possible to observe individual ordered molecules, nuclei, monocrystals, and fibrils, and to determine the conditions for their formation. On the other hand, the flexible polyethylene showed neither individual molecules nor fibrils, despite extreme variations of molecular weight and crystallization conditions.

The experimental results, particularly the temperature-dependence of the lengths of the folded chain segments and of the sizes of the nuclei, are compared with the predictions of *Lauritzen* and *Hofmann*'s kinetic theory of chain folding[14]. The deviations from the theory can be discussed in relation to the flexibility of the chains.

Examples of the Flow Birefringence of Viscoelastic Systems

By *H.. Janeschitz-Kriegl*[*]

Macromolecular liquids exhibit pronounced elastic properties. This is demonstrated by their partial recovery on removal of a load causing plastic deformation. The recoverable shear in the rotation viscometer (constrained recoverable shear) is found on removal of the shear stress required for stationary laminar flow. Normal stresses acting perpendicular to the boundary surfaces of the liquid play an important part as constraining forces. However, the only material properties are differences in the normal stresses, which one would like to determine as functions of the (stationary) shear gradient, but which cannot be measured directly without disturbing the flow. One method for the indirect measurement of $p_{11} - p_{22}$ (difference of the normal stresses in the flow direction and in the direction of the shear gradient) consist in the determination of the axial force (normal thrust) in the rheogoniometer. The present investigations arose from a desire to use the flow birefringence of macromolecular liquids for photoelastic investigations.

Comparison with the measurements carried out with the rheogoniometer showed that an investigation of this nature is quite feasible at low shear gradients. It was also confirmed that molten polymers having a wide molecular weight distribution have more pronounced elastic properties than those having a narrow distribution and having approximately the same viscosity. Two polypropylenes were studied[15].

Experiments were also carried out to determine whether results for polymer melts can be compared with those for dilute solutions. This is important in connection with the interpretation of the influence of the molecular weight distribution, since the known theoretical relationships are really valid only for dilute systems, for which good agreement with experiment has been found. The dimensionless stress quantities used lead to an excellent reduction with respect to molecular weight, temperature, and concentration for anionically polymerized polystyrenes. The reduction with respect to the concentration is subject to an interesting limitation. Using a technical polystyrene, it is shown that solutions of medium concentration are more elastic in relation to their viscosities than dilute solutions and melts, which correspond to each other.

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[*] Dr. H. Janeschitz-Kriegl
TNO Centraal Laboratorium Julianalaan 134
Delft (Netherlands)

[15] Joint investigation by: Kon. Shell Plastics Laboratorium and Centraal Laboratorium TNO.

Investigations on the Flow Behavior of Polymers in Relation to their Molecular Structure

By *H. H. Meyer* and *W. Ring*[*] (delivered by *H. H. Meyer*)

The flow behavior of polymers in the melt and in concentrated solution is mainly determined by the average molecular weight, the molecular weight distribution, and the degree of branching. To study these relationships, model substances were prepared by polymerization of butadiene in benzene with n-butyl-lithium as the catalyst. The reaction of these "living polymers" with alkylchlorosilane or $SiCl_4$ led to macromolecules with a defined degree of branching.

The pure substances and a series of mixtures were characterized by solution viscosity, osmometry, and light scattering, and in some cases by gel permeation chromatography. The Weissenberg rheogoniometer was used to determine the flow behavior in concentrated solution and in the melt at shear rates between about 10^{-3} and 10^3 sec^{-1}. The normal stresses were measured as well as the tangential stresses. The results were largely in agreement with those obtained by *Kraus* and *Gruver*[16]; however, we have found that for 10% solutions of polybutadiene branching in four directions and having molecular weights up to $\bar{M}_w = 700000$, the course of the viscosity-molecular weight line (logarithmic graph, gradient 3.4) is parallel to that for linear polybutadiene, the branched polybutadiene always having a lower viscosity than a linear polybutadiene of the same molecular weight. No intersection of the two curves is observed up to a molecular weight of $\bar{M}_w = 2.5 \times 10^6$. This in agreement with a theory recently proposed by *F. Bueche*.

The normal stress differences have been found to be proportional to the square of the shear rate in the low shear rate range for linear, narrow distribution polybutadiene of various molecular weights (10% solution). A reduced plot showed good superposition. Moreover, application of a recently published phenomenological theory of *Ninomiya* and *Ferry*[17], which allows calculation of the equilibrium compliance essentially from intrinsic viscosity data, and of a specific result from "second order" fluid theory[18] yielded normal stress differences in good agreement with those directly measured by the rheogoniometer.

Torsional Vibration Measurements on High Polymers in the Rubber-Elastic Range

By *E. E. Schäfer* and *G. Rehage*[**] (delivered by *E. E. Schäfer*)

The elastic properties of dry and swollen elastomers that are cross-linked *via* principal valences were studied above the glass transition point. Experiments were carried out to determine whether the theories derived from statistical thermodynamics for the entropy-elastic state of matter can be applied to torsional vibration measurements. These measurements should give the principal parameters for the description of the elastic behavior of real networks, the degree of cross-linking, and the energy-elastic component of the storage modulus G'.

For this purpose we constructed a torsional pendulum that permits the determination of the temperature-dependence of the storage modulus, even for highly swollen elastomers, with an accuracy of at least 0.5%.

[*] Dr. H. H. Meyer and Dr. W. Ring
Chemische Werke Hüls AG.
437 Marl (Germany)

[16] *G. Kraus* and *J.T. Gruver*, J. Polymer Sci. *A 3*, 105 (1965).

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[**] Dr. E. E. Schäfer and Prof. Dr. G. Rehage
Physikalisch-Chemisches Institut
der Technischen Hochschule
Adolf-Römer-Str. 2 A
3392 Clausthal-Zellerfeld (Germany)

The investigations were carried out on polymethyl methacrylate that had been cross-linked in bulk or in a chlorobenzene solution with ethylene glycol dimethacrylate, and on natural rubber cross-linked with dicumyl peroxide. After extraction for about three weeks with *m*-xylene, nearly all the specimens showed a linear increase in storage modulus G' with temperature over a wide temperature range.

The physically effective degree of cross-linking could be calculated from the slope of these straight lines. The result is independent of the swelling agent used for a given specimen.

The energy-elastic component G'_4 of the storage modulus was found from the intercept of the lines $G'(T)$ on the axis, which was determined both graphically and analytically. G'_U was based on the total storage modulus, since the errors arising in the determination of the dimensions of the specimen are then eliminated. The energy-elastic component of the storage modulus for the unswollen polymethyl methacrylate specimens is less than 5 %, *i.e.* these specimens are almost ideally rubber-elastic in this temperature range. The values for the dry rubber specimens were 21 to 32 %, depending on the degree of cross-linking. G'_4 always increases with the degree of cross-linking.

In every case, the energy-elastic component of the storage modulus increases with the degree of swelling at a constant degree of cross-linking. We assume that the networks studied by us contain not only chains whose contour length is so great that their behavior is entropy-elastic, but also short chains, which are braced by the swelling process and energetically loaded on deformation.

Thermodynamic (Maximum) Melting Points of Oligomeric and Polymeric Single-Component and Multi-Component System

By *H. G. Kilian*[*]

Formulae are given for the thermodynamic equilibrium melting points of oligomeric and polymeric single-component systems of linear, perfectly stereo-regular chains. Under these conditions the chains are always built into crystal lamellae of the same thickness in the extended state (molecular folding is impossible). According to *Flory* and *Vrij*, the melting point of such a system is partly determined by a characteristic additional entropy term, which takes into account the nematic mixing of the chains in an otherwise invariant crystal lattice. This additional term is also significant for eutectic, ideally athermic polymeric multi-component systems. In this case it is accompanied by the entropy of mixing, which is due to the mixing of chains of various lengths in the melt. In the fully-crystalline eutectic state, the chains of various lengths in the eutectic multi-component system are arranged according to chain length and built into the crystal lamellae in the extended state, the length of these lamellae being the same as that of the chains themselves.

However, complete fractionation of the chains of various lengths during crystallization can seldom be achieved. It must therefore be assumed that there is limited miscibility of the chains of various lengths in the solid state and a limited possibility of nematic translation of the chains of various lengths in the crystal. These deviations from the equilibrium outlined above can be theoretically taken into account by a single "internal" parameter at the maximum melting point. The limited miscibility in the solid state and the possibility of nematic translation raise the maximum melting point in relation to that of the equilibrium system, since the "total" entropy of melting is decreased.

The melting points of several n-paraffins, the melting points of several fractions of linear polyethylene (in which there is no molecular folding), and the maximum melting points of quasi-eutectic copolymers can all be quantitatively described by an invariable set of phenomenological constants with the aid of the formulae discussed here. The polymeric single-component systems have consistently higher melting points than the multi-component systems, while the maximum melting points of the quasi-eutectic copolymers with statistical length distribtions of the crystallizable sequences show higher melting point depressions than the fractions with gaussian length distributions.

[*] Doz. Dr. H.-G. Kilian
Institut für Polymere der Universität
Marbacher Weg 15
355 Marburg (Germany)

Investigation of the Melting Behavior of Crystalline Polyethylene Produced by Degradation with HNO_3

By *K. H. Illers*[*]

Partially crystalline samples of linear and branched polyethylene, the crystallinities of which varied between 0.46 and 0.96; were treated with 100 % HNO_3 for up to 40 hours at 70 °C. According to *Palmer* and *Cobbold*[19], this leads to selective oxidation and breakdown of the amorphous regions. Investigations on the residual highly crystalline skeleton should provide information about the size, morphology, and properties of the crystalline regions in the partially crystalline starting material.

A differential calorimeter (DSC1, Perkin-Elmer) was used to find the melting point and the enthalpy of fusion as a function of the reaction time and rate of heating. The molecular weights $\overline{M}_n$ and $\overline{M}_w$ of the completely degraded samples were also determined, and electronmicroscope and X-ray measurements were carried out. The results can besummarized as follows:

1. The average crystal thickness in chain direction as calculated from the average molecular weights $\overline{M}_n$ and $\overline{M}_w$ of the degraded samples agree closely with the larger of the two X-ray periods. This shows that the dimension of the crystal in the chain direction is given by the larger X-ray period, and not by the smaller.
2. The molecular weight distributions of the degraded samples are very narrow, and probably approximately agree with the crystallite size distribution before degradation. The morphological structure of the original samples is evident in the molecular weight distribution of the degraded samples.
3. The melting point (position of endothermic peak extrapolated to a heating rate of zero) is not affected by treatment with HNO_3. On crystallization of the degraded samples from the melt, the melting point rises slightly for previously short crystallized chains, and falls for long chains.
4. The marked increase in the melting point of samples crystallized under high pressure with increasing heating rate ("superheating effect") is no longer observed after degradation.
5. The heat of melting increased with increasing reaction time, and reaches a limiting value after a time which decreases with increasing crystallinity of the original sample. The limiting value for annealed (130 °C) samples and samples crystallized under high pressure is 70 ± 1 cal/g. This value agrees with the heat of fusion of the infinitely large, 100 % crystalline polyethylene crystal, which could previously be determined only by extrapolations. In the case of branched and quenched linear polyethylene, a small amorphous fraction (15 and 10 % respectively) is still present even after the limiting value has been reached.
6. After degradation, the chains are crystallized in the extended state. When the degraded samples are subsequently crystallized from the melt, the heat of fusion again decreases, the decrease becoming more pronounced with increasing original crystal size. This is attributed to the combined influence of renewed chain folding and of the crystallite size. [VB 58 IE]

German version: Angew. Chem. *79*, 416 (1967)

[*] Dr. K. H. Illers
Badische Anilin- und Soda-Fabrik AG.
67 Ludwigshafen (Germany)

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Oxidation Reactions of the Thioamide Group

By *W. Walter* [*]

On oxidation with H_2O_2, thioamides afford thioamide *S*-oxides *(1)*, which can be clearly differentiated from the isomeric thiohydroxamic acids. The vibrations of the C=S group of thioamides couple so strongly with other vibrations that they cannot be used for identification, but the S=O vibration of the >C=S=O system offers a key band for this group. The equilibrium between a thioamide and an imido thiol corresponds to the equilibrium between *(1)* and the iminomethanesulfenic acid *(2)* in the oxidation products.

$$R^1\text{-}\underset{\underset{S=O}{\|}}{C}\text{-}NHR^2 \rightleftharpoons R^1\text{-}\underset{SOH}{C}=NR^2$$

(1) *(2)*

Reactions of thioamide *S*-oxides have been found in which the form *(2)* takes part; in the thiourethane series compounds of structure *(2)* can be isolated, *e.g.* when R^1 = $-O-C_6H_4-C_6H_5$-*o*, and R^2 = $-C_6H_3(CH_3)_2$-*o,o'*. The hydrogen bond shown in *(1)* plays a part in the stability of compounds *(1)* and *(2)*.

Thioamides show *cis-trans*-isomerism at their partial C=N double bonds. One isomer of an *N*-benzyl-*N*-methylthioformamide has been isolated and the other has been enriched to the extent of 75 %; the activation energy for their interconversion has been determined as 25.16 ± 0.66 kcal/mole. Their respective structures were assigned on the basis of NMR and X-ray diffraction data.

N-Isobutylthioformamide is an equilibrium mixture of 82 % of the *trans*- and 18 % of *cis*-form, but after oxidation to the *S*-oxide only the *cis* isomer remains; thus the intramolecular hydrogen bond is so strongly stabilizing that the barrier to rotation cannot be overcome at room temperature.

Lecture at Krefeld (Germany) on November 24th, 1966 [VB 45 IE]
German version: Angew. Chem. 79, 426 (1967)

[*] Prof. W. Walter
Chemisches Staatsinstitut Hamburg,
Institut für Organische Chemie
2 Hamburg 13 (Germany)
Papendamm 6

Nicotinamide *N*-Oxide: A Biological Oxidant

By *S. Chaykin* [*]

Hog liver xanthine oxidase can catalyse the reduction of nicotinamide *N*-oxide [1]. Either reduced nicotinamide adenine dinucleotide (NADH), hypoxanthine, or xanthine can be oxidized by the *N*-oxide. Since the enzyme also catalyses reactions with oxidizing agents that can act only as electron acceptors, it has been generally assumed that oxidizing agents always function solely as electron acceptors in xanthine oxidation. Water would serve as an oxygen donor when required. Although the *N*-oxide certainly is an electron acceptor in the oxidation of NADH, the possibility existed that it might act as an oxygenating agent in the oxidation of hypoxanthine or xanthine. The latter reactions were therefore investigated using ^{18}O-labeled oxidants.

When xanthine is oxidized in an atmosphere of $^{18}O_2$ no oxygen-18 is found in the uric acid which is formed. If the reaction is carried out in $H_2^{18}O$ and an atmosphere of $^{16}O_2$ oxygen-18 is found in the uric acid. However, when ^{18}O-labeled nicotinamide *N*-oxide is used, direct transfer of oxygen to xanthine occurs and 0.67 g-atom of ^{18}O per mole of uric acid are found. The *N*-oxide also functions as an electron acceptor, but to a much lesser extent; on oxidation with unlabeled *N*-oxide in the presence of $H_2^{18}O$ 0.18 g-atoms of ^{18}O were incorporated per mole of uric acid.

Similar results were obtained with milk and liver xanthine oxidases. If the properties of nicotinamide *N*-oxide are representative of those of heterocyclic *N*-oxides in general, then these compounds can be classified as biological oxidizing agents and should be investigated as potential electrophilic hydroxylating agents.

Lecture at Freiburg (Germany), November 11th, 1966 [VB 49 IE]
German version: Angew. Chem. 79, 476 (1967)

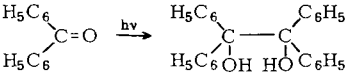
[*] Prof. Dr. S. Chaykin
Chemisches Laboratorium der Universität
Albertstr. 21
78 Freiburg (Germany)

[1] *K. N. Murray* and *S. Chaykin*, J. biol. Chemistry *241*, 3468 (1966).

Photoreduction of Ketones and Ketimines

By *M. Fischer* [*]

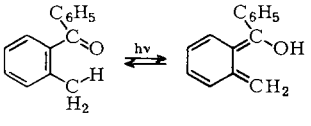
On irradiation by UV light, benzophenone *(1)* is reduced by hydrogen donors such as alcohols and hydrocarbons to benzopinacol *(2)* [1]. The quantum yield for the photoreduction reaches an optimal 2.0 in 2-propanol since hydrogen is abstracted relatively easily from this solvent, and it is vanishingly small in benzene whose hydrogen atoms are more firmly bound [2]. Studies with quenchers [3] show that



(1) *(2)*

the triplet state is the excited state responsible for the light-induced reaction.

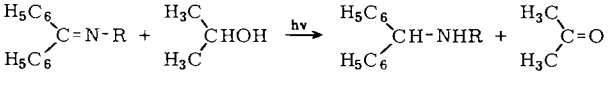
2-Methylbenzophenone *(3)* cannot be reduced to the pinacol [4] because the excitation by light causes an intramolecular migration of hydrogen to give the dienol *(4)*, which spontaneously reverts to the ketone. Formation of the dienol *(4)* was demonstrated by Diels-Alder addition to dimethyl acetylenedicarboxylate.



(3) *(4)*

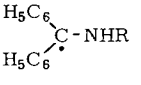
Photoreduction is also not observed with those benzophenones [2] that have substituents with electron-donor properties at the *o*- or *p*-position, since on irradiation electron shifts lead to a π,π^* triplet instead of the reactive n,π^* triplet.

Ketimines derived from benzophenone, *e.g.* benzophenone methylimine *(5)*, with R = CH_3, are reduced by 2-propanol under the influence of UV light to the corresponding amines *(6)* [5]. Quantum yield: 0.01 on irradation with light of wavelength 265 nm. Reaction conditions: Hanau immersion lamp TQ 81; Solidex filter; yield: 90%.



(5), R = CH_3, $C_6H_5CH_2$, C_6H_5 *(6)*

The aminodiphenylmethyl radical *(7)* is formed in the primary photochemical process, as could be shown by means of radical trapping agents and by isotope experiments.



(7)

Sensitizers such as xanthone with triplet energies of at least 62 kcal/mole sensitize the photoreduction of *(5)*.

Lecture at Isny/Allgäu on December 12th, 1966 [VB 53 IE]
German version: Angew. Chem. *97*, 425 (1967)

[*] Dr. M. Fischer
Chemisches Institut der Universität
Wilhelmstrasse 33
74 Tübingen (Germany)

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[5] *M. Fischer*, Tetrahedron Letters *1966*, 5273.

Side-Chain Interactions in Polypeptides. Experiments with Donor-Acceptor Complexes

By *R. Schwyzer* [*]

Synthetic chemical work has shown that the information held in the amino acid sequences of biologically active polypeptides is grouped in individual words of specific biological meaning [1]. For angiotensin and adrenocorticotropin (the first protein hormone synthesized in a pure state [2]) it has been shown that the regions responsible for the receptor mechanism, for blocking and for qualitative and quantitative alternation of activity, for transport, and for antigenic properties lie next to one another and are spelled out with different amino acid sequences. These results are important in the development of drugs.

The conformational possibilities of the active materials and their binding to the receptor molecule play a large part in translation of the sequence information into biological activity ("2nd translation of biochemical genetics"). Sidechain interactions are particularly important in this respect. In order to obtain information on side chain interactions in solution, we are attempting to build such amino acids into synthetic polypeptides whose side-chains might, given favorable conformations, form electron-donor-acceptor (EDA) complexes with one another. Complex formation can be detected spectroscopically by appearance of charge-transfer (CT) bands.

Our present experiments concern the following questions:

1. Which amino acids can form EDA complexes? 2. What are the properties of their intermolecular complexes? 3. Can one establish the existence of intramolecular complexes and what are their properties?

Our preliminary findings can be summarized as follows:

1. Amino acids with donor sidechains are: pentamethylphenylalanine, *p*-dimethylaminophenylalanine, tryptophan.

2. Amino acids with acceptor side chains are: *p*-nitrophenylalanine, 2,4-dinitrophenylalanine, 2,4,6-trinitrophenylalanine, N^{ε}-(4-nitrophthaloyl)lysine, N^{δ}-(4-nitrophthaloyl)ornithine, N^{ε}-(tetrachlorophthaloyl)lysine, N^{δ}-(tetrachlorophthaloyl)-ornithine.

3. Some intermolecular EDA complexes of 4-nitrophthaloylglycine ethyl ester: *N*-(benzyloxycarbonyl)pentamethylphenylalanine (in ethanol, λ_{CT} = 370 nm, ε_{CT} = 500, K_{ass} = 2.3, distance between ring planes 3.4 Å); *N*-acetyl-*p*-dimethylaminophenylalanine ester (in ethanol, λ_{CT} = 460 nm, ε_{CT} = 664, K_{ass} = 0.54); *N*-(benzyloxycarbonyl)tryptophan (in ethanol, λ_{CT} = 355 nm, ε_{CT} = 712, K_{ass} = 1.56).

4. Some intramolecular EDA complexes of the simplest *N*-phthaloylamino acid type: *N*-(4-nitrophthaloyl)pentamethylphenylalanine ester, yellow crystals (in $CHCl_3$, λ_{CT} = 345 nm, ε_{CT} = 310; mean distance for electron transfer 3.85 Å); *N*-(4-nitrophthaloyl)-*p*-dimethylaminophenylalanine ester, violet crystals (in ethanol, λ_{CT} = 430 nm, ε_{CT} = 17); *N*-(4-nitrophthaloyl)tryptophan ester, orange-red crystals (in $CHCl_3$, λ_{CT} = 428 nm, ε_{CT} = 470).

Lecture at Marburg on December 2nd, 1966 [VB 54 IE]
German version: Angew. Chem. *79*, 425 (1967)

[*] Prof. Dr. R. Schwyzer
Laboratorium für Molekularbiologie der
Eidgenössischen Technischen Hochschule
Universitätsstrasse 6
CH-8006 Zürich (Switzerland)

[1] *R. Schwyzer*, Ergebnisse Physiologie *53*, 1 (1963).

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Siderochromes, Iron-Containing Substances from Microorganisms

By *H. Zähner* [*]

When grown in an iron deficient environment, numerous microorganisms excrete compounds that can form iron complexes. Study of these products from different microorganisms disclosed a new group of natural compounds, the siderochromes. These are characterized by the presence of three hydroxamic acid groups per molecule, arranged in such a way that formation of a stable iron(III) complex is possible. Three types of complex can be distinguished on the basis of their biological activities:

a) *Sideramines.* Growth factors for various sideramine-heterotropic microorganisms (*Pilobolus kleinii*, strains of *Microbacterium lacticum*, *Arthobacter terregens*) and also antagonists of iron-containing antibiotics, namely the sideromycins. The group includes: ferrichrome, ferrichrysin, ferricrocin, ferrirubin, ferrirhodin, ferrioxamines A_1, A_2, B, C, D_1, D_2, E, F, and G, coprogen, and the terregen factor; probably also schizokinen.

b) *Sideromycins.* Iron-containing antibiotics that can be considered as antimetabolites of sideramines (albomycin, grisein, ferrimycin A_1 and A_2, succinimycin, A 22765, danubomycin).

c) *Siderochromes* without detectable biological activity, *e.g.* ferrichrome A.

All the sideramines from molds contain three ornithine units, their amino groups being hydroxylated and acylated. Varations in structure either consist in the mode of union of the three ornithine groups, *e.g.* through three glycine residues to a hexapeptide (here the glycine residues may be partially replaced by serine), or in the presence of different acid components (acetic acid or *cis*- or *trans*-anhydromevalonic acid).

The biological function of the sideramines is not yet clear. Hypotheses deal on the one hand with an influence on iron transport and on the other with a "coenzyme" action in the incorporation of iron into Fe-containing enzymes; but other possibilities cannot yet be ruled out.

The various hypotheses can be experimentally tested by means of the antagonism between sideramines and sideromycins. Iron-free ferrioxamin B is used as its methanesulfonate (Desferal®) for treatment of disturbance of iron storage. Formation of iron-free sideramines can be regulated by varying the amount of iron offered (deficiency of iron leads to increased production; with sufficient supply of iron no sideramine is produced). The mechanism and site of this control are unknown.

Lecture at Wuppertal on December 14th, 1966 [VB 55 IE]
German version: Angew. Chem. *79*, 424 (1967)

[*] Prof. Dr. H. Zähner
Institut für Mikrobiologie der Universität Tübingen
Im Schönblick 47
74 Tübingen (Germany)

Oxidation and Elimination Reactions of the Diazomethane–2,2-Bi-(1,4-naphthoquinone) Adduct

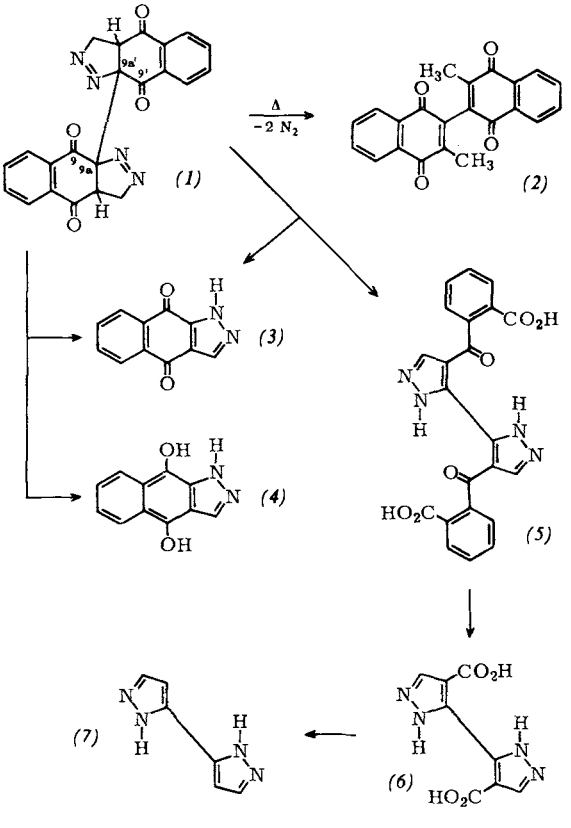
By *A. Zeeck* [*]

Both half-molecules of 2,2′-bi-(1,4-naphthoquinone) react with diazomethane in a cycloaddition yielding the adduct *(1)* [1]. This compound can be stabilized in three ways, each of which involve attack on the bonds from C-9a and C-9′a and aromatization:

1. Warming the adduct in anhydrous toluene gives 3,3′-dimethyl-2,2′-bi-(1,4-naphthoquinone) *(2)* (thermal elimination of nitrogen).

2. In the presence of electrophilic agents disproportionating fragmentation occurs, yielding benz[*f*]indazole-4,9-quinone *(3)* and its hydroquinone *(4)*. The latter is rapidly oxidized by air to the former. *(3)* and *(4)* can be identified in admixture by means of acetic anhydride/pyridine (with exclusion of air) when the *N*-acetyl derivative of *(3)*, and the leucotriacetate derivative of *(4)* are obtained. In a side reaction, *(1)* loses half of its nitrogen before the two molecular fragements have separated; a nitrogenous quinone of molecular weight 352 but unknown structure results.

3. Oxidation in 2 to 4 N alkali hydroxide solution leads to (a) decoupling of the C-9a/C-9′a bond, yielding two molecules of *(3)*, or (b) fission of the C-9/C-9a and the C-9′/C-9′a bonds, yielding 4,4′-bis(2-carboxybenzoyl)-5,5′-bipyrazole *(5)*. Use of hydrogen peroxide as oxidizing agent gives mainly *(3)* [1], and use of potassium hexacyanoferrate(III) gives (energetically more favorable) mainly *(5)*. Both reactions are expected to occur by way of an dianion of *(1)* and a



radical anion, which either splits into two parts or, when attacked by hydroxide ions at C-9 or C-9′, initiates another reaction path (oxidative-hydrolytic scission of two C–C bonds).

The structures of *(5)* and some of its derivatives can be proved by IR, NMR, and mass spectrometry. The position of the hydrogen atom in the pyrazole rings cannot be determined by these methods. Since *(5)* contains the structural units of *o*-aroylbenzoic acids, ring-chain tautomerism also occurs. Reaction with diazomethane yields the normal dimethyl ester, whereas acetylation or reduction result in ring closure in both halves of the molecule to yield 1,1′-diacetyl-4,4′-bis(3-acetoxyphthalid-3-yl)-5,5′-bipyrazole or 4,4′-bis-(phthalid-3-yl)-5,5′-bipyrazole, respectively.

The parent of *(5)*, namely, 3,3′- or 5,5′-bipyrazole *(7)* (m.p. 259 °C) is obtained on decarboxylation of the dicarboxylic acid *(6)*; it is formed, with benzoic acid, in an alkali melt at 160 °C.

Lecture at Göttingen on December 15th, 1966 [VB 56 IE]
German version: Angew. Chem. *79*, 477 (1967)

[*] Dr. A. Zeeck
Organisch-Chemisches Institut der Universität
Windausweg 2
34 Göttingen (Germany)

[1] Oxidative degradation of diazomethane adducts of type *(1)* can be used for determination of the structure of biquinones. – *H. Brockmann, K. van der Merwe*, and *A. Zeeck*, Chem. Ber. *97*, 2555 (1964); *H. Brockmann, A. Zeeck, K. van der Merwe*, and *W. Müller*, Liebigs Ann. Chem. *698*, 209 (1966).

Commercial Processes for Antibiotic Fermentation

By *R. Kreutzfeldt* [*]

Industrial fermentation has recently achieved increased importance, principally by production of antibiotics. Some 1000 antibiotics have been discovered in the last 25 years, of which about 50 have acquired economic significance, notably the penicillins, tetracyclins, and streptomycins. About 3000 tons of antibiotics were prepared in USA in 1964 (*ca.* 50 % of the world production), at a value of *ca.* $ 400 million. The world production of penicillins can be estimated as about 1500 tons a year.

In spite of many years' experience, penicillin production remains one of the most difficult and most sensitive. *Fleming* achieved yields of 2–10 units/ml in his first fermentations: today 10000 units/ml are considered normal. The fermentations are carried out in a technically similar way for all antibiotics, and the technique for penicillin fermentation alone will be described more closely here.

The penicillin-forming mold is preserved as a permanent culture in the anhydrous state at about −5 °C in order to exclude any metabolism. From this permanent culture subcultures are made on the laboratory scale, and further cultures are grown in prefermenters. The amount of inoculum for the main fermenter is chosen to be between 2 and 20 % of the amount to be harvested; larger amounts of inoculum shorten the fermentation time.

The fermenters are fitted with an aeration system, a stirrer, and a cooling system that keeps the temperature constant within ± 0.5 °C. Provision of oxygen and formation of penicillin are closely related. Fermenters in commercial use today may have a capacity of 400 m³. Antibiotic fermentations must be carried out without admission of foreign infections: Only sterilization by steam (at least 120 °C for at least 20 min) comes into consideration for large-scale production.

Fermentation conditions: 7 Days at 25 ± 0.5 °C; 0.3 m³ of air per min per 1 m³ of liquor. The following are required for production of 100 kg (4.3 % yield) of penicillin-Na: 1200 kg of carbohydrate, 60 kg of animal and vegetable fats, 770 kg of corn steep liquor, 220 kg of inorganic substances (as buffer, and as source of sulfur and phosphorus), and 100 kg of phenylacetic acid for formation of penicillin G.

The material balance of penicillin production from these quantities (input 2350 kg of raw materials) is: 100 kg of penicillin-Na (4 wt-%), 825 kg of mould mycelium (35 %), 660 kg of residual substances in the culture solution (28 %), 765 kg of CO_2 (33 %).

The energy change of penicillin fermentation is as follows (heats of combustion of raw materials and of the metabolic products are compared: mechanical energy, *e.g.* heat generated by stirring of the culture liquor, is not considered):

Energy contained in	kcal	%
Penicillin-Na	586000	7
Mycellium	2805000	33
Residual substances in liquor	1923000	23
Heat of combustion evolved	3147000	37
Total consumption of energy of the raw materials	8461000	100

Further, every 100 kg of penicillin require: 3000 kWh of electrical energy (mainly for stirring), 4 tons of steam (sterilization and sealing), 50000 Nm^3 of crude air, 900 m^3 of cooling water (cooling of the sterilized solution, removal of the heat produced by stirring and by biochemical combustion).

Costs of penicillin production (exclusive of amortization) can be divided as follows: for raw materials 50 %, for energy 20 %, for repairs 10 %, personel costs 15 %, other costs 5 %. These complicated biological processes are very liable to disturbance and require detailed supervision and exact analytical control. Even with fermentation processes that have been well established variations of yield amounting to ± 15 % are to be expected. In general, the following factors are responsible for this: variation of the penicillium strain or of the quality of raw materials; infection by foreign molds; errors in servicing and technical disturbances. The quality of the raw materials is decisive for fermentation yields, and as these materials are mostly of natural origin they are subjected to analytical and biological control.

Lecture at Frankfurt am Main on October 21st, 1966 [VB 57 IE]
German version: Angew. Chem. 79, 478 (1967)

[*] Dr. R. Kreutzfeldt
Farbwerke Hoechst A.G.
Pharma-Fabrik/Antibiotika-Betriebe
6230 Frankfurt/(M)-Höchst, Postfach 70 (Germany)

Electrochemical Oxidation of Formic Acid and Carbon Monoxide on Platinum Catalysts in Acid Electrolytes

By *H. Binder*, *A. Köhling*, and *G. Sandstede*[*]

Fuel cells containing acid electrolytes are advantageous for electrochemical oxidation of carbon-containing fuels because the resulting carbon dioxide is obtained as a gaseous combustion product, whereas in alkaline electrolytes it remains dissolved as carbonate. In addition to hydrocarbons and methanol, other carbon-containing fuels are carbon monoxide (which can be obtained mixed with hydrogen on conversion of hydrocarbons or coal) and also formic acid. Their use has hitherto been restricted because they poison platinum catalysts, the electrodes becoming strongly polarized and the output of the cells lowered. When the platinum surface is partially covered with sulfur, the anodic oxidation to carbon dioxide is greatly accelerated. This result could lead to development of fuel cells utilizing either carbon monoxide and hydrogen, or formic acid.

On a Raney platinum catalyst that is partially covered with a monatomic sulfur sorbate, carbon monoxide in 3 N sulfuric acid at 90 °C leads to a potential of 250 mV (at a current density of 200 mA/cm^2) against a hydrogen reference electrode in the same solution. Anodic oxidation of formic acid (the hydrate of carbon monoxide) is still more strongly accelerated, so that under similar conditions a current density of 200 mA/cm^2 is obtained, even at 30 °C. At 90 °C the current density reaches a stationary value of *ca.* 2 A/cm^2. At an untreated Raney platinum electrode, however, a current density of less than 1 mA/cm^2 is obtained.

The sulfur sorption layer can be easily placed on any platinum catalyst, including platinum black, *e.g.* by treatment with hydrogen sulfide. It is stable at anodic regions up to 600 mV; oxidation to sulfur dioxide begins only at higher potentials. The degree of coverage of the platinum surface has a large effect on the reaction rate of carbon monoxide or formic acid; the rate is a maximum when about one third of the total surface platinum atoms is covered with sulfur.

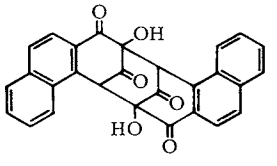
Lecture at Essen (Germany) on February 10th, 1967 [VB 66 IE]
German version: Angew. Chem. 79, 477 (1967)

[*] Dr. H. Binder, A. Köhling, and Dr. G. Sandstede
Battelle-Institut
Wiesbadener Str.
6 Frankfurt/Main (Germany)

Specific Oxidation of Phenols by Dipotassium Nitrosobissulfate

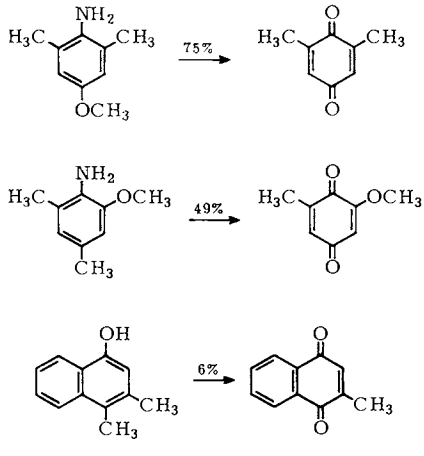
By *H.-J. Teuber*[*]

Reaction of 2,3-phenanthrenediol with dipotassium nitrosobissulfate, $ON(SO_3K)_2$, yields 3-hydroxy-1,2-phenanthraquinone, which is obtained as the colorless dimer *(1)*[1] whose UV spectrum corresponds substantially to that of 3,4-dihydro-1(2*H*)-phenanthrone but not to that of 2,3-dihydro-4(2*H*)-phenanthrone. The (dimeric) 2-hydroxy-3,4-phenanthraquinone is thus not formed.



(1)

In the formation of *p*-quinones from monohydric phenols, substituents may be eliminated from the *para*-position; not merely COOH, OCH_3, and Cl but even CH_3 may be eliminated, so that blocking of *para*-positions by methyl groups cannot always be reliably accomplished:



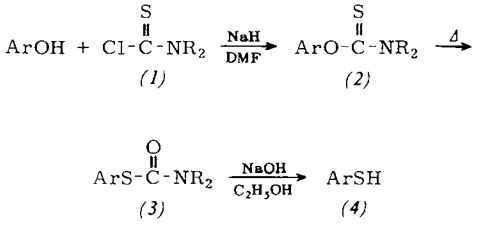
Formation of the *N*-methyliminobissulfate, $H_3C{-}N(SO_3K)_2$, during demethylating oxidations has been demonstrated.

Lecture at Hamburg on January 10th, 1967 [VB 59 IE]
German version: Angew. Chem. 79, 426 (1967)

[*] Prof. Dr. H.-J. Teuber
Institut für Organische Chemie der Universität
Robert-Mayer-Str. 7/9
6 Frankfurt/Main (Germany)

[1] Cf. *H.-J. Teuber* and *G. Steinmetz*, Chem. Ber. *98*, 666 (1965); *H.-J. Teuber*, *P. Heinrich*, and *M. Dietrich*, Liebigs Ann. Chem. *696*, 64 (1966).

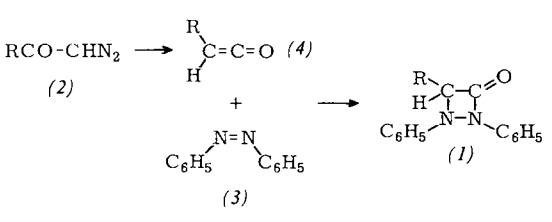
The conversion of phenols into thiophenols, according to *M. S. Newman* and *H. A. Karnes*, can generally be achieved by the reaction sequence *(1)–(4)*. The decisive step is the thermal rearrangement of *o*-aryl dialkylthiocarbamate *(2)* into *S*-aryl dialkylthiocarbamate *(3)*. This rearrangement proceeds



at 130–300 °C (depending on Ar) in high yields. The reaction has been used with numerous phenols and hydroxyheterocyclic compounds. 2- and 4-pyridyl esters can rearrange at 25 °C with acidic reagents. / 152nd Meeting Amer. chem. Soc. *1966*, p. 111 / –Ma. [Rd 608 IE]

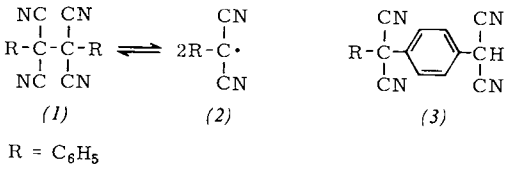
The formation of cyanogen *N*-oxide, NC–C≡N→O *(1)*, from cyanoformhydroximyl chloride NC–C(Cl)=NOH with tertiary amines or aqueous organic bases has been detected by *Ch. Grundmann* and *H.-D. Frommeld* by means of typical 1,3-dipolar additions. Preparation of the oxide in the presence of active dienophiles such as styrene, acrylonitrile, 1,3-butadiene, phenylacetylene, and dimethyl acetylenedicarboxylate led to substituted 3-cyano-4,5-dihydro-1,2-oxazoles or 3-cyano-1,2-oxazoles. *(1)* forms an explosive solid polymer. Unlike cyanogen bis-*N*-oxide ONC–CNO, which is an unusually stable aliphatic nitrile oxide because of the large number of possible resonance structures, *(1)* is typically unstable. / 152nd Meeting Amer. chem. Soc. *1966*, p. 49 / –Ma. [Rd 612 IE]

1,2-Diazetidinones *(1)* have been synthesized by *W. Fischer* and *E. Fahr*. These authors irradiated (high-pressure mercury lamp) diazoketones *(2)* in CH_2Cl_2 in the presence of azobenzene *(3)*. The initially formed aldoketenes *(4)* add to azobenzene. *(1)* are pale yellow or colorless substances,



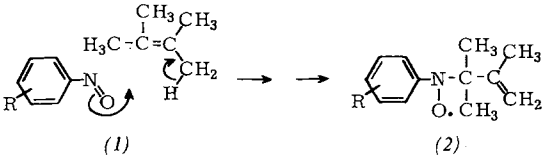
which can be recrystallized from ethanol. Examples: R = *m*-$NO_2C_6H_4$, m.p. 125 °C, yield 43%; *p*-ClC_6H_4, m.p. 131 °C, 42%; α-naphthyl, m.p. 147 °C, 30%; *m*-CH_3O–C_6H_4, m.p. 142 °C, 57%. / Tetrahedron Letters *1966*, 5245 / –Ma. [Rd 613 IE]

Polycyano radicals such as *(2)* have been studied by *H. D. Hatzler*. The α,α-dicyanobenzyl radical *(2)*, which is formed from phenylmalodinitrile and t-butylperoxide or from symtetracyanodiphenylethane *(1)*, dimerizes to give *p*-(α,α-dicyanobenzyl)phenylmalodinitrile *(3)*. *(2)* reacts with NO_2, NO, Br_2, and 2,2-diphenylpicrylhydrazyl, but not with O_2. It abstracts hydrogen from THF, but does not initiate the polymerization of styrene. Radicals are also formed at room



temperature in solutions of 1,2-bis-(4-nitrophenyl)tetracyanoethane, sym-dicyanotetraphenylethane, and hexacyanoethane, and these can be intercepted with 2,2-diphenylpicrylhydrazyl. The reactions of polycyanoethylenes such as *(1)* are best interpreted by assuming easy homolytic dissociation. 9-Cyano-9-tricyanomethylfluorene undergoes homolysis much more slowly than the compounds mentioned above. / J. org. Chemistry *31*, 2654 (1966) / –Ma. [Rd 614 IE]

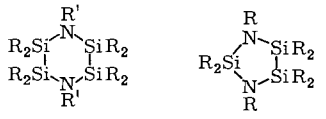
Very stable nitroxide radicals are formed from nitrosoaromatic-olefin adducts. Nitrosoaromatic compounds react with olefins in a Diels-Alder type of reaction, as indicated in *(1)*, to give *N,N*-disubstituted hydroxylamines, which are oxidized to the radical *(2)* by an excess of nitroso compound.



In order to obtain the simplest possible ESR spectra, *A. B. Sullivan* used 2,3-dimethyl-2-butene (0.01 N in benzene). The unstable nitroxide radicals could not be detected; however, *N*-(trimethylprop-2-enyl)aniline could be isolated by reduction with sodium in n-butanol. The radicals are formed in a second-order reaction. The coupling constants for a series of *m*- and *p*-substituted compounds (*e.g.* R = Cl, CH_3, OCH_3, OC_6H_5) can be linearly related to the Hammett σ values. The effects of the substituents on the ESR spectra are the same as for the nitrobenzene radical-anions. / J. org. Chemistry *31*, 2811 (1966) / –Bu. [Rd 622 IE]

The aromatization of cyclohexanecarboxylic acid to benzoic acid is catalysed by an enzyme which has been enriched from liver and liver mitochondria by *B. M. Babior* and *K. Bloch*. Cyclohexane carboxyl CoA is substrate, cyclohexene-1-carboxyl CoA is intermediate. All three isomers of cyclohexene carboxyl CoA are converted to benzoyl CoA. The reaction does not proceed *via* hydroxylation and dehydratation but has the character of an oxidation similar to acyl-CoA-dehydrogenation in fatty acid catabolism. FAD acts as coenzyme and is removable at lower pH, FAD addition then reactivates the enzyme. The aromatization requires oxygen, which, however, can be replaced by 5-methylphenaziniummethyl sulfate and iron(III) cyanide. The Michaelis constant for cyclohexane carboxyl CoA is 9.1×10^{-5}, for cyclohexene-1-carboxyl CoA 3.4×10^{-5} moles/l. The natural substrate is not known. / J. Biol. Chemistry *241*, 3643 (1966) / –Hö. [Rd 634 IE]

New five- and six-membered silicon-nitrogen ring systems have been reported by *U. Wannagat* and *O. Brandstätter*. The previously unknown 1,4-diazatetrasilacyclohexanes *(1)* (R′ = H, m.p. 1 °C; R′ = CH_3, m.p. 23 °C) were prepared by the reaction of ammonia or methylamine with 1,2-dichlorotetramethyldisilane.



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

The reaction of 1,2-dichlorotetramethyldisilane with *N,N'*-dilithiumbis(methylamino)dimethylsilane yields the new 1,3-diazatrisilacyclopentane derivative *(2)* (m.p. −12 °C). / Mh. Chem. *97*, 1352 (1966) / −WG. [Rd 635 IE]

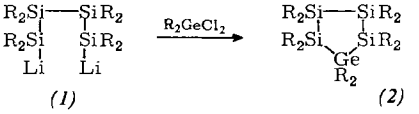
A new reaction of geminal bis(ethoxycarbonyl) compounds is reported by *A. P. Krapcho, G. A. Glynn,* and *B. J. Grenon.* On heating *(1)* with at least one equivalent of NaCN to about 160 °C in dimethylsulfoxide for *ca.* four hours, the ester *(2)* is produced in good yield. This simple method is superior to the classical decarboxylation reaction.

$$\underset{(1)}{R^1R^2C(CO_2C_2H_5)_2} \xrightarrow[DMSO]{NaCN} \underset{(2)}{R^1R^2CHCO_2C_2H_5}$$

Examples: Diethyl 1,1-cyclobutanedicarboxylate → ethyl cyclobutanecarboxylate (yield 75 %); diethyl 1,1-cyclopentanedicarboxylate → ethyl cyclopentanecarboxylate (75 %); $CH_3-CH_2-CH(CO_2CH_5)_2$ → $CH_3CH_2-CH_2-CO_2C_2H_5$ (80 %). / Tetrahedron Letters *1967*, 215 / −Ma. [Rd 638 IE]

Gas chromatographic capillary columns of high resolution in direct combination with a mass spectrometer is the basis of a new technique reported by *J. A. Völlmin, I. Omura, J. Seibl, K. Grob,* and *W. Simon.* The apparatus permits of the routine operation of packed columns, as well as capillary columns, coupled to a single focusing mass spectrometer. The most important feature is the arrangement of the separator, glass connecting tubes, and stopcock, on a carrier which is screwed onto the ion source, and by means of which these parts may be removed from the rest of the mass spectrometer without breaking any glass joints. The system may be heated to a maximum temperature of 250 °C. The change from capillary to packed column can be accomplished without modifying the rest of the apparatus. Evaluation and interpretation, *e.g.* of the mass spectrum of the substances contained in cigarette smoke, can be carried out at least ten times faster than the conventional gas chromatographic characterization. / Helv. chim. Acta *49*, 1768 (1966) / −WG. [Rd 636 IE]

Tetrasilacyclopentanes containing an additional hetero atom in the ring have been prepared by *E. Hengge* and *U. Brychcy.* Members of this little investigated class of compounds may be synthesized in the following way: Cleavage of octaphenylcyclotetrasilane by halogens or by lithium yields bifunctional tetrasilanes, *e.g. (1)*, which further react with other bifunctional molecules to yield the desired heterocyclic compound



(1) *(2)*

R = C_6H_5

e.g. (2). Compound *(2)* contains a hetero atom which has no lone pair of electrons. The compound is of interest for purposes of spectral comparison. / Mh. Chem. *97*, 1309 (1966) / −WG. [Rd 637 IE]

BOOK REVIEWS

Dünnschichtchromatographie in der Aminosäure- und Peptidchemie (Thin-Layer Chromatography in Amino-acid and Peptide Chemistry). By *G. Pataki.* de Gruyter & Co., Berlin 1966. 1st ed., xviii, 250 pp., 128 illustrations, 52 tables, 1 fold-out table, bound DM 38.– (*ca.* $10.–).

Owing to the many applications of thin-layer chromatography, the number of publications has become so large that the need has arisen for a special treatise on thin-layer chromatography in amino acid and peptide chemistry. The author has provided a useful aid in the form of a handy (*octavo*) laboratory manual with clear working procedures.

After reading the short description of the technique and theory of thin-layer chromatography in the first part of the book, the reader can carry out and evaluate separations without referring to the original literature. In the second part, the chromatography and electrophoresis of amino acids and iodine-containing amino acids are discussed in detail, and brief hints on the separation of peptides and intermediates are offered. The third and most detailed part gives data on the thin-layer chromatographic separation of derivatives of terminal amino acids and on the "fingerprint" technique, as well as guidance in the determinatron of the amino-acid sequence of proteins and peptides. The last part describes the preparation ot starting materials for the analysis of amino acids and related compounds in biological materials.

The most important publications up to November 1964 are covered (457 references). The subject index could have been more detailed, and the quality of some photographs of instruments might have been better. The reader misses a description of molecular-sieve chromatography with the aid of the thin-layer technique, which yields information on the molecular weights of peptides and proteins too.

The publication of this (unfortunately expensive) laboratory manual will undoubtedly be welcomed by all amino acid and peptide chemists. *A. Arens* [NB 526 IE]

Handbuch für das Eisenhüttenlaboratorium. Bd. 2: Die Untersuchung der metallischen Stoffe (Handbook for the iron foundry laboratory. Vol. 2: The investigation of metallic substances). Edited by the Chemikerausschuß des Vereins Deutscher Eisenhüttenleute. Verlag Stahleisen, Düsseldorf 1966. 2nd Edit., xxiii, 441 pp., 117 figures, cloth DM 88.– [*].

This manual gives detailed analytical procedures for pig iron, steel, ferrous alloys, filler metals, metallic coatings, and (more briefly) cemented carbides and structural components. It also contains sections in which analytical methods (photoemission spectrometry, X-ray emission spectrometry, microchemical analysis) are discussed. The advisability of this division is not easy to judge.

Apart from numerous improvements in individual procedures, a number of important changes have been made to the first edition. The chapters entitled "Sampling and "The examination of metals and metal alloys" have been omitted, as have the procedures for the determination of the beryllium, thorium, and uranium contents, which are of little practical importance. The section on "Photoemission spectrometry",

however, has been enlarged and a chapter on "X-ray emission spectrometry" has been introduced. The latter is the only chapter that does not describe experimental procedures, but simply gives a description of the method and a list of references to applications in the steel industry.

The great value of the book lies in the description of proven analytical methods, incorporating the experience of numerous large laboratories of the steel industry. Rather surprisingly, however, relatively little or no mention is made of a number of more modern methods, such as polarography, X-ray analysis, and atomic absorption. Moreover, there may be some doubt as to the usefulness of the method given for the determination of selenium.

The updating of this work in the new edition is very welcome, and the book itself should take an important place in the library of any iron-foundry laboratory.

R. Bock [NB 558 IE]

[*] For a review of Vol. 1 see Chemie-Ing.-Techn. *36*, 569 (1964).

Advances in Structure Research by Diffraction Methods, Vol. 2 Fortschritte der Strukturforschung mit Beugungsmethoden, Bd. 2[*] Edited by *R. Brill* and *R. Mason*. Friedr. Vieweg & Sohn, Braunschweig – Interscience Publishers, a Division of John Wilev & Sons, Inc., New York-London-Sydney 1966. 1st Edit., iii, 166 pp., 73 figures, 11 tables, DM 34.–.

Progress reports of this nature fulfil a very important function in scientific literature. They present a summary of the latest results of special fields of research within a relatively short time of the publication of the original papers. The book contains four articles written by experts.

On pages 1 to 33, *G. E. Bacon* discusses the investigation of magnetic structures by neutron diffraction. Corresponding to the great technical interest of this topic, very many publications have appeared; the author presents a good general review.

An important question is discussed in the article by *R. Mason* and *G. B. Robertson* (Diffraction Methods and Quantum Chemistry). The authors show how accurate X-ray analyses (particularly accurate measurements of bond lengths and angles) can provide experimental bases for quantum-mechanical calculations.

The longest article (*D. C. Phillips*: Advances in Protein Crystallography) deals with one of the most modern aspects of X-ray structure analysis. It also shows how quickly articles of this type become out of date. For example, the latest work by *Phillips* on lysozyme is not included. However, it is still very valuable because of its discussion of methods.

The last, short article by *P. Corradini* (New Results of Structural Researches on High Polymers) deals mainly with recent work in the Italian high-polymer school.

W. Hoppe [NB 572 IE]

[*] Vol. 1, cf. Angew. Chem. *77*, 184 (1965); Angew. Chem. internat. Edit. *4*, 175 (1965)

Immunopathology. IVth International Symposium, Monte Carlo 1965. Edited by *P. Grabar* and *P. A. Miescher*. Schwabe & Co., Publishers. Basel-Stuttgart 1966. 1st. Edit., 467 pp., 153 figures, 1 color plate, DM 80.–.

The present volume IV of the series on immunopathology is a fit companion for the earlier volumes, and needs no special recommendation in expert circles.

The subjects discussed at this symposium were: The question of tumor-specific antigens, and the closely related problem of the histocompatibility antigens, the chemistry of which is still largely unknown. A second lecture cycle deals with immune globulins and "paraproteins" in the widest sense; finally light is thrown from various sources on autoimmunization, special emphasis being rightly placed on "immunovasculitis". The choice of lecturers is excellent, and the discussions are terse and trimmed to the essentials. It may be asked, however, whether it might not have been better to translate the French contributions, for example one as important as that by *Voisin*, into English. The overall presentation is such as to make the high price appear justifiable.

This book is more than mere leisure readin and it is recommended to the biochemist, who is nowadays faced to an increasing extent with immunobiological questions as integral parts of his own field. Some topics, such as immunochemical questions in the structure of proteins, will already be familiar to him, and these will encourage him to turn to the apparently complex "immunobiological" phenomena, which are presented here as a huge field of research.

G. Uhlenbruck [NB 575 IE]

The Amino Sugars. Vol. IIB: Metabolism and Interactions. Edited by *E. A. Balazs* and *R. W. Jeanloz*. From the series "The Chemistry and Biology of Compounds Containing Amino Sugars". Academic Press, Inc., New York-London 1966. 1st Edit., xvii. 516 pp., numerous figures and tables, $22.00.

The latest contribution on the amino sugars[1] contains 14 chapters (38–51 in the consecutive numbering system), which can be grouped according to subject. The first group (38–41) deals with metabolic processes of the monomeric amino sugars as well as of the polymeric compounds, the second (42–47) with the enzymatic and non-enzymatic degradation of glycosaminoglycanes, and the third (48–51) with the relationships between amino sugars or polymers containing amino sugars and various biological systems.

The individual topics discussed are: the metabolism of amino sugars *(E. A. Davidson)*, of glycosaminoglycans *(H. Boström, L. Rodén)*, of glycoproteins, glycopeptides, and glycolipids *(I. Yamashina)*, the influence of steroid hormones on the glycosaminoglycans of secondary sex characteristics *(J. A. Szirmai)*, hexosaminidases *(P. G. Walker)*, neuraminidases *(M. E. Rafelson jr., M. Schneir, V. W. Wilson jr.)*, glycosaminoglycan-degrading enzymes *(H. Gibian)* glycosaminoglycan sulfatases *(K. S. Dodgson)*, activation and inhibition of enzymes by polyanions containing amino sugars *(P. Bernfeld)*, chemical and physical changes of glycosaminoglycans and glycoproteins by redox systems and irradiation *(L. Sundblad, E. A. Balazs)*, interactions of polyanions with blood components *(P. Bernfeld)*, immunochemistry *(G. F. Springer)*, interactions between glycoproteins and viruses *(A. Gottschalk)*, and interactions between amino sugars or polymers containing amino sugars and viruses cells, and tissues *(E. A. Balazs, B. Jacobson*

The literature is generally covered up to 1963, and publications from 1964 and 1965 are listed as an appendix in some chapters. In the article on amino sugar metabolism, the data unfortunately do not proceed beyond 1963, though numerous papers on this topic were published after 1963, particularly in the bacteriological sector. *H. Gibian*'s chapter on glycosaminoglycan-degrading enzymes is particularly well documented (up to 1965). Many of the articles also contain additional literature surveys on individual problems (*e.g.* on the incorporation of ^{35}S into connective tissue and cartilage; p. 52).

Like its predecessors in the series, the present volume again demonstrates the importance of amino sugars in biological systems. The authors do not confine themselves to listing and discussing results, but present detailed information about the methods used and point out the advantages and disadvantages of certain techniques. (*Gibian*: hyaluronidase tests; *Walker*: working-up of hexosaminidases; *Springer*: immunological techniques).

The excellent article by *G. F. Springer* on the immunochemistry of substances containing amino sugars describes in detail the structure and immunology of the blood-group substances, but also deals with other immunologically interesting polymers from higher organisms, bacteria, and protozoa, and describes relationships between the various systems. Special mention should also be made of the article by *A. Gottschalk*, which clearly describes results on virus receptors, RDE, and analogies between the receptors and various glycoproteins.

The book is an important addition to the literature, and can be warmly recommended. *H. J. Risse* [NB 571 IE]

[1] Cf. Angew. Chem. *78*, 1027 (1966); Angew. Chem. internat. Edit. *5*, 979 (1966).

Advances in Free-Radical Chemistry. Vol. 1. Edited by *G. H. Williams*. Logos Press – Academic Press, London 1965. 1st Edit., xi. 291 pp., several figures and tables, $12.00; 75s.

The chemistry of free radicals has developed independently in physical chemistry (gas-phase reactions) and organic chemistry (solution reactions; stable radicals). It is to be hoped that the new series "Advances in Free-Radical Chemistry" will help to bring these two branches together.

In what is probably the most interesting article in the first volume, *A. F. Trotman-Dickenson* critically sifts and comments upon the literature on "The Abstraction of Hydrogen Atoms by Free Radicals". The articles by *N. J. Friswell* and *B. G. Gowenlock* ("Inorganic Hydrogen- and Alkyl-Containing Free Radicals") and by *E. S. Huyser* ("Solvent Effects in Free-Radical Reactions") are first interim reports on current research topics, the object of which is to describe new departures and to stimulate new work by formulations that are occasionally rather too subtle.

An important report on the little known but surprisingly smooth "Vapor-Phase Halogenation of Aromatic Compounds", which has been studied mainly in the author's own laboratory since 1957, is presented by *E. C. Kooyman*. *R. Kh. Freidlina*'s article on "Rearrangments of Radicals in Solution" emphasizes the Russian work, and particularly her own; this article therefore complements a recent review by *Ch. Walling*. However, the choice of subject matter is not always absolutely satisfactory. For example, the important 1,5-hydrogen shifts are discussed only on the basis of the earliest examples, while no mention is made of more recent reviews. "Free-Radical Reactions of Bridged Cyclic Systems" are discussed by *D. I. Davies* and *S. J. Cristol*. In contrast to the chemistry of the carbonium ions, these free-radical reactions show few unusual features; the article points out some useful relationships.

With a few exceptions, the literature is covered only up to 1964, and even for this period the coverage is unfortunately not always complete. The authors should have specified the completeness and the period covered. The presentation and the index are good, but the references might have been better inserted as footnotes. *C. Rüchardt* [NB 574 IE]

The Molecular Orbital Theory of Conjugated Systems, by *L. Salem*. W. A. Benjamin, Inc., New York-Amsterdam 1966. 1st Edit., xvi, 576 pp., numerous illustrations, cloth $ 22.50.

The MO theory of conjugated systems is probably the most extended and one of the most successful sectors of quantum chemistry. *Salem* makes a commendable attempt to present a methodically complete description of the theory in its present state.

This book should not be approached without a previous knowledge of the elementary theory of chemical bonding. The first chapter is a recapitulation of, rather than an introduction to, Hückel MO theory. Unfortunately, no serious foundation is given for the distinction between σ and π electrons nor for the fundamentally important σ–π separation. This is particularly regrettable since some aspects of σ–π separation are currently regarded as very doubtful, and since joint treatments of σ and π electrons (though within the framework of the σ–π separation) are becoming increasingly important. Among the basic assumptions for which no convincing justification is given are the "neglect of overlap" and of "differential overlap". The short section on electron correlation deals only with some aspects of this important concept.

The review of the refined methods in the second chapter is arbitrary rather than systematic. The strength of the book does not lie in the discussion of fundamental questions, but in the detailed description of the current and possible applications of the MO theory. The author goes into detail on the relationship between theoretical delocalization energies and resonance energies, the Hückel rule, and the semi-empirical calculation of dipole moments, bond lengths, force constants, and ionization energies. Special attention is given to the magnetic properties of π-electron systems, particularly to 'ring currents", the theory of "chemical shifts", and spin densities and their relation to ESR spectra. Further chapters deal with the theory of the chemical reactivity and that of the UV spectra of unsaturated molecules. The author makes extensive and profitable use of the simple rules derived by the "English school" for the Hückel MO's of alternant hydrocarbons, *e.g.* the scheme for obtaining the coefficients of a non-bonding MO without calculation.

The final chapter is devoted, apart from the Jahn-Teller effect, to a phenomenon on which the author himself has worked successfully, *i.e.* bond alternation in polyenes and other conjugated systems.

Though the book is quite extensive and includes treatments of some uncustomary problems, such as conjugated rings containing d electrons, the author has omitted the theory of a number of interesting unsaturated systems, *e.g.* that of the non-classical carbonium ions, as well as conjugation in non-planar systems. The main emphasis is placed on the treatment of alternant hydrocarbons. The reader experiences little of the special problems of the theory of heteroaromatic compounds.

The recent literature is abundantly cited, though sometimes the selection is somewhat arbitrary.

The rather high price of this book may preclude purchase by individuals, but chemical libraries should not do without the information it contains. *W. Kutzelnigg* [NB 560 IE]

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Electron-Impact Induced Rearrangement Reactions of Organic Molecules [**]

BY P. BROWN AND C. DJERASSI [*]

Hydrogen migrations accompany many mass spectrometric fragmentation processes and a detailed study of these migrations, largely by means of deuterium labeling, has shed much light on electron-impact induced bond fissions. More recently, it has been found that groups other than hydrogen, such as alkyl, aryl, hydroxyl, etc., also can migrate after electron bombardment and the present article is concerned with a discussion of such molecular rearrangements among organic compounds. These observations are not only of intrinsic mechanistic interest, but a detailed knowledge of the occurrence of such migration reactions is crucial to the proper interpretation of mass spectra and to the avoidance of misinterpretations in "element mapping".

1. Introduction

One of the most significant developments in organic chemistry during this decade has been the very rapid acceptance and extremely wide use of mass spectrometry for the solution of structural problems. *Stenhagen*'s [1] prediction in 1961 "Es wird wahrscheinlich nicht lange dauern, bis der massenspektrometrischen Analyse bei Strukturbestimmungen in der organischen Chemie dieselbe Stellung zukommt wie jetzt z.B. der Infrarotspektrometrie und der magnetischen Kernresonanz" has become a statement of fact in less than five years. The pursuit of natural products chemistry without mass spectrometry has become unthinkable [2].

Whereas the rapid acceptance of UV, IR, and NMR spectroscopy or optical rotatory dispersion by the organic chemist was triggered to a large extent by the commercial availability of suitable instruments, this was not the case with mass spectrometry. Adequate mass spectrometers were available at least ten years prior to their extensive utilization for structural organic investigations and it seems that one of the principal motivating factors has been the recent "mechanistic" studies which led to the conclusion [3] that many fragmentation reactions of organic molecules induced by electron impact are interpretable in the every-day language of the organic chemist. To a certain extent, the word "mechanism" is a euphemism since the products of such fragmentations in the mass spectrometer are not isolable, but are only detected in terms of their mass and one is thus dependent on indirect evidence. For this purpose, the most useful technique is isotopic labeling [4], but recognition of metastable ions, high resolution mass measurements, and appearance potential determinations also play important roles.

Many of the bond fissions promoted by electron bombardment in the mass spectrometer are accompanied by transfer of one or more hydrogen atoms. Such hydrogen migrations shed considerable light on the probable fragmentation paths of organic molecules. Much of the work in our laboratory [5] has concentrated on detailed studies of such hydrogen migrations triggered by a variety of functional groups. As an example of the relevance of such hydrogen migrations to mass spectrometric fragmentation "mechanisms" one may cite the "McLafferty rearrangement" [6] of ketones such as n-dibutylketone *(1)*, which has been shown [7] by deuterium

[*] Dr. Peter Brown and Prof. Carl Djerassi
Department of Chemistry, Stanford University
Stanford, Calif. (U.S.A.)

[**] Part of this material was covered in a lecture by *C. Djerassi* at the EUCHEM Conference on Mass Spectrometry, Sarlat (France) September 1965.

[1] *E. Stenhagen*, Z. analyt. Chem. *181*, 462 (1961).

[2] *H. Budzikiewicz, C. Djerassi*, and *D. H. Williams*: Structure Elucidation of Natural Products by Mass Spectrometry. Holden-Day, San Francisco, 1964. Vol. I, Alkaloids. Vol. II, Steroids, Terpenoids, Sugars and Miscellaneous Classes.

[3] See for instance *H. Budzikiewicz, C. Djerassi*, and *D. H. Williams*: Mass Spectrometry of Organic Compounds. Holden-Day, San Francisco 1967.

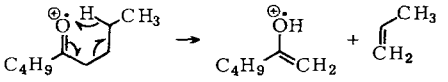
[4] For reviews see [2] ,Vol. I, chapter 2 as well as *K. Biemann*: Mass Spectrometry. Organic Chemical Applications. McGraw-Hill, New York 1962, Chapter 5.

[5] 129th paper in the Stanford series "Mass Spectrometry in Structural and Stereochemical Problems"; *A. M. Duffield, W. Carpenter*, and *C. Djerassi*, Chem. Commun. *1967*, 109.

[6] *F. W. McLafferty*, Analytic. Chem. *31*, 82 (1959).

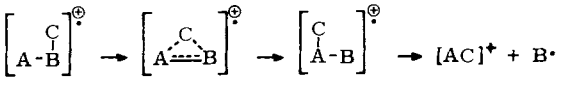
[7] For most recent investigation and leading references see *H. Budzikiewicz, C. Fenselau*, and *C. Djerassi*, Tetrahedron *22*, 1391 (1966).

labeling to involve transfer of the γ-hydrogen and fission of the β-bond with production of the enol ion radical *(2)* [8] and a neutral olefin *(3)* [*]. The "McLafferty rearrangement" is thus the mass spectrometric equivalent of the well known "Type II" Norrish photochemical decomposition of ketones [9].



(1) *(2)* *(3)*

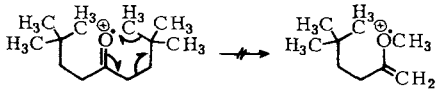
The frequent occurrence of hydrogen rearrangements raises the question whether other moieties are also prone to migrate after electron impact. Answers to this question are not only of intrinsic mechanistic interest, but they also have a crucial bearing on the scope and limitation of *Biemann*'s "element mapping" computer technique [10], which either requires that such rearrangements do not proceed to a significant extent or that their occurrence be predictable and hence discountable. The electron impact induced migration of alkyl, aryl, and other functional groups has attracted considerable attention during the past two years and apparently occurs with much greater frequency than has hitherto been realized. It is with this subject that the present review is concerned and for our purpose, we are principally concerned with the following process:



in which the migrating group C is at no time bound to the rest of the molecule by more than one σ-bond.

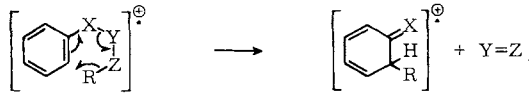
2. Simple Alkyl and Aryl Rearrangements

The first question that may be asked is whether alkyl rearrangements can take place in lieu of isotopically documented hydrogen migrations in substances where all implicated hydrogen atoms have been replaced by alkyl groups. The answer is decisively negative [11,12]. Thus 2,2,8,8-tetramethylnonan-5-one *(4)* is the completely methylated analogue of n-dibutylketone *(1)* and a "McLafferty rearrangement" of one of its methyl groups should then lead to an ion *(5)* of mass 142, which was not observed [11].



(4) *(5)*

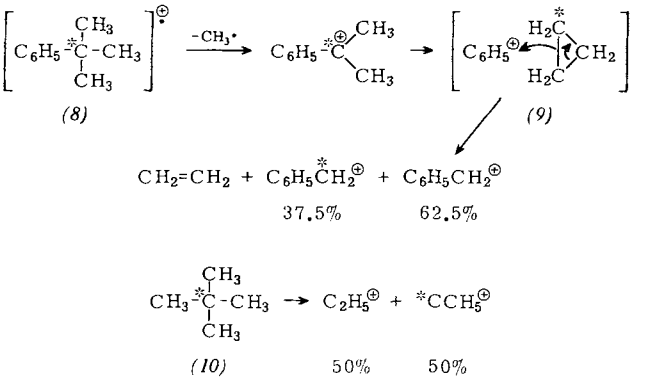
Similarly, a variety of benzene derivatives of type *(6)* have been shown by isotopic labeling [13] to fragment by hydrogen transfer [*(7)*, R = H], but no analogous methyl migration [*(7)*, R = CH_3] was encountered [12] when the appropriate hydrogen atoms were substituted by methyl groups.



(6) R = H, CH_3; X = CH_2, O, S, NH; Y = CH_2, O; Z = CH_2, O

(7) R = H; X = CH_2, O, S, NH

These results would seem to offer a poor prognosis for the prevalence of methyl migrations. On the other hand, some of the early mass spectral results with ^{13}C-labeled hydrocarbons showed quite definitely that methyl migrations do occur, presumably through the intermediacy of cationated cyclopropanes [14]. Thus, the mass spectrum of t-butylbenzene *(8)* exhibits a peak at *m/e* = 91 (benzyl or tropylium cation) which in the ^{13}C-labeled analogue [see asterisked carbon atom in *(8)*] is distributed between *m/e* = 91 and 92 in the indicated proportions, thus supporting the suggestion that cyclopropane *(9)* is an intermediate. A similar conclusion [14] can be reached from the observation [15] that the C_2 species in the mass spectrum of neopentane *(10)* labeled with ^{13}C at the central carbon atom are equally represented by labeled and unlabeled fragments.



(8) *(9)*

$CH_2{=}CH_2$ + $C_6H_5\overset{*}{C}H_2^{\oplus}$ + $C_6H_5CH_2^{\oplus}$

37.5% 62.5%

(10) 50% 50%

Another type of methyl migration, which cannot really be subjected to the same type of experimental scrutiny as the above mentioned examples, is one

[8] The relevant evidence is summarized by *S. Meyerson* and *J.D. McCollum* in *C. N. Reilly*: Advances in Analytical Chemistry and Instrumentation. Interscience, New York 1963, Vol. 2, pp. 184–199.

[*] A single "fishhook" (cf. [2], Vol. II, pp. 1–2) denotes homolytic fission ($-\overset{\frown}{C}-C- \rightarrow C\bullet + \bullet C-$), while the conventional arrow refers to heterolysis ($-\overset{\frown}{C}-C- \rightarrow -C^{\oplus} + -C^{\ominus}$). Several of the fragmentations are indicated as concerted processes, but this is only done for the sake of convenience since no experimental method is available at the present time of differentiating between concerted or stepwise processes.

[9] *J. G. Calvert* and *J. N. Pitts jr.*: Photochemistry. Wiley & Sons, New York 1966. See also *P. J. Wagner* and *G. S. Hammond*, J. Amer. chem. Soc. *87*, 4009 (1965).

[10] *K. Biemann*, Pure appl. Chem. *9*, 95 (1964) and later papers.

[11] *R. R. Arndt* and *C. Djerassi*, Chem. Commun. *1965*, 578.

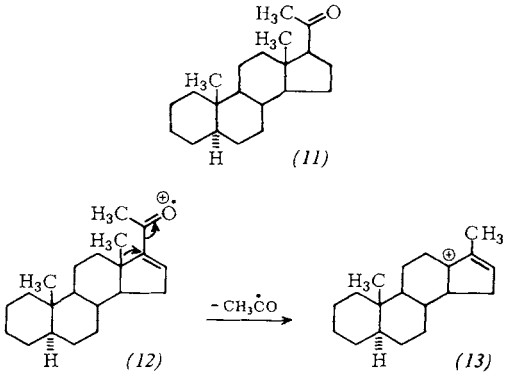
[12] *M. Fischer* and *C. Djerassi*, Chem. Ber. *99*, 750 (1966).

[13] For leading references see [12].

[14] *P. N. Rylander* and *S. Meyerson*, J. Amer. chem. Soc. *78*, 5799 (1956).

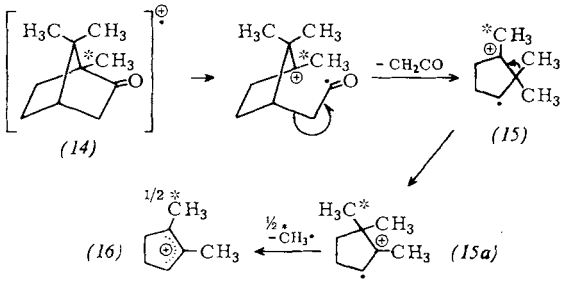
[15] *C. P. Johnson* and *A. Langer*, J. physic. Chem. *61*, 1010 (1957).

where only the observed fragmentation mode suggests its occurrence. For instance, the M − 43 peak (loss of CH_3CO) in 5α-pregnan-20-one *(11)* is much smaller than the corresponding one in Δ^{16}-5α-pregnen-20-one *(12)*, which is a surprising result since vinylic fissions are usually very unfavorable processes in mass spectrometry. Consequently, it has been suggested [16] that the expulsion of the acetyl radical in *(12)* is accompanied by concerted migration of the angular methyl group to furnish the highly stabilized carbonium ion *(13)*.



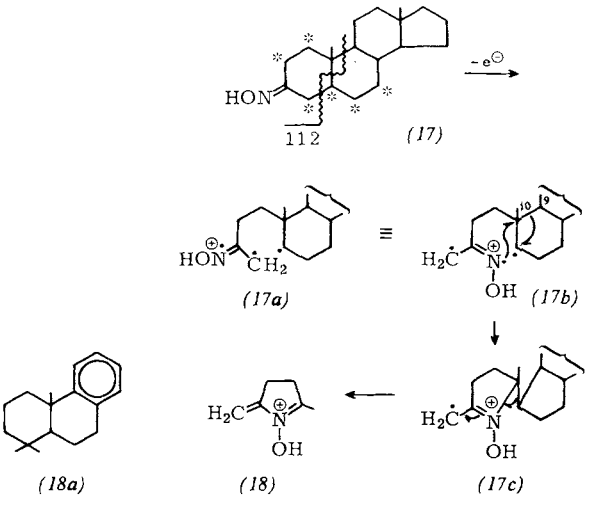
(11) *(12)* *(13)*

A similar case is provided by the mass spectrum [17] of camphor *(14)*, whose base peak occurs at $m/e = 95$ (C_7H_{11}) *(16)* owing to the loss of ketene and a methyl radical. As shown by isotopic labeling, nearly 50 % rather than the expected 33 % of the methyl loss originates from C-1. This is best interpreted by assuming that the fragment ion *(15)*, resulting from expulsion of ketene, first suffers methyl migration to *(15a)* (the driving force being the generation of an "ionized double bond") in which either the labeled or unlabeled methyl group would be expected to be lost to an equal extent.



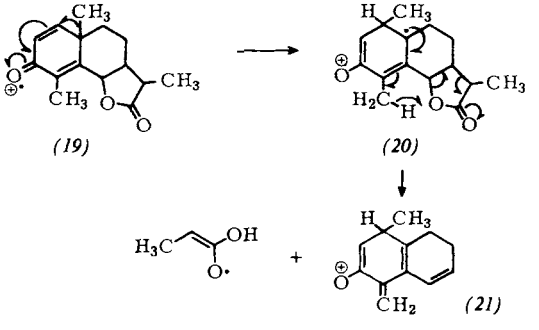
(14) *(15)* *(16)* *(15a)*

Yet another example is provided by the most abundant fragment ion of mass 112 ($C_6H_{10}NO$) in the mass spectrum of 5α-androstan-3-one oxime *(17)*, which by deuterium labeling (see asterisked positions) was shown [18] to arise formally by the bond cleavages indicated by the wavy line in formula *(17)*. Such a formulation would require the very unfavorable fission of two bonds connected to one carbon (C-10) and it is for this reason that migration of the 9–10 bond [*] in the hypothetical intermediate *(17b)* was postulated [18], the final $C_6H_{10}NO$ fragment then being depicted as *(18)*, which is completely consistent with the deuterium labeling results.



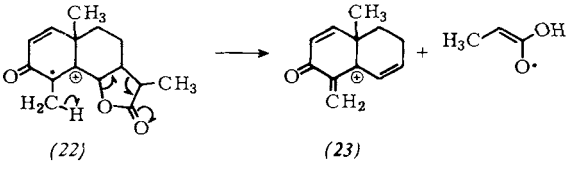
(17) *(17a)* *(17b)* *(17c)* *(18)* *(18a)*

The postulation of such "undetectable" migrations typified by *(12)*, *(15)*, and *(17b)* is tempting and great caution should be exercised before resorting to such mechanistic rationalizations. An example of an unnecessary postulation of a methyl migration is provided by the recently proposed [19] reaction path *(19)* → *(20)* → *(21)* to account for the appearance of an ion of mass 173 in the spectrum of santonin *(19)*.



(19) *(20)* *(21)*

In fact a more plausible decomposition path can be formulated as *(22)* → *(23)*, which does not require the intervention of a methyl migration nor does it utilize the unfavorable electron sextet depicted in *(20)* and *(21)*, simply by assuming that the fragmentation is initiated by the molecular ion *(22)*.



(22) *(23)*

With the above material as background, it is now possible to consider recent authenticated cases of alkyl or aryl migrations. They may be divided into reactions

[16] *L. Tökés* and *C. Djerassi*, Steroids 6, 493 (1965).

[17] *D. S. Weinberg* and *C. Djerassi*, J. org. Chemistry *31*, 115 (1966); *D. R. Dimmel* and *J. Wolinsky*, J. org. Chemistry *32*, 410 (1967).

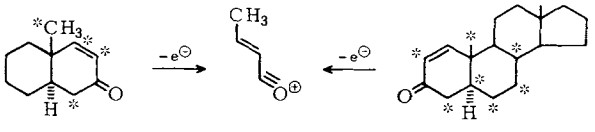
[18] *D. Goldsmith*, *D. Becher*, *S. D. Sample*, and *C. Djerassi*, Tetrahedron, Suppl. 7, 145 (1966).

[*] A very similar rationale has been offered (see *H. E. Audier*, *S. Bory*, *G. Defaye*, *M. Fétizon*, and *G. Moreau*, Bull. soc. chim. France, *1966*, 3181) for the presence of an intense peak at m/e=117 in the mass spectrum of the diterpenoid hydrocarbon *(18a)*.

[19] *D.G.B. Boocock* and *E.S. Waight*, Chem. Commun. *1966*, 90.

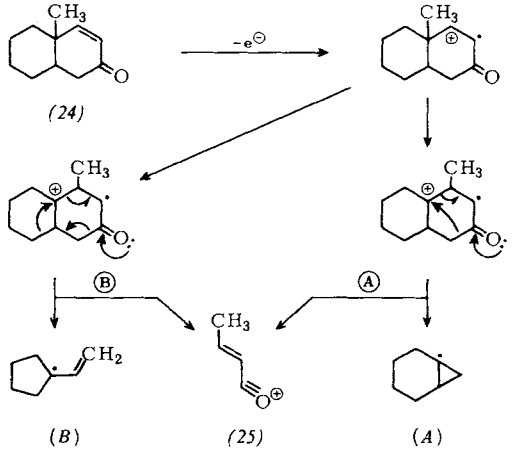
where the principal driving force appears to be the generation of favorable carbonium ion or radical intermediates and those where the migration is accompanied by the expulsion of a stable neutral molecule such as CO or CO_2. It is the latter type of rearrangement reaction that is most likely to lead to erroneous results in "element mapping" [10], unless its occurrence is readily recognized.

The first example of an authentic 1,2-alkyl migration is provided by the mass spectra of *trans*-Δ^3-10-methyl-2-octalone *(24)* and related bicyclic ketones, which exhibit an intense peak at $m/e = 69$ that was shown by high resolution mass measurements to correspond to the composition C_4H_5O. Isotopic labeling [20] (see asterisked positions in *(24)*) demonstrated that methyl migration had occurred and that the resulting fragment is probably best expressed in terms of *(25)*. Similar conclusions could be reached [21] from the mass spectrum of Δ^1-5α-androsten-3-one *(26)* and its labeled analogues.



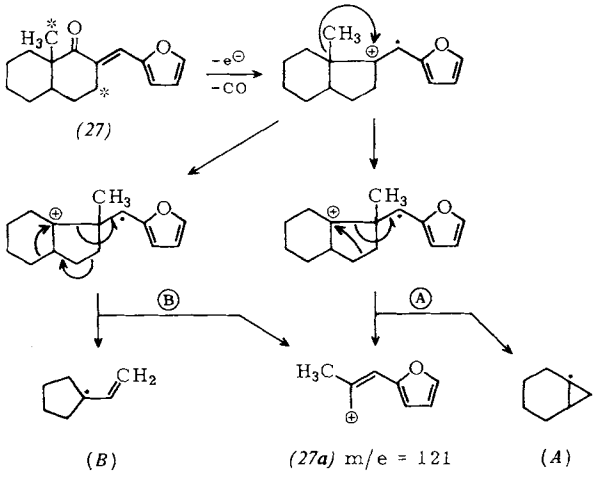
(24) *(25)* m/e = 69 *(26)*

Two plausible pathways to the rearrangement ion *(25)* are outlined below, the principal difference being the nature of the uncharged species which may result from either a 1,3-(path A) or two consecutive 1,2-(path B) [22] shifts.

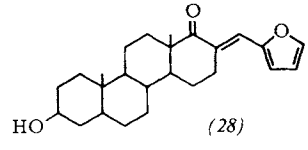


(B) *(25)* *(A)*

A similar methyl migration process was discovered [23] through appropriate deuterium labeling (see asterisks in *(27)*) in 2-arylidene- and 2-furfurylidene-1-decalones *(27)* as well as analogous D-homo steroids *(28)*, whose mass spectra displayed the most intense peak at $m/e = 121$ *(27a)* and which was displaced by the appropriate mass increment in the various arylidene derivatives. Again two reaction paths (A and B) can be entertained [23] which are analogous to those proposed in the fragmentation of the octalone *(24)* or the steroid *(26)*.

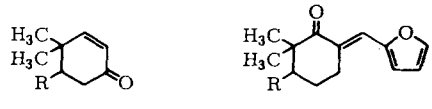


(27) *(B)* *(27a)* m/e = 121 *(A)*



(28)

A possible distinction between paths A and B can be made by examining the minimum structural requirements for such methyl migration. The striking observation was made [24] that whereas 4,4-dimethylcyclohex-2-en-1-one *(29)* and 2-furfurylidene-6,6-dimethylcyclohexanone *(30)* exhibit practically no methyl rearrangement peaks in their mass spectra, introduction of an additional methyl substituent (see *(31)* and *(32)*) at the site of the original ring juncture restores again the proclivity towards methyl transfer observed in their bicyclic analogues (*(24)* and *(27)*). Since the presence of this additional methyl function in *(31)* and *(32)* should play no noticeable role in reaction path A, route B may be considered to be more plausible.



(29) R = H *(30)* R = H
(31) R = CH_3 *(32)* R = CH_3

Not only methyl groups, but other alkyl and aryl groups have also been shown [24] to participate in such rearrangements. These observations raise the question about the relative migratory aptitudes of various substituents in electron impact promoted rearrangements as compared to the migratory aptitudes of the same substituents in carbonium ion or free radical

[20] *F. Komitsky jr.*, *J. E. Gurst*, and *C. Djerassi*, J. Amer. chem. Soc. *87*, 1398 (1965).

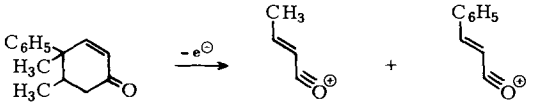
[21] *R. H. Shapiro* and *C. Djerassi*, J. Amer. chem. Soc. *86*, 2825 (1964), as well as unpublished high resolution mass measurements which showed that 70% of the m/e=69 peak in the mass spectrum of *(26)* corresponds to C_4H_5O.

[22] This possibility was first raised by Dr. *W. J. Richter* at the EUCHEM Conference on Mass Spectrometry, Sarlat (France) 1965.

[23] *C. Djerassi*, *A. M. Duffield*, *F. Komitsky jr.*, and *L. Tökes*, J. Amer. chem. Soc. *88*, 860 (1966).

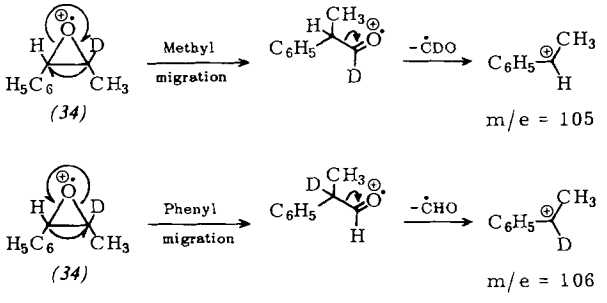
[24] *R. L. N. Harris*, *F. Komitsky jr.*, and *C. Djerassi*, J. Amer. chem. Soc., in press.

rearrangements[25]. Thus a comparison[24] of the relative intensities of the m/e = 69 and 131 peaks in the mass spectrum of 4,5-dimethyl-4-phenylcyclohex-2-en-1-one *(33)* indicates a ten-fold preference for phenyl as compared to methyl migration. Such a conclusion is only qualitative, since it presupposes an identical rate (or lack) of further decomposition of the rearrangement ions of mass 69 and 131.



(33) *(25)* m/e = 69 *(25a)* m/e = 131

A similar conclusion about the preference of phenyl over methyl migration can be reached by comparing the relative intensity of the hydrocarbon portion (C_8H_9) of the m/e = 105 peak in the mass spectrum[26] of [2-D]-1-phenyl-1,2-epoxypropane *(34)* with that of the m/e = 106 peak. The virtue of this comparison is that these two hydrocarbon species yield effectively the same ion and any difference in their subsequent decomposition would be relatively small since it would be only due to an isotope effect.



(34) *(34)*

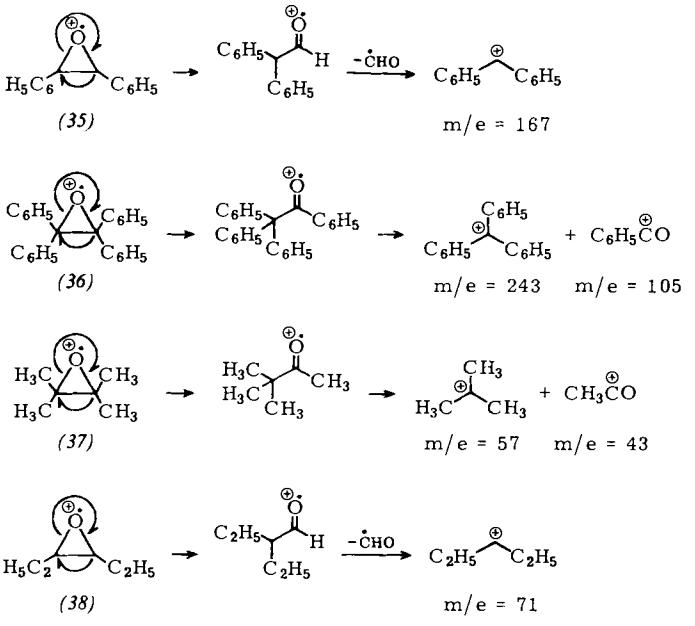
Epoxides appear to be a relatively fertile field for encountering molecular rearrangements. Thus the presence of m/e = 167 and m/e = 243 peaks in the mass spectra[26] of stilbene oxide *(35)* and tetraphenylethylene oxide *(36)* demonstrates the occurrence of phenyl migrations, while high resolution and isotope labeling experiments[27] in dialkyl epoxides such as 2,3-dimethyl-2,3-epoxybutane *(37)* and 3,4-epoxyhexane *(38)* revealed the occurrence of ethyl and methyl migrations, respectively.

These skeletal rearrangements among epoxides would complicate or confuse the interpretation of "element maps"[10] were it not for the rather low abundance of such rearrangement peaks. However, much more substantial rearrangement peaks, which could affect conclusions from "element mapping"[10], have been encountered in other compounds and three such examples involving aryl or benzyl migration may be cited in this connection.

[25] See *e.g. E. S. Gould*: Mechanism and Structure in Organic Chemistry. Henry Holt and Co., New York 1959, pp. 607and 758.

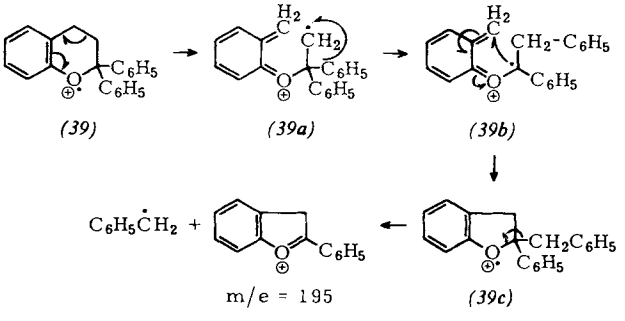
[26] *H. Audier, J. F. Dupin, M. Fétizon*, and *Y.Hoppilliard*, Tetrahedron Letters *1966*, 2077, and personal communication from Professor *Fétizon*.

[27] *P. Brown, J. Kossanyi*, and *C. Djerassi*, Tetrahedron Suppl.*8*. Pt. 1, 241 (1966).



(35) *(36)* *(37)* *(38)*

2,2-Diphenylchroman *(39)* exhibits in its mass spectrum[28] a significant peak at m/e = 195, which by high resolution mass measurements and isotopic labeling has been shown[29] to involve a phenyl migration resulting in the eventual expulsion of a benzyl radical, a moiety which is not present in the original molecule *(39)*. One plausible mechanism, though by no means the sole one[29], is depicted below:



(39) *(39a)* *(39b)* *(39c)*

A second case is illustrated by *Biemann*'s observation[30] that the tribenzylamine *(40)* mass spectrum contains an appreciable peak at m/e = 181 of composition $C_{14}H_{13}$. Since the parent amine *(40)* does not contain an uninterrupted sequence of fourteen carbon atoms, a benzyl rearrangement must have occurred in the genesis of the m/e 181 fragment.

$$(C_6H_5CH_2)_3\overset{\oplus\bullet}{N} \longrightarrow C_{14}H_{13}^{\oplus}$$

(40) $m/e = 181$

A third example is the production of a $C_9H_{10}N_2S$ ion (m/e = 178) from 3-(β-hydroxy-β-phenylethyl)-2-iminothiazolidine *(41)* (R = OH; R′ = H) in a one-step process (as shown by the presence of the appropriate metastable ion), which may be depicted[31] as a six-center phenyl migration, although the structural requirements for such a migration must be fairly specific since no such rearrangement is encountered[32]

[28] *C. S. Barnes, M. I. Strong*, and *J. L. Occolowitz*, Tetrahedron *19*, 839 (1963).

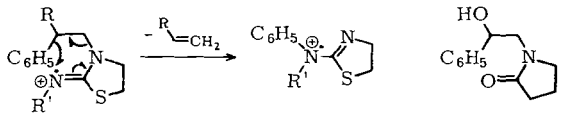
[29] *S. D. Sample* and *C. Djerassi*, unpublished.

[30] *K. Biemann*, Abstracts of 13th Annual Conference on Mass Spectrometry, ASTM Committee E-14, St. Louis, Mo., 1965, p. 427.

[31] *B. R. Webster*, Chem. Commun. *1966*, 124, and personal communication.

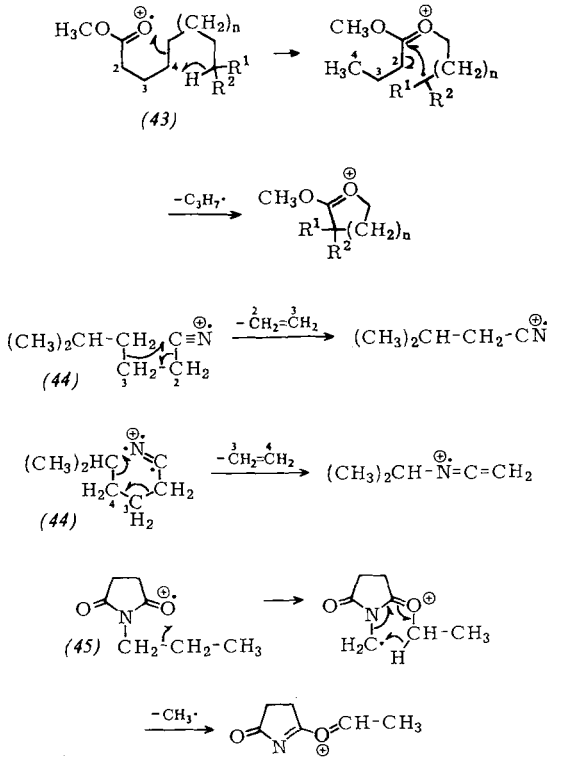
[32] Unpublished experiments by Dr. *J. K. MacLeod*.

in the related pyrrolidone *(42)* nor in the ketone *(41)* (R = O; R′ = H) or various *N*-acetyl derivatives *(41)* (R′ = $COCH_3$; R = O or OH)[31].



(41) m/e = 178 *(42)*

It must be borne in mind that there are many skeletal rearrangements, which are mechanistically important and readily detectable by isotopic labeling, but where the occurrence of such a rearrangement, irrespective of its abundance, has no bearing on the interpretation of "element maps". Such isotopically documented examples include the loss of a propyl radical[33] encompassing carbon atoms 2, 3, and 4 of long chain fatty acid methyl esters *(43)*, the loss of ethylene[34] from positions 2 and 3 (22 %) or 3 and 4 (78 %) in isohexyl cyanide *(44)*, and finally the apparent ethyl migration[35] involved in the expulsion of a methyl radical in *N*-propylsuccinimide *(45)*.



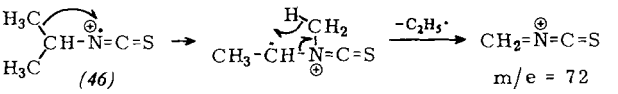
(43)

(44)

(44)

(45)

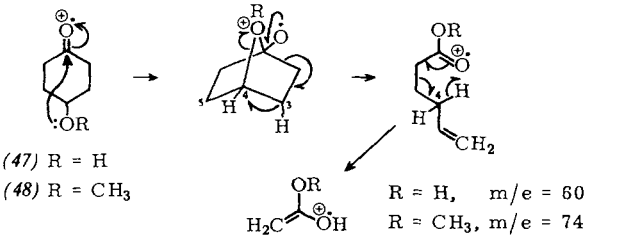
The expulsion of an ethyl radical[36] in 2-propylisothiocyanate *(46)* would be misleading in "element mapping", but fortunately it is of low abundance.



(46) m/e = 72

Alkyl or aryl groups are not the only molecular species that can suffer migration. When the migrating group contains a heteroatom, then it follows automatically that the composition of the resulting peak will afford misleading information in "element mapping". Whether such information will be fatal depends on the number of such rearrangement peaks in one such molecule, their relative abundance, and whether their occurrence can be pinpointed as a result of internal inconsistency of the computer-analysed data. The net result of such rearrangements, namely a combination in the fragment ion of heteroatoms and carbon atoms which is not present in the molecular ion, can also arise from the expulsion of neutral molecules such as carbon monoxide, formaldehyde, nitriles, *etc.* Before discussing them, it is worth while discussing some recent examples of oxygen rearrangements.

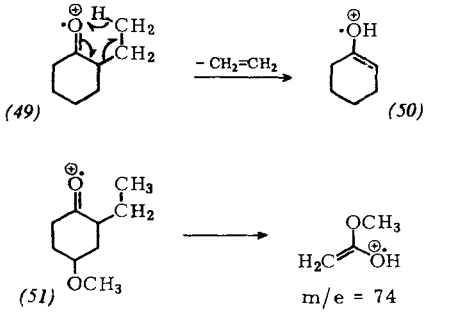
One of the most abundant ions in the mass spectrum[37a] of 4-hydroxycyclohexanone *(47)* corresponds to $C_2H_4O_2$ (*m/e* = 60). Similarly, the base peak in the spectrum of 4-methoxycyclohexanone *(48)* is associated with an ion of mass 74 ($C_3H_6O_2$). The presence of two oxygen atoms in a two-carbon fragment from *(47)* and in a three-carbon moiety from *(48)* requires the intervention of an oxygen rearrangement in each instance. By labeling all of the positions with deuterium, it was found[37a] that one of the hydrogen atoms at C-3 or C-5 becomes equivalent to the C-4 hydrogen atom, and a reaction path consistent with these data is depicted below.



(47) R = H
(48) R = CH_3

R = H, m/e = 60
R = CH_3, m/e = 74

These results raise the question of how general such transannular rearrangements might be and how they are able to compete with other fragmentation reactions. In this regard, it is relevant to point out that the second most intense peak in the mass spectrum of 2-ethylcyclohexanone *(49)* is due to a standard McLafferty rearrangement (see *(1)* → *(2)*) with loss of ethylene to give *(50)*, while in 4-methoxy-2-ethylcyclohexanone *(51)* this fragmentation is greatly



(49) *(50)*

(51) m/e = 74

[33] *E. Stenhagen*, Z. analyt. Chem. *205*, 109 (1964); *N. Dinh-Nguyen, R. Ryhage, S. Ställberg-Stenhagen*, and *E. Stenhagen*, Ark. Kemi *18*, 393 (1961).

[34] *R. Beugelmans, D. H. Williams, H. Budzikiewicz*, and *C. Djerassi*, J. Amer. chem. Soc. *86*, 1386 (1964).

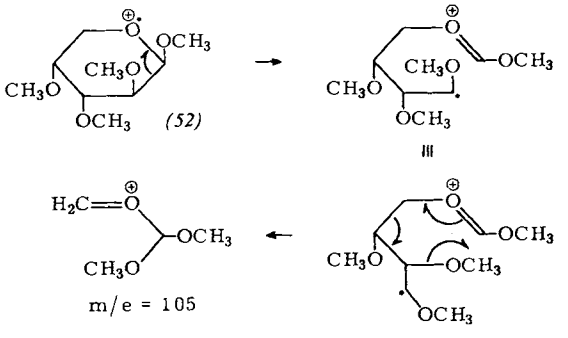
[35] *A. M. Duffield, H. Budzikiewicz*, and *C. Djerassi*, J. Amer. chem. Soc. *87*, 2913 (1965).

[36] *E. Bach, A. Kjaer, R. H. Shapiro*, and *C. Djerassi*, Acta chem. scand. *19*, 2438 (1965).

reduced [37a] at the expense of the transannular methoxyl rearrangement with eventual production of the $m/e = 74$ ion.

In the related cyclohexane diol system, rearrangement ions of composition CH_3O_2 ($m/e = 47$) and abundance $\Sigma_{35} = 1.1\ \%$ (70 eV) [*] have recently been reported [37b] for the 1,3- and 1,4-isomers, but no evidence for hydroxyl migration was found in the 1,2-compound [37b].

Methoxyl rearrangements have also been encountered in mass spectrometric investigations [38a] of permethylated sugars, an instructive example being the genesis of the $m/e = 105$ peak in the mass spectrum of methyl 2,3,4-tri-*O*-methyl-β-L-*arabo*-pyranoside *(52)*, as proved by appropriate deuterium labeling. An analogous acetoxy migration has been proposed [38b] in the fragmentation of pyranose penta- and hexa-acetates.



Rearrangements involving hydroxyl migration have been observed in benzoic acid [39,40], and in oximes of benzophenone [18] and acetophenone [41]; these examples are further discussed below.

3. Rearrangements Accompanied by Ejection of a Stable Neutral Molecule

Many of the skeletal reorganization processes encountered in mass spectrometry have in common the loss of a stable neutral moiety from a non-terminal position in the original molecule. The consequence of such rearrangements, especially if they occur to a significant extent, on the element map [10] of a particular compound is obvious. Entries will be recorded for ions comprising atoms that were not in fact bonded together as a contiguous chain in the original molecule, and may prove misleading unless the scope of these reactions is vigorously explored and delineated.

Kinetic methods [42,43] have so far proved inapplicable to the interpretation of the mass spectra of all but the simplest organic compounds; the role of thermodynamic considerations has consequently been enhanced. Thus one finds that major fragmentation pathways can almost always be rationalized (if not yet predicted) by stabilizing the positive charge (and radical, if present) at all intermediate stages, and by finally losing a stable neutral (or radical) species [44].

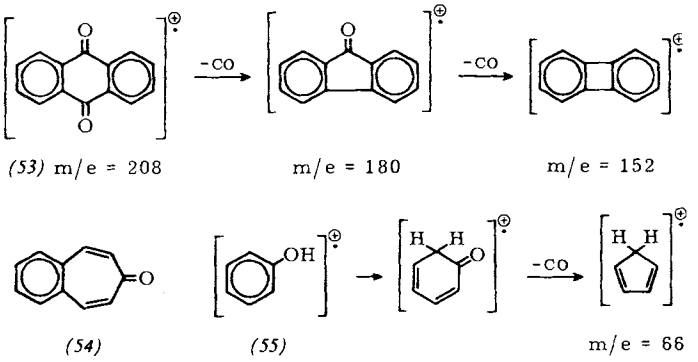
It is not very surprising then, to discover that a large proportion of electron impact induced skeletal rearrangements are accompanied by expulsion of such neutral entities as carbon dioxide, carbon monoxide, sulfur dioxide, formaldehyde, *etc.*, all of which have favorably negative heats of formation [45] (Table 1).

Table 1. Heats of formation (gas) at 298 °K.

Compound	ΔH_f^0 (kcal mole^{-1})	Compound	ΔH_f^0 (kcal mole^{-1})
CO_2	−94.05	C_2H_4	12.50
SO_2	−70.96	SO	19.02
COS	−32.8	CS_2	27.55
CH_2O	−27.7	HCN	31.2
CO	−26.42	C_2H_2	54.19

a) Loss of Carbon Monoxide

In an important paper, *Beynon* [46] called attention to the ejection of carbon monoxide from *p*-benzoquinones, *e.g.* anthraquinone *(53)*, and from benzotropone *(54)* and phenol *(55)*. In each instance, major peaks result from such rearrangement.



[37a] *M. M. Green, D. S. Weinberg*, and *C. Djerassi*, J. Amer. chem. Soc. *88*, 3883 (1966).

[*] Σ_{35} signifies the intensity of a peak relative to the sum of intensities of all peaks from $m/e = 35$ to the molecular ion peak.

[37b] *H. F. Grützmacher, J. Winkler*, and *K. Heyns*, Tetrahedron Letters *1966*, 6051.

[38a] *K. Heyns* and *D. Müller*, Tetrahedron *21*, 55 (1965); *N. K. Kochetkov* and *O. S. Chizhov, ibid. 21*, 2029 (1965).

[38b] *K. Heyns* and *D. Müller*, Tetrahedron Letters *1966*, 6061.

[39] *S. Meyerson* and *J. L. Corbin*, J. Amer. chem. Soc. *87*, 3045 (1965).

[40] *J. H. Beynon, B. E. Job*, and *A. E. Williams*, Z. Naturforsch. *20a*, 883 (1965).

[41] *K. G. Das* and *P. S. Kulkarni*, 14th Annual Conference on Mass Spectrometry, A.S.T.M. Committee E-14, Dallas, Texas, 1966.

[42] *H. M. Rosenstock, M. B. Wallenstein, A. L. Wahrhaftig*, and *H. Eyring*, Proc. nat. Acad. Sci. U.S.A. *38*, 667 (1952).

[43] See, however, *M. M. Bursey* and *F. W. McLafferty*, J. Amer. chem. Soc. *88*, 529 (1966); *88*, 4484 (1966); *F. W. McLafferty, M. M. Bursey*, and *S. M. Kimball, ibid. 88*, 5022 (1966); *M. M. Bursey* and *F. W. McLafferty, ibid. 88*, 5023 (1966); *89*, 1 (1967).

[44] *F. W. McLafferty* in *F. W. McLafferty*: Mass Spectrometry of Organic Ions. Academic Press, New York 1963, p. 318.

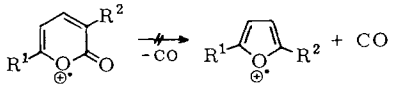
[45] Selected Values of Chemical Thermodynamic Properties, Circular of the National Bureau of Standards No. 500, U.S. Government Printing Office, Washington, D.C., 1952.

[46] *J. H. Beynon, G. R. Lester*, and *A. E. Williams*, J. physic. Chem. *63*, 1861 (1959).

However, the elimination of a neutral molecule from a ring falls outside our definition of "group migration" (see Introduction). The term "migration" implies movement of a group from one site to another, accompanied by bond breakage and bond formation in the transition state. In many cases of expulsion of a stable, neutral species from a cyclic ion, recyclization is not a mechanistic necessity[47], although it is almost universally depicted as such in fragmentation schemes.

The perils inherent in assuming that loss of carbon monoxide from cyclic carbonyl compounds will generate a simple recyclized ion are apparent from a study[48a] of 2-pyrone *(56)* and its deuterated analogues *(57)* and *(58)*. If a symmetrical species such as *(59)* were formed, then the mass spectra of [3-D]-2-pyrone *(57)* and [6-D]-2-pyrone *(58)* would be identical. In fact they were not, gross differences being noted in the isotope distribution in ions formed by further decomposition of the M−CO species. However, the

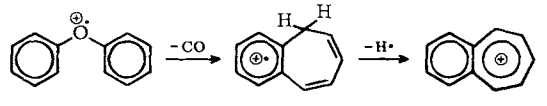
(56) $R^1 = R^2 = H$
(57) $R^1 = H, R^2 = D$
(58) $R^1 = D, R^2 = H$



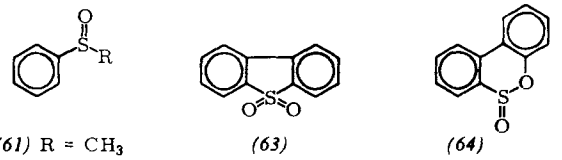
(59)

interpretation of these labeling results by *Pirkle*[48a] have recently been critically questioned[48b] and the intermediacy of a cyclic M − CO ion *(59)* in the fragmentation of 2-pyrone remains an open question.

Elimination of carbon monoxide occurs somewhat unexpectedly in the mass spectra of diphenyl ether[46,49,50] *(60)* and various aryl substituted sulfones[51,52] and sulfoxides[52]. For example, methyl phenyl sulfoxide[52] *(61)*, diphenyl sulfoxide[52] *(62)*, and dibenzothiophene sulfone[51,52] *(63)* all display high intensity peaks, corresponding to operation of an M−CO process. It has been suggested[51,52] that isomerization of the molecular ion of *(63)* to that of the sulfinate ester *(64)* occurs prior to the ejection of



(60) m/e = 142 m/e = 141



(61) R = CH_3
(62) R = C_6H_5

(63) *(64)*

carbon monoxide. Skeletal rearrangements leading to M−CO ions were not encountered to any significant extent in dialkyl sulfones and sulfoxides[52,53].

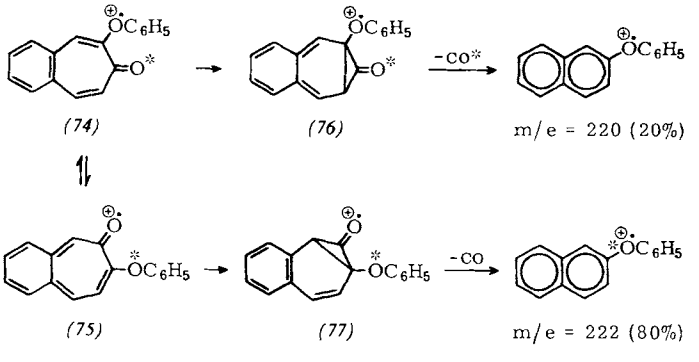
Carbon monoxide loss has also been discerned in the spectra of acetylacetone[46,54,55] *(65)*, methyl and ethyl acetoacetate[54,56] *(66)* and *(67)*, isopropenyl acetate[57] *(68)*, distyryl ketone[54] *(69)*, phenyl styryl ketone[46,54] *(70)*, benzoic acid[39,40] *(71)*, benzophenone[49,50] *(72)*, and trichlorotrifluoroacetone[58a] *(73)* (Table 2), and a variety of other carbonyl compounds containing at least one additional site of unsaturation[58b].

Table 2. Rearrangement peaks involving loss of carbon monoxide.

Compound		Relative abundance of M−CO peak (%)	Ref.
$CH_3-CO-CH_2-CO-CH_3$	*(65)*	10	[46,54,55]
$CH_3-CO-CH_2-CO_2-CH_3$ [*]	*(66)*	6	[54,56]
$CH_3-CO-CH_2-CO_2-C_2H_5$ [*]	*(67)*	4	[54,56]
$CH_3-CO-O-C(=CH_2)CH_3$	*(68)*	6	[57]
$(C_6H_5-CH=CH)_2CO$	*(69)*	17	[54]
$C_6H_5-CH=CH-CO-C_6H_5$	*(70)*	10	[46,54]
$C_6H_5-CO_2H$	*(71)*	5	[39,40]
$C_6H_5-CO-C_6H_5$	*(72)*	5	[49,50]
$CCl_3-CO-CF_3$	*(73)*		[58a]

[*] ^{18}O labeling showed [54] that principally the ketone carbonyl is lost as carbon monoxide.

The operation of a 1,4-phenyl migration associated with CO expulsion has been uncovered[59] by isotope labeling studies with 2-phenoxy-4,5-benzotropone *(74)*. Separate scrutiny of both the ^{18}O-labeled carbonyl compound and the ^{18}O-labeled ether analogue disclosed that in the formation of the two most important high mass peaks (M−OH, 26 %; M−CO, 60 %) both oxygen atoms are involved. In the carbon mon-



(74) *(76)* m/e = 220 (20%)

(75) *(77)* m/e = 222 (80%)

[47] For evidence concerning acyclic ions in the mass spectra of aromatic hydrocarbons, see *P. Natalis* and *J. L. Franklin*, J. physic. Chem. *69*, 2935 (1965), and references cited therein.

[48a] *W. H. Pirkle*, J. Amer. chem. Soc. *87*, 3022 (1965).

[48b] *P. Brown* and *M. M. Green*, J. org. Chemistry, *32*, 1681 (1967).

[49] *P. Natalis* and *J. L. Franklin*, J. physic. Chem. *69*, 2943 (1965).

[50] *J. H. D. Eland* and *C. J. Danby*, J. chem. Soc. (London) *1965*, 5935.

[51] *E. K. Fields* and *S. Meyerson*, J. Amer. chem. Soc. *88*, 2836 (1966).

[52] *J. H. Bowie, D. H. Williams, S.-O. Lawesson, J. O. Madsen, C. Nolde*, and *G. Schroll*, Tetrahedron *22*, 3315 (1966).

[53] *R. G. Gillis* and *J. L. Occolowitz*, Tetrahedron Letters *1966*, 1997; *I.D. Entwistle, R.A.W. Johnstone*, and *B.J. Millard*, J. chem. Soc. (London) *C*, *1967*, 302.

[54] *J. H. Bowie, R. Grigg, D. H. Williams, S.-O. Lawesson*, and *G. Schroll*, Chem. Commun. *1965*, 403.

[55] *J. H. Bowie, D. H. Williams, S.-O. Lawesson*, and *G. Schroll*, J. org. Chemistry *31*, 1384 (1966).

[56] *J. H. Bowie, S.-O. Lawesson, G. Schroll*, and *D. H. Williams*, J. Amer. chem. Soc. *87*, 5742 (1965).

[57] *A. S. Newton* and *P. O. Strom*, J. physic. Chem. *62*, 24 (1958).

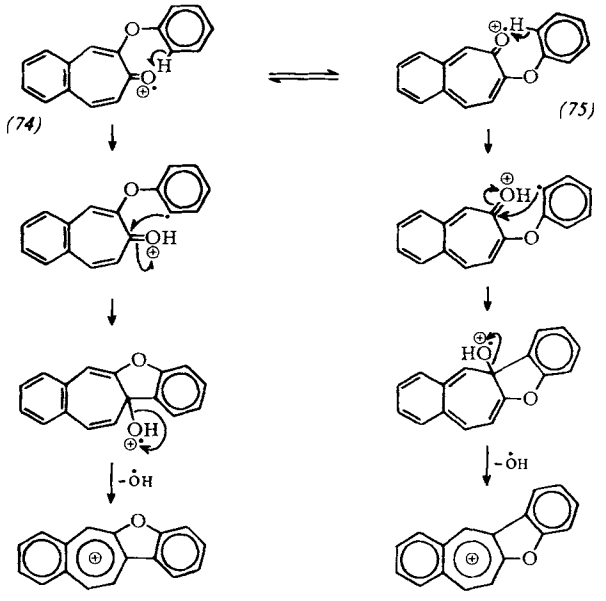
[58a] *F. W. McLafferty*, Appl. Spectroscopy *11*, 148 (1957).

[58b] *J. H. Bowie, R. G. Cooks, S.-O. Lawesson, P. Jakobsen*, and *G. Schroll*, Chem. Commun. *1966*, 539.

[59] *O. L. Chapman, T. H. Kinstle*, and *M.T. Sung*, J. Amer. chem. Soc. *88*, 2618 (1966).

oxide loss (M−CO), 80 % of the oxygen involved derives from the ether position, which can be readily accounted for by consideration of the relative stabilities of the two postulated intermediates *(76)* and *(77)*.

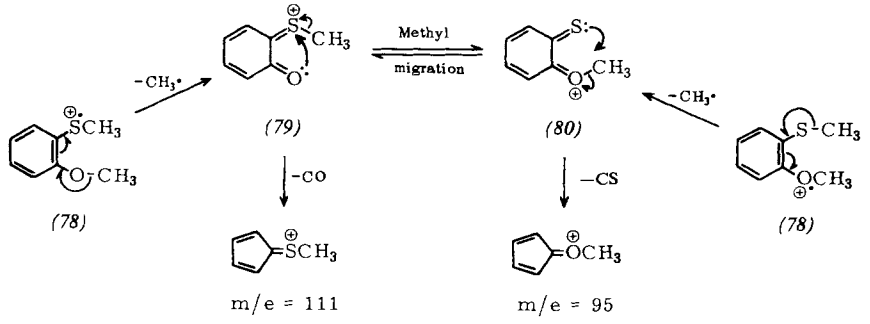
In the loss of OH (M − 17) process, the oxygen originates to approximately equal extent from each position[59], implicating again 1,4-phenyl migration [*(74)* ⇆ *(75)*]. No thermal phenyl migration was observed in this system but other instances of photochemically induced phenyl shifts (1,5 in *cis*-dibenzoylethylene) to oxygen are on record[60,61].



(74) *(75)*

m/e = 231 (M-17)

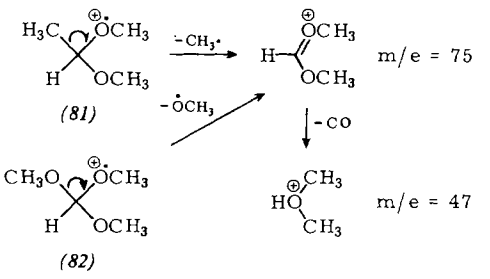
A closely related methyl migration has been reported[62] in the electron impact induced fragmentation of 2-methoxythioanisole *(78)*. An appropriate metastable ion verifies the expulsion of carbon monosulfide from the M − 15 species *(80)*, furnishing an ion of mass 95. In the *S*-trideuteriomethyl analogue, approximately 65 % of *m/e* = 95 increases to *m/e* = 98, and again a corresponding metastable ion is observed, indicating that methyl migration between sulfur *(79)* and oxygen *(80)* precedes loss of carbon monosulfide.



(78) *(79)* *(80)* *(78)*

m/e = 111 m/e = 95

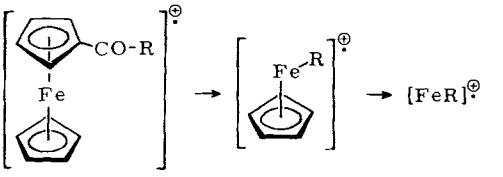
A further example of carbon monoxide elimination attended by skeletal rearrangement is apparent in the fragmentation of dimethyl acetal[6,46] *(81)* and trimethyl orthoformate[63]



(81) *(82)*

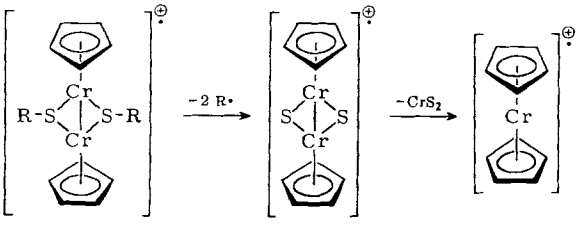
(82) on electron impact. In both compounds, α-cleavage affords an ion of mass 75, which then expels carbon monoxide to give the rearrangement species at *m/e* = 47. The relative abundance of this peak is 8 % for *(81)* and 47 % for *(82)*.

Also falling in this category are the recent reports[64,65] of carbon monoxide loss from certain π-bonded organometallic compounds. For example, with the ferrocene derivatives



(83) R = CH_3, OH

(83), migration of the group R to the metal atom apparently occurs. This type of rearrangement is common to a wide range of suitably substituted π-complexes of Fe, Cr, and Mn[65].



(84) R = CH_3, C_6H_5 m/e = 298 m/e = 182

Another reorganization process in the mass spectra of some binuclear transition metal π-complexes has been observed by *Reed*[66]. Thus the chromium complex *(84)* decomposes to an ion of mass 298,

[60] *G. W. Griffin* and *E. J. O'Connel*, J. Amer. chem. Soc. *84*, 4148 (1962).

[61] *H. E. Zimmerman, H. G. C. Durr, R. G. Lewis*, and *S. Braun*, J. Amer. chem. Soc. *84*, 4149 (1962).

[62] *J. H. Bowie, S.-O. Lawesson, J. O. Madsen, C. Nolde*, and *D. H. Williams*, J. chem. Soc. (London) *B 1966*, 951.

[63a] *G. Schroll, H. J. Jakobsen, S.-O. Lawesson, P. Brown*, and *C. Djerassi*, Ark. Kemi *26*, 279 (1966).

[63b] *M. J. Rix, A. J. C. Wakefield*, and *B. R. Webster*, Chem. Commun. *1966*, 748.

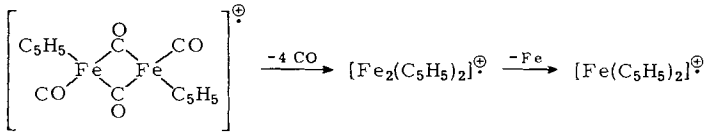
[64] *A. Mandelbaum* and *M. Cais*, Tetrahedron Letters *1964*, 3847.

[65] *N. Maoz, A. Mandelbaum*, and *M. Cais*, Tetrahedron Letters *1965*, 2087.

[66] *F. J. Preston* and *R. J. Reed*, Chem. Commun. *1966*, 51.

which in turn loses the elements of CrS_2. This behavior was also noted for the corresponding Fe and Ni analogues.

Skeletal rearrangement ions have also been observed [67] in the mass spectra of a variety of other transition metal complexes [*(85)*, *(86)*, *(87)*].



(85)

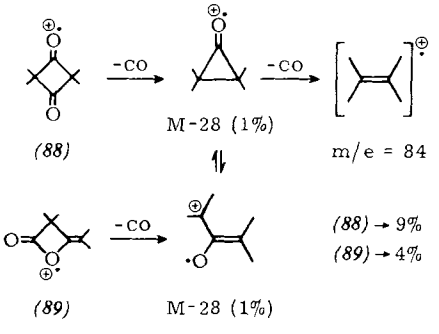
$$[(C_6H_5)_3SnMn(CO)_5]^{\oplus\cdot} \xrightarrow{-5\,CO} [(C_6H_5)_3SnMn]^{\oplus\cdot} \rightarrow [(C_6H_5)Mn]^{\oplus\cdot}$$

(86)

$$[(C_6H_5)SnFe(CO)_2(C_5H_5)]^{\oplus\cdot} \rightarrow [Sn(C_5H_5)]^{\oplus\cdot}$$

(87)

In the spectra of tetramethylcyclobutane-1,3-dione *(88)* and its photoisomer *(89)*, peaks [68] are seen which correspond to the sequential loss of two carbon monoxide molecules. Although the structures of the ions

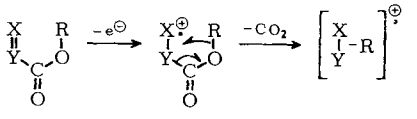


depicted are no less tentative than those proposed in many mass spectral mechanistic schemes, nevertheless, carbon-carbon bond formation must accompany or precede the final ejection of carbon monoxide in order to furnish the ion of mass 84. The observation of a metastable peak for the decomposition of the molecular ion to $m/e = 84$ betrays the simultaneous operation of a concerted M−2CO process. Certain correlations between the electron impact induced and the photochemical behavior of ketene dimers such as *(88)* have been made [68].

b) Loss of Carbon Dioxide

Skeletal rearrangement accompanied by expulsion of carbon dioxide in the mass spectrometer is a well documented process, occurring particularly in certain types of esters, and closely related compounds (Table 3).

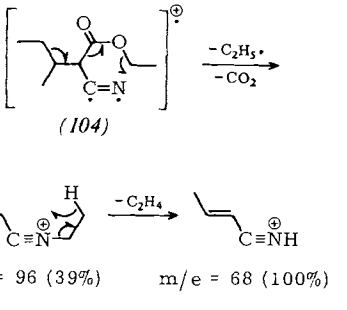
Significant rearrangement peaks have been noted in the mass spectra of all the compounds given in the table. For all the compounds listed, except the cyanoacetates *(94)*–*(97)* and the diethyl malonates *(98)*, an unsaturated system is in conjugation with the ester carbonyl group [69]. Effective localization of the charge on the adjacent group *(102)* would then provide an electron deficient site for alkyl migration [*(102)* → *(103)*], attended by simultaneous loss of carbon dioxide. Only the simpler alkyl groups (*e.g.* methyl, ethyl) give significant rearrangement peaks, probably due to the larger number of alternative reactions possible in the more complex groups.



(101) *(102)* *(103)*

However, although the migration of the alcohol R group in α-β unsaturated esters seems to be a fairly general process [73], only one case of the converse situation (*i.e.* a vinyl ester of a saturated acid) expelling carbon dioxide with concomitant alkyl shift has been reported [*(100)*, Table 3] [12]. Migration of the t-butyl group in phenyl pivalate is observed, but no corresponding methyl migration in phenyl acetate has been detected [12, 73].

The substituted cyanoacetates *(96)* and *(97)* are believed [70] to suffer synchronous γ-cleavage (to the carbonyl group), alkyl migration, and loss of carbon



(104)

m/e = 96 (39%) m/e = 68 (100%)

[67] *J. M. Wilson* and *M. Haas*, Symposium on "Newer Physical Methods in Structural Chemistry", Oxford 1966.

[68] *N. J. Turro*, *D. C. Neckers*, *P. A. Leermakers*, *D. Seldner*, and *P. D'Angelo*, J. Amer. chem. Soc. *87*, 4097 (1965).

[69] *J. H. Bowie*, *D. H. Williams*, *P. Madsen*, *G. Schroll*, and *S.-O. Lawesson*, Tetrahedron *23*, 305 (1967).

[70] *J. H. Bowie*, *R. Grigg*, *S.-O. Lawesson*, *P. Madsen*, *G. Schroll*, and *D. H. Williams*, J. Amer. chem. Soc. *88*, 1699 (1966).

[71] *J. H. Bowie*, *D. H. Williams*, *S.-O. Lawesson*, and *G. Schroll*, J. org. Chemistry *31*, 1792 (1966).

[72] *F. Weiss*, *A. Isard*, and *G. Bonnard*, Bull. Soc. chim. France *1965*, 2332.

[73] It must be conceded that although rearrangement occurs in t-butyl benzoate [12], no significant analogous methyl migration is apparent with methyl benzoate [12].

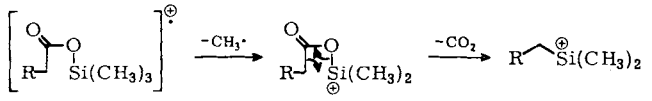
Table 3. Loss of carbon dioxide from unsaturated carboxylic esters.

Compound	R	Rearrangement peak	Relative abundance %	Ref.
$CH\equiv C-CO_2R$ *(90)*	CH_3	$M - CO_2$ $M - HCO_2$	20 15	[69]
	C_2H_5	$M - CO_2$ $M - HCO_2$	< 1 10	
	n-C_3H_7	$M - CO_2$ $M - HCO_2$	2 8	
	i-C_4H_9	$M - CO_2$ $M - HCO_2$	< 1 3	
	sec-C_4H_9	$M - CO_2$ $M - HCO_2$	1 3	
	$CH_2CH=CH_2$	$M - CO$ $M - CO_2$ $M - HCO_2$	– 4 8	
	$CH_2-C_6H_5$	$M - CO_2$ $M - HCO_2$	34 67	
$RO_2C-C\equiv C-CO_2R$ *(91)*	CH_3 C_2H_5	$M - CO_2$ $M - CO_2$	40 7	[54] [69]
cis $RO_2C-CH=CH-CO_2R$ *(92)*	CH_3	$M - CO_2$	1	[69]
trans $RO_2C-CH=CH-CO_2R$ *(93)*	CH_3 $CH_2CH=CH_2$	$M - CO_2$ $M - HCO_2$	4 6	[69]
$NC-CH_2-CO_2R$ *(94)*	CH_3 C_2H_5	$M - CO_2$ $M - HCO_2$ $M - HCO_2$	14 10 10	[69] [70]
	n-C_3H_7	$M - CO_2$ $M - HCO_2$ $M-(CH_3 + CO_2)$	3 3 5	
	$CH_2CH=CH_2$	$M - HCO_2$	16	
$C_6H_5-CH(CN)-CO_2R$ *(95)*	C_2H_5	$M - CO_2$	8	[54] [70]
$R^1R^2CH-CH(CN)-CO_2C_2H_5$ *(96)*	$R^1 = CH_3$ $R^2 = CH_3$	$M-(CH_3 + CO_2)$	27	[54] [70]
	$R^1 = CH_3$ $R^2 = C_2H_5$	$M-(C_2H_5 + CO_2)$	39	
	$R^1 = H$ $R^2 = n\text{-}C_3H_7$	$M-(C_3H_7 + CO_2)$	54	
	$R^1 = H$ $R^2 = i\text{-}C_3H_7$	$M-(C_3H_7 + CO_2)$	43	
$R^1R^2CH-CH(CN)-CO_2CH_3$ *(97)*	$R^1 = H$ $R^2 = C_3H_7$	$M-(C_3H_7 + CO_2)$	75	[70]
$C_6H_5-CR(CO_2C_2H_5)_2$ *(98)*	H	$M - CO_2$	17	[54]
	C_2H_5	$M - CO_2$	8	[71]
$C_6H_5-CO_2R$ *(99)*	t-C_4H_9	$m/e = 91$	7	[12]
	$CH_2-C_6H_5$	$M - HCO_2$	6	[72]
$(CH_3)_3C-CO_2R$ *(100)*	C_6H_5	$M - CO_2$	3	[12]

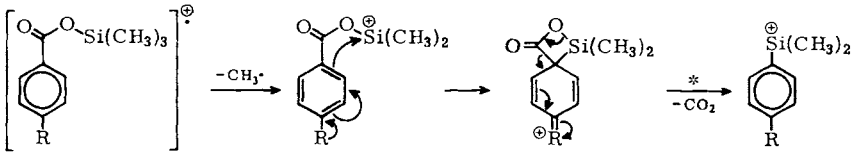
dioxide, as outlined for ethyl s-butylcyanoacetate *(104)*. Further elimination of ethylene from the rearrangement ion (mass 96) provides one route to the species (m/e = 68) responsible for the base peak in the spectrum.

Both alkyl and aryl group migrations have been described [74] in the electron impact induced decomposition of trimethylsilyl esters. Rearrangement peaks [M − (15 + 44)] were apparent in the spectra of the trimethylsilyl derivatives of octanoic, decanoic, and octadecanoic acids *(105)*, and also alanine. In the case of aromatic acid derivatives, support for the scheme *(106)* → M − 15 → M − (15 + 44) is provided by the presence of appropriate metastable peaks, and also by an increase in the intensity of the M − (15 + 44) peak relative to M − 15 as R is varied from an electron withdrawing to an electron donating group. In the mesitoic acid derivative, the rearrangement is still operative.

[74] *R. M. Teeter*, Abstracts Tenth Annual Conference on Mass Spectrometry, ASTM Committee E-14, New Orleans, La., 1962, p. 51.

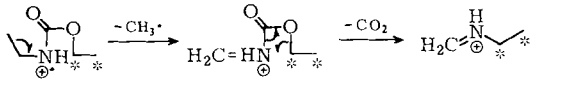


(105) M-15 M-(15 + 44)

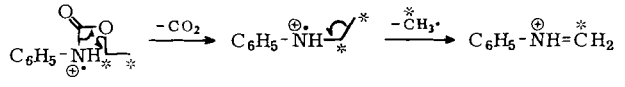


(106) M-15 M-(15 + 44)

Similar rearrangements have been noted [75,76] with *N*-substituted ethyl carbamates. Where α-cleavage to nitrogen is possible [*e.g.*, ethyl *N*-ethylcarbamate *(107)*], it apparently precedes ethyl migration and carbon dioxide loss. In instances where such cleavage is prohibited [*e.g.* ethyl *N*-phenylcarbamate *(108)*], the sequence of events appears to be reversed. Deuterium labeling studies [see asterisks in *(107)* and *(108)*] were undertaken in support of the proposed pathways.

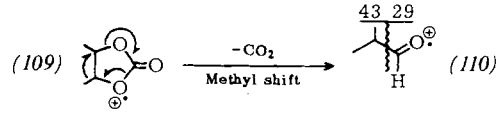


(107) m/e = 102 (M-15) M-(15 + 44)

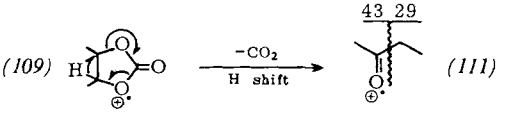


(108) m/e = 121 (M-44) M-(44 + 15)

Both hydrogen and methyl shifts accompanied by carbon dioxide elision are found [77] in the fragmentation of certain cyclic carbonates. Analogous rearrangements with loss of sulfur dioxide are also encountered [77] in the corresponding cyclic sulfites, further discussed below. As an example of the former, the two largest peaks in the mass spectrum of butane-2,3-diol cyclic carbonate *(109)* are at *m/e* = 43 (100 %) and *m/e* = 29 (38 %). Each peak is a doublet by exact mass measurements, indicating that both rearrangement species *(110)* and *(111)* are formed in approximately 1:3 ratio.

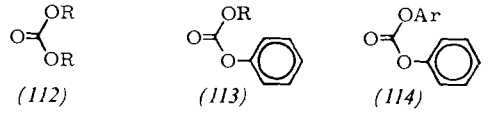


(109) (110)



(109) (111)

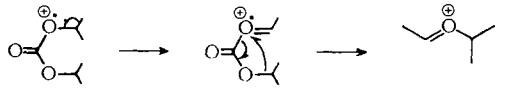
This type of rearrangement is also prevalent [78] in the mass spectra of symmetrical dialkyl carbonates *(112)*, alkyl phenyl carbonates *(113)*, and aryl phenyl carbonates *(114)*. The rearrangement peak is of high intensity for the methyl compounds *(112)* (R = CH_3, 53.2 % Σ_{40}) and *(113)* (R = CH_3, 11.8 % Σ_{40}), and likewise for the diphenyl compound *(114)* (Ar = C_6H_5,



(112) (113) (114)

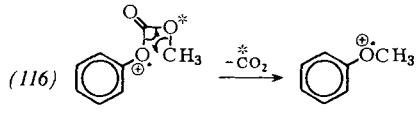
R = CH_3, C_2H_5, n-C_3H_7, i-C_3H_7, n-C_4H_9, sec.-C_4H_9, i-C_4H_9, i-C_5H_{11} Ar = C_6H_5, *p*-$CH_3C_6H_4$

8.3 % Σ_{40}), but rapidly falls off with the larger R groups. Evidence was adduced [78] for a two stage decomposition of the dialkyl carbonates *(112)*, with alkyl migration and loss of carbon dioxide following initial α-cleavage (see *(115)*, diisopropyl carbonate). With the alkyl phenyl carbonates *(113)* (except for R = CH_3), both this decomposition path and the converse (initial loss of carbon dioxide, then α-cleavage) appear to operate, while the diaryl compounds *(114)* expel carbon dioxide [79], followed by carbon monoxide from the diaryl ether [46] rearrangement ion.

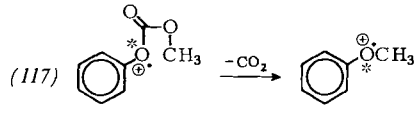


(115) m/e = 131 (M-15) m/e = 87 M-(15 + 44)

A more detailed study has since been undertaken [80a] in an attempt to clarify further the mechanism of methyl migration in methyl phenyl carbonate [*(113)*, R = CH_3]. Previous results [78] already indicated that migration was taking place to aryl oxygen, rather than to the *ortho* ring position, and two separate ^{18}O-labeling experiments [see asterisks in *(116)* and *(117)*]



(116)



(117)

[75] *C. P. Lewis*, Analyt. Chem. *36*, 176 (1964).

[76] *C. P. Lewis*, Analyt. Chem. *36*, 1582 (1964).

[77] *P. Brown* and *C. Djerassi*, unpublished.

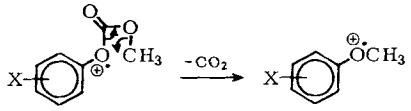
[78] *P. Brown* and *C. Djerassi*, J. Amer. chem. Soc. *88*, 2469 (1966).

[79] The pyrolytic analogue of this rearrangement has been reported by *P. D. Ritchie*, J. chem. Soc. (London) *1935*, 1054.

[80a] *P. Brown* and *C. Djerassi*, J. Amer. chem. Soc. *89*, 2711 (1967).

verified[80a] that the aryl oxygen was indeed retained exclusively in the M – 44 rearrangement ion.

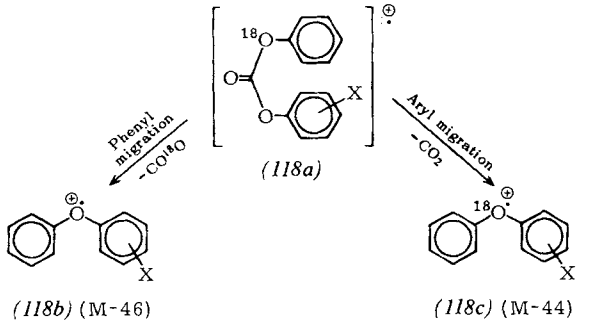
By variation of the *meta*- and *para*-substituents [X in *(118)*] in the aromatic ring, the propensity for rearrangement was expressed[80a] in kinetic terms[43], and a Hammett ρσ plot of positive slope obtained. A reasonable interpretation of these data is that methyl migration takes place in this system preferentially to the more positively charged site.



(118) M-44

In this connection, it is worth recalling that alkyl migration in dialkyl carbonates[78] *(112)* and ethyl *N*-ethylcarbamate[75] *(107)* occurs only after initial α-cleavage. This cleavage removes the inductively stabilizing effect of an alkyl group on the ion radical, and simultaneously generates a full positive charge on the "receptor site". Alkyl migration takes place in the molecular ion of methyl phenyl carbonate[78] [*(113)*, R = CH_3] and ethyl *N*-phenyl carbamate[75] *(108)*, where the phenyl substituent can inductively enhance the positive character of the "receptor site". The data for trimethylsilyl derivatives of substituted benzoic acids[74] *(106)* also support the hypothesis that the migrating group will be a nucleophilic species and the "receptor site" electrophilic in nature.

A substituent effect study has also been performed[80a] on the electron impact induced decarboxylation of aryl phenyl carbonates. In this reaction, phenyl migration [*(118a)* → *(118b)*] was distinguished from aryl migration [*(118a)* → *(118c)*] by ^{18}O-labeling. Thus relative migratory aptitudes of the aryl groups could be assigned (Table 4).



(118a)

(118b) (M-46) *(118c)* (M-44)

Table 4. Relative migratory aptitudes of aryl groups in the electron impact induced decarboxylation of aryl phenyl carbonates.

$[C_6H_5O{-}CO{-}OC_6H_4X]^{\oplus}_{\bullet} \rightarrow [C_6H_5{-}O{-}C_6H_4X]^{\oplus}_{\bullet} + CO_2$

Substituent	Migrating group		Aryl migratory aptitudes	
	Phenyl	Aryl	Carbonates	Pinacols [80b]
p-OCH_3	48	52	1.1	500
m-OCH_3	30	70	2.3	1.6
o-OCH_3	>98	< 2	< 0.02	0.3
α-Naphthyl	95	5	0.05	–
p-C_6H_5	39	61	1.6	11.5
2,6-Dimethyl	6	94	15.7	–
p-CH_3	63	37	0.6	15.7
m-CH_3	23	77	3.4	1.9
o-CH_3	21	79	3.8	–
H	50	50	1.0	1.0
p-CO_2CH_3	80	20	0.25	–
p-Br	>99	< 1	< 0.01	0.7
p-F	>99	< 1	< 0.01	–
p-CN	>99	< 1	< 0.01	–
p-NO_2	>99	< 1	< 0.01	–

It was found that charge distribution in the molecular ion and the relative nucleophilicities of the migrating species are major factors controlling the overall migration tendencies. Very generally, electron withdrawing substituents on the aryl group favored phenyl migration, and electron releasing substituents produced more aryl migration. Correlation of these migratory aptitudes (1,3–O to O shift) with those obtained in solution chemistry for the pinacol rearrangement (1,2–C to C shift)[80b] is only qualitative (see Table 4).

As a logical extension of our previous work[78], we have studied[81] the relative ease of elimination of various possible neutral molecules from the series of

$H_3C{-}X{-}C(=Z){-}Y{-}C_6H_5$ $C_6H_5{-}X{-}C(=Z){-}Y{-}C_6H_5$

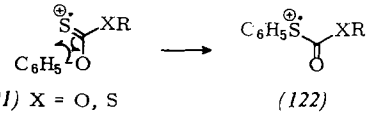
(119) X,Y,Z = O or S *(120)*

all possible methyl phenyl *(119)* and diphenyl *(120)* mono-, di-, and trithiocarbonates (Table 5). In addition to this rearrangement, a further process involving

Table 5. Rearrangement peaks in the mass spectra of thiocarbonates (all numerical values refer to Σ_{40}).

Compound	M – CO	M – CS	M – CO_2	M – COS	M – CS_2
$C_6H_5O{-}CO{-}OCH_3$	–		11.8		
$C_6H_5O{-}CO{-}SCH_3$	13.8		–	2.4	
$C_6H_5S{-}CO{-}OCH_3$	–		7.4	0.1	
$C_6H_5O{-}CS{-}OCH_3$	0.1	–	9.0	3.9	
α-Naphthyl-O–CS–OCH_3	–	–	2.7	4.2	
β-Naphthyl-O–CS–OCH_3	–	–	2.9	4.6	
$C_6H_5S{-}CO{-}SCH_3$	14.0			1.1	
$C_6H_5O{-}CS{-}SCH_3$	4.8	–		0.2	0.1
$C_6H_5S{-}CS{-}OCH_3$	–	–		14.3	–
$C_6H_5S{-}CS{-}SCH_3$		0.7			0.7
$C_6H_5O{-}CO{-}OC_6H_5$	–		8.3		
$C_6H_5O{-}CO{-}SC_6H_5$	10.0		<0.3	–	
$C_6H_5O{-}CS{-}OC_6H_5$	7.8	–	<0.2	0.2	
$C_6H_5O{-}CS{-}SC_6H_5$	6.7	–		0.4	
$C_6H_5S{-}CO{-}SC_6H_5$	12.0			0.8	
$C_6H_5S{-}CS{-}SC_6H_5$		0.7			1.5

isomerization of the molecular ion of compounds containing the part structure $C_6H_5O{-}CS$ was disclosed [see *(121)* → *(122)*]. This latter type of rearrangement has good analogy in the corresponding thermal process.



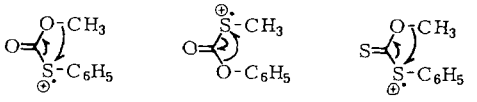
(121) X = O, S R = CH_3, C_6H_5 *(122)*

The observed eliminations (Table 5) can be rationalized by locating the charge at a favorable site, and assuming a relative migratory order of $CH_3 > OC_6H_5 > SC_6H_5 > C_6H_5$. In this way, neutral species with negative heats of formation are preferentially produced (see Table 1), but this factor alone does not exert the sole

[80b] *W. E. Bachmann* and *J. W. Ferguson*, J. Amer. chem. Soc. *56*, 2081 (1934).

[81] *J. B. Thomson*, *P. Brown*, and *C. Djerassi*, J. Amer. chem. Soc. *88*, 4094 (1966).

controlling influence. Thus in *(123)*, carbon dioxide is lost to a greater extent than carbonyl sulfide, whereas in *(124)* carbon monoxide loss prevails over that of carbonyl sufide or carbon dioxide, and in *(125)* only



(123) *(124)* *(125)*

elision of carbonyl sulfide is apparent. In the diphenyl series, *(126)* suffers loss of carbon monoxide rather than carbon dioxide or carbonyl sulfide, and *(127)* eliminates carbon monoxide rather than carbonyl sulfide.

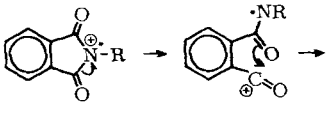


(126) *(127)*

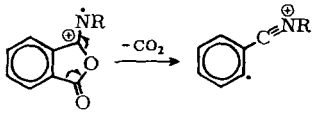
In the course of this work [81], it was noted [77] that the spectrum of phenyl chloroformate *(128)* contains two rearrangement peaks, due to loss of carbon monoxide (4 % relative abundance), and of carbon dioxide (14 %).

C_6H_5–O–CO–Cl *(128)*

Two recent reports call attention to the expulsion of carbon dioxide from certain aromatic imides, *e.g. N*-methylphthalimide *(128a)*, R = CH_3 [82a] and the *N*-phenyl analogue *(128a)*, R = C_6H_5 [82b]. *(128a)*, R = C_6H_4-*p*-C_6H_5, also gives rise to carbon dioxide elimination, but an *o*-phenyl substituent *(128a)*, R = C_6H_4-*o*-C_6H_5, results in different fragmentation pathways [82b].



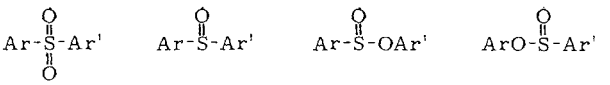
(128a)



M-44

c) Loss of Sulfur Dioxide and Sulfur Monoxide

The mass spectra of diaryl sulfones [52,83,84] *(129)* and sulfoxides [52,84] *(130)* have recently been published, and it is apparent (Table 6) that skeletal rearrange-



(129) *(130)* *(131)* *(132)*

ments in these compounds are more pronounced than in the dialkyl analogues [53]. In addition to the unexpected carbon monoxide expulsion discussed in one of the preceding sections, loss of sulfur dioxide from sulfones and sulfur monoxide from sulfoxides seems to require at least one aromatic ring (site of unsaturation) in the molecule. Analogous eliminations of sulfur dioxide from sulfones have been observed under radiolytic [85] and pyrolytic [86] (600–700 °C) conditions.

Table 6. Some rearrangement peaks in the mass spectra of sulfoxide and sulfones.

Compound	Rearrangement peak	Relative abundance (%)	Ref.
$(CH_3)_2SO$	M – SO	0	[52]
CH_3SO–CH=CH_2	M – SO M – HSO	10.6 17.0	[53]
(n-$C_3H_7)_2SO$	M – SO	0	[52]
$(C_6H_5CH_2)_2SO$	M – SO M – H_2SO	30 16	[84]
C_6H_5–SO–CH_3	M – SO M – HSO	5 10	
$(C_6H_5)_2SO$	M – SO M – HSO	64 10	
(*p*-$CH_3C_6H_4)_2SO$	M – SO M – HSO	100 18	
$(CH_3)_2SO_2$	M – SO_2	0	
CH_3–SO_2–CH=CH_2	M – SO_2 M – HSO_2	4.7 4.2	[53]
(i-$C_4H_9)_2SO_2$	M – SO_2	0	[52]
C_6H_5–SO_2–CH_3	M – SO_2	0	
C_6H_5–SO_2–C_2H_5	M – SO_2	0	
$(C_6H_5)_2SO_2$	M – SO_2 M – HSO_2 M – H_2SO_2	2 4 5	[83]
(*o*-$CH_3C_6H_4)_2SO_2$ [*]	M – SO_2 M – HSO_2 M – H_2SO_2	5 21 67	[83]
(*m*-$CH_3C_6H_4)_2SO_2$ [*]	M – SO_2 M – HSO_2 M – H_2SO_2	1 2 0	
(*p*-$CH_3C_6H_4)_2SO_2$ [*]	M – SO_2 M – HSO_2 M – H_2SO_2	1 1 0	
3,3'-dithiophene sulfone	M – SO_2	10	[52]

[*] These are only representative examples of a large number of methyl-substituted diphenyl sulfones listed in ref. [83].

A further rearrangement of the unsymmetrical diaryl sulfone *(129)* molecular ion to sulfinate esters *(131)* and *(132)* is envisaged [83] to account for the presence of aryloxy ions in the mass spectra. Significantly, the more highly methyl

[82a] *R. A. W. Johnstone, B. J. Millard,* and *D. S. Millington,* Chem. Commun. *1966*, 600.

[82b] *J. L. Cotter* and *R. A. Dine-Hart,* Chem. Commun. *1966*, 809.

[83] *S. Meyerson, H. Drews,* and *E. K. Fields,* Analyt. Chem. *36*, 1294 (1964).

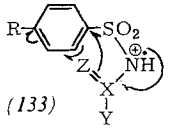
[84] *J. O. Madsen, C. Nolde, S.-O. Lawesson, G. Schroll, J. H. Bowie,* and *D. H. Williams,* Tetrahedron Letters *1965*, 4377.

[85] *L. Kevan, P. L. Hall,* and *E.T. Kaiser,* J. physic. Chem. *70*, 853 (1966).

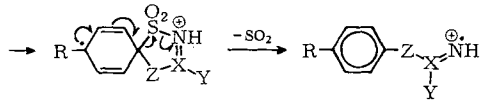
[86] *E. C. Leonard,* J. org. Chemistry *30*, 3258 (1965).

substituted aromatic nucleus was found to migrate preferentially in every case.

Loss of sulfur dioxide from sulfonamides on electron impact has also been reported [87] (Table 7). Since the intensity of the M – SO_2 peak increases as the basicity of Z increases (see *(133)* and Table 7), and taking into account steric considerations, a general scheme can be proposed *(133)* → *(134)* → *(135)*][87]. In support



(133)



(134) *(135)* M-SO_2

of this rationalization, it should be noted that 4-aminobenzosulfonamide (Table 6, R = H) exhibits no M – SO_2 peak, whereas with 4-nitrobenzosulfonamide, this process is responsible for the base peak.

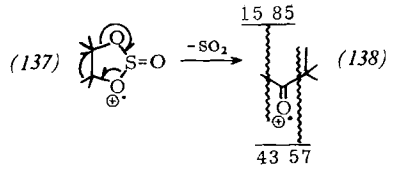
More recently, an analogous expulsion of sulfur dioxide from *N*-n-butyl-*N'*-*p*-toluenesulfonylurea *(136)* has been detected [88]. By a combination of exact mass measurements and deuterium labeling techniques, two fragmentation pathways were established, the main process being identical to that described above for other sulfonamides[*(133)* → *(134)* → *(135)*]. At low ionizing voltage (19 eV), the relative importance of the rearrangement was enhanced.

p–CH_3–C_6H_4–SO_2–NH–CO–NH–C_4H_9 *(136)*

Table 7. Rearrangement peaks in the mass spectra of sulfonamides. *p*-R–C_6H_4–SO_2–NH–R' [87].

R	R'	Rearrangement peak	Relative abundance (%)
NH_2	H	M – SO_2	–
NH_2	$COCH_3$	M – SO_2	–
NH_2	CONH–n-C_4H_9	M – SO_2	4
NH_2	C(=NH)–NH_2	M – SO_2	6
NH_2	4,5-Dimethyl-2-oxazolyl	M – SO_2	7
NH_2	1-Phenyl-5-pyrazolyl	M – SO_2	10
NH_2	2-Thiazolyl	M – SO_2	75
NH_2	[1,3]-Diazin-2-yl	M – SO_2	100
		M – HSO_2	87
NH_2	5-Methyl-[1,3]-diazin-2-yl	M – SO_2	86
		M – HSO_2	100
NH_2	5-Methoxy-[1,3]-diazin-2-yl	M – SO_2	100
		M – HSO_2	75
NH_2	2,6-Bis(methoxy)-[1,3]-diazin-4-yl	M – SO_2	100
		M – HSO_2	33
NH_2	3,4-Dimethyl-5-isoxazolyl	M – SO_2	–
NO_2	H	M – SO_2	100

As previously mentioned,certain cyclic sulfites undergo alkyl migration accompanied by sulfur dioxide loss [77], analogous to the corresponding cyclic carbonates losing carbon dioxide [*(109)* → *(110)*]. For example, 2,3-dimethylbutane-2,3-diol cyclic sulfite *(137)* ap-

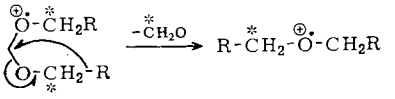


(137) *(138)*

pears to rearrange to the 3,3-dimethyl-2-butanone molecular ion *(138)*, in what may be described as an electron impact induced pinacol rearrangement. The peaks at *m/e*=43 and 57 have the compositions expected, and together comprise 52 % Σ_{40}.

d) Loss of Formaldehyde

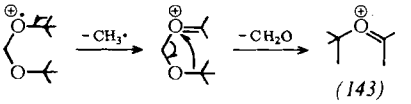
One of the few well documented cases of skeletal rearrangement with formaldehyde expulsion taking place in the mass spectrometer has been described [89] for formaldehyde acetals. The primary alcohol derivatives *(139)* display low intensity M – CH_2O peaks



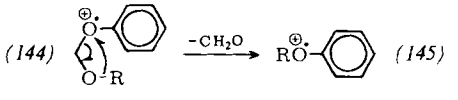
(139) *(140)* M-30

R = C_2H_5, i-C_3H_7, t-C_4H_9

(140), that surprisingly involve loss of the α-carbon of the alcohol. Acetals of secondary and tertiary alcohols, on the other hand, first suffer α-cleavage and then rearrangement [*(141)* → *(142)* → *(143)*], exactly as in the dialkyl carbonates *(112)*. Alkyl aryl acetals *(144)* eliminate formaldehyde directly from the molecular ion, again paralleling the behavior of the corresponding carbonates *(113)*, in which alkyl migration takes place preferentially to the most positive site. It should be noted that the analogous rearrangement process apparently does not operate in dithioacetals [90].



(141) *(142)* M-15 *(143)* M-(15 + 44)



(144) *(145)*

During the course of deuterium labeling studies on butyl acetate [91]*(146)*, a small but characteristic M – 30 peak was detected. Loss of formaldehyde from butyl acetate *(146)* and of acetaldehyde from 1-methyl-propyl acetate *(147)* was confirmed by precise mass measurements. Similar rearrangements occur with neopentyl esters of acetic, propionic, benzoic, and some substituted benzoic acids [92]. In an independent investiga-

[87] *G. Spiteller* and *R. Kaschnitz*, Mh. Chem. *94*, 964 (1963).

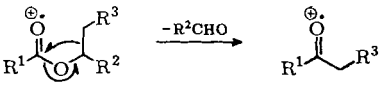
[88] *H. F. Grostic*, *R. J. Wnuk*, and *F. K. MacKellar*, J. Amer. chem. Soc. *88*, 4664 (1966).

[89] *P. Brown*, *C. Djerassi*, *G. Schroll*, *H. J. Jakobsen*, and *S.-O. Lawesson*, J. Amer. chem. Soc. *87*, 4559 (1965).

[90] *T. M. Shuttleworth*, Appl. Spectroscopy *18*, 78 (1964).

[91] *D. R. Black*, *W. H. McFadden*, and *J. W. Corse*, J. physic. Chem. *68*, 1237 (1964).

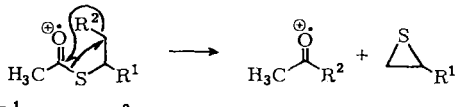
[92] *W. H. McFadden*, *K. L. Stevens*, *S. Meyerson*, *G. J. Karabatsos*, and *C. E. Orzech*, J. physic. Chem. *69*, 1742 (1965).



(146) $R^1 = CH_3$, $R^2 = H$, $R^3 = C_2H_5$ *(149)*
(147) $R^1 = R^2 = R^3 = CH_3$
(148) $R^1 = C_2H_5$, $R^2 = H$, $R^3 = C_2H_5$

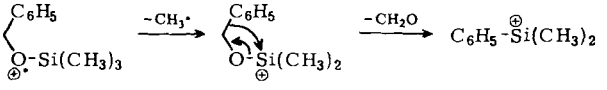
tion[93] using deuterium labeled esters, expulsion of formaldehyde from butyl propionate *(148)* was noted. The rearrangement ion was written as the ketone molecular ion *(149)*, since α-cleavage in *(149)* could then account simply for an otherwise anomalous peak (C_4H_7O) at *m/e* = 71.

It is noteworthy in this connection that thioesters[94] do not lose thioformaldehyde, but rather thiiranes *(153)*. The rearrangement peak corresponds to 3.8 % Σ_{40} for *(150)*, and 1.2% Σ_{40} for *(151)*.



(150) $R^1 = CH_3$, $R^2 = C_2H_5$ *(152)* *(153)*
(151) $R^1 = R^2 = C_2H_5$

In a series of experiments designed to explore the feasibility of elimination of various neutral species (particularly formaldehyde) from trimethylsilyl derivatives of alcohols, a large rearrangement peak (62 % relative abundance) was detected[95] in the mass spectrum of the benzyl alcohol derivative *(154)*. This process is obviously closely related to the loss of

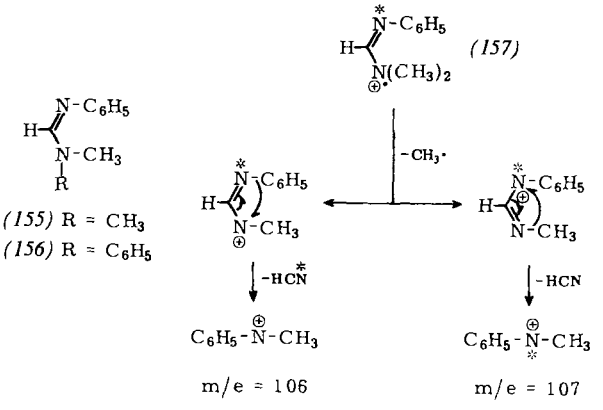


(154) M-15 M-(15 + 30)

carbon dioxide by trimethylsilyl derivatives of benzoic acid[74] *(106)*. A similar study of the effect of substituents in the aromatic ring on the migratory propensity of the aryl group in this system is in progress[95].

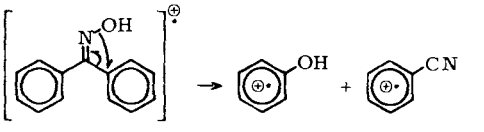
e) Loss of Hydrogen Cyanide and Nitriles

Skeletal rearrangement accompanied by elimination of hydrogen cyanide as a neutral species has been observed[96] in the spectra of certain amidines. In N^1,N^1-dimethyl-N^2-phenylformamidine *(155)*, the rearrangement peak appears at *m/e* = 106 [M − (CH_3 + HCN), 45 % relative abundance], and in N^1-methyl-N^1,N^2-diphenylformamidine *(156)* it is shifted to *m/e* = 168 [M−(CH_3 + HCN)]. By using the ^{15}N-labeled analogue [*(157)*, see asterisks], it was shown that both methyl and phenyl migrations are taking place, since some of the *m/e* = 106 peak moved to *m/e* = 107.



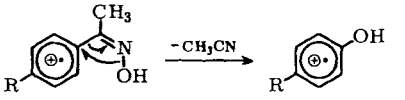
(155) R = CH_3
(156) R = C_6H_5
(157)

The occurrence of two rearrangement peaks at *m/e* = 94 and *m/e* = 103 in the mass spectrum of benzophenone oxime *(158)* has been attributed[18] to a hydroxyl migration, producing benzonitrile as one of the species. Operation of this scheme is supported by both precise mass measurements and observation of a metastable peak for the transition.

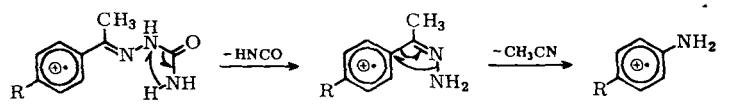


(158) m/e = 94 m/e = 103

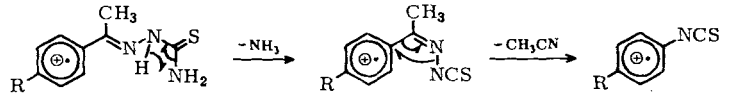
Similar rearrangements have been claimed[41] in the spectra of oximes *(159)*, semicarbazones *(160)*, and thiosemicarbazones *(161)* of *p*-substituted acetophenones.



(159)
R = H, CH_3, OCH_3, Br, NO_2



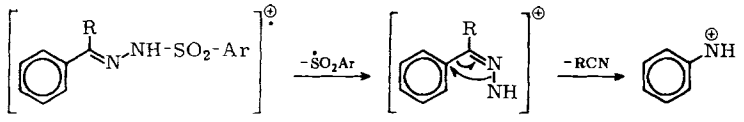
(160)



(161)

A recent study[97] of the electron impact induced fragmentation of alkyl and aryl sulfonylhydrazones has uncovered some important rearrangement processes which fall in this category. For example,

[93] *C. Djerassi* and *C. Fenselau*, J. Amer. chem. Soc. *87*, 5756 (1965).
[94] *W. H. McFadden, R. M. Seifert*, and *J. Wasserman*, Analyt. Chem. *37*, 560 (1965).
[95] *J. B. Thomson, J. Diekman*, and *C. Djerassi*, unpublished.
[96] *A. K. Bose, I. Kugajevsky, P.T. Funke*, and *K. G. Das*, Tetrahedron Letters *1965*, 3065.
[97] *A. Bhati, R. A.W. Johnstone*, and *B. J. Millard*, J. chem. Soc. *C 1966*, 358.

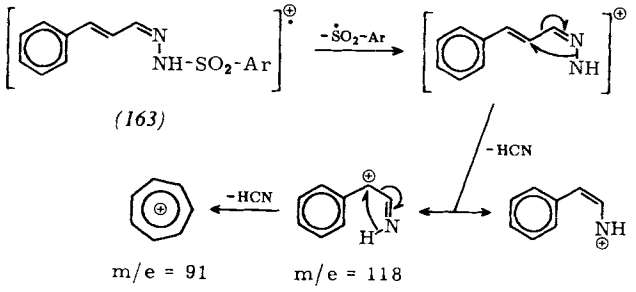


(162)

R = H, CH_3, $OCOCH_3$, C_6H_5

m/e = 92

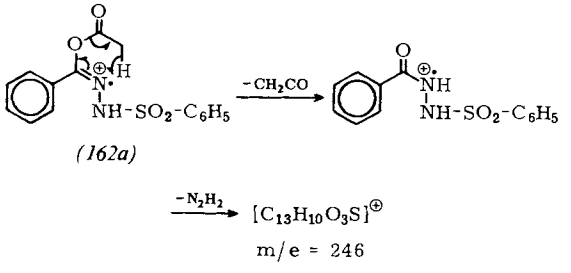
benzenesulfonylhydrazones and toluene-*p*-sulfonylhydrazones of aromatic aldehydes and ketones *(162)* generate characteristic peaks at *m/e* = 92. With the cinnammaldehyde derivatives *(163)* two rearrangement peaks are seen at *m/e* = 118 and *m/e* = 91, produced by successive eliminations of hydrogen cyanide. A further reorganization process has been



(163)

m/e = 91 m/e = 118

recognized in the acetyl derivative *(162a)*. After conventional cleavage of ketene, a subsequent loss of diimide apparently occurs, furnishing a rearrangement peak at *m/e* = 246.



(162a)

m/e = 246

f) Loss of Sulfur

Systematic studies on sulfides [53,62,84] and disulfides [84,98,99a] have clearly shown that many skeletal rearrangements with attendant sulfur loss are possible (Table 8). However, as with rearrangements involving carbon dioxide expulsion [69], it has been proposed [62,98] that an unsaturated site in the molecule is a necessary prerequisite for significant rearrangement. The absence of skeletal rearrangement peaks in the mass spectra of higher dialkyl sulfides [99b] may be cited in favor of this suggestion. Also, the much greater proclivity of methyl compounds (*e.g.* dimethyl sulfide [53], dimethyl disulfide [98], and thioanisole [62]) to undergo skeletal rearrangement compared with other alkyl substituted analogues has been attributed [62,98] to the lack of competing reactions possible with the simplest alkyl group.

Table 8. Skeletal rearrangement peaks in the mass spectra of sulfides and disulfides.

Compound	Rearrangement peak	% Relative abundance	Ref.
$(CH_3)_2S$	M − H_2S	3	[49,53]
$CH_3S-CH=CH_2$	M − S	3.6	[53]
	M − HS	95.1	
$CH_3-S-CH_2-CH=CH_2$	M − HS	2.6	
	M − H_2S	1.5	
$CH_3-S-CH=CH_2-CH_3$	M − HS	5.5	
	M − H_2S	2.2	
$CH_3-S-C\equiv CH$	M − HS	10.0	
$(CH_3)_2S_2$	M − S	1.5	[53,98]
	M − HS	13.5	
	M − H_2S	100	
$(C_2H_5)_2S_2$	M − S	1.5	[98]
	M − 2 S	3.2	
$(CH_2=CH-CH_2)_2S_2$	M − S	9	
	M − SH	5	
	M − CH_3S_2	58	
$C_6H_5-S-CH_3$	M − HS	25	[62,84]
β-Naphthyl-S-CH_3	M − HS	13	
$C_6H_5-S-CH_2CH=CH_2$	M − HS	39	
$(C_6H_5)_2S$	M − S	4	[49, 62,84]
	M − HS	6	
	M − H_2S	10	
	M − CS	3	
	M − CHS	4	
	M − CH_2S	2	
$C_6H_5CH_2-S-C_6H_5$	M − H_3S	4	[62,84]
$(C_6H_5CH_2)_2S$	M − S	2	
$C_6H_5-S-S-CH_3$	M − S	5	[98]
	M − HS	5	
	M − HS_2	10	
$(C_6H_5)_2S_2$	M − S	16	[62,84]
	M − HS	15	
	M − 2 S	11	
$(C_6H_5CH_2)_2S_2$	M − S	19	
	M − CH_2S	10	
	M − 2 S	11	
R = C_2H_5	M − 4 S	13	[99a]
R = n−C_3H_7	M − 4 S	7	
R = i−C_3H_7	M − 4 S	1	
$(R_2N-C(S)-S-)_2$,	M − S	2	
R_2 = $-(CH_2)_5-$	M − 2 S	7	
	M − 4 S	5	

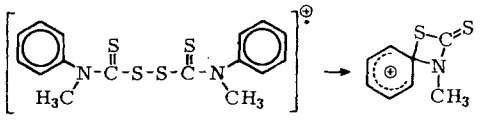
[98] *J. H. Bowie, S.-O. Lawesson, J. O. Madsen, C. Nolde, G. Schroll,* and *D. H. Williams,* J. chem. Soc. (London) *B 1966,* 946.

[99a] *J. Ø. Madsen, S.-O. Lawesson, A. M. Duffield,* and *C. Djerassi,* J. org. Chemistry, in press.

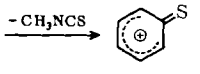
[99b] *S. D. Sample* and *C. Djerassi,* J. Amer. chem. Soc. *88,* 1937 (1966).

In phenyl substituted sulfides and disulfides, the $C_7H_7^{\oplus}$ ion of mass 91 is virtually ubiquitous, occurring for example to the extent (Table 8) of 25 % with thioanisole[62], and 12 % with phenyl allyl sulfide. It is also worth noting that although the M – CO process in diphenyl ether[46,49,50] *(60)* is a relatively favorable one (15–25 % relative abundance[46,49]), with diphenyl sulfide the corresponding M – CS peak is much less important (3 %, Table 8).

Thiuramdisulfides[99a] such as *(163a)* have small peaks corresponding to the loss of four sulfur atoms (Table 8), In addition, a more important (47 % relative abundance) rearrangement peak appears at $m/e = 109$, which can be most simply visualized as arising by phenyl migration to sulfur, followed by elimination of the elements of methyl isothiocyanate.



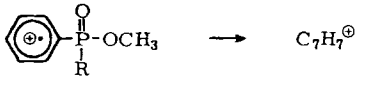
(163a)



m/e = 109

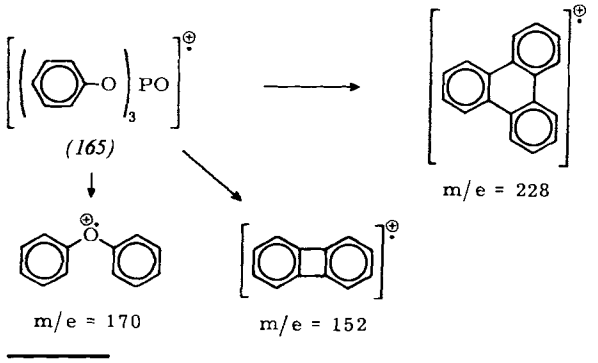
g) Miscellaneous Rearrangements

A rearrangement peak at $m/e = 91$, amounting to 20 % relative abundance, has been reported[100] in the mass spectra of a series of alkyl aryl phosphonates *(164)*.



(164) R = H, CH_3, C_2H_5 m/e = 91

Many relatively intense peaks in the spectra of triaryl phosphates[101] [*e.g.* triphenyl phosphate *(165)*] must involve complex skeletal rearrangements. For example, peaks at $m/e = 228$ (12 % relative abundance), $m/e = 170$ (40 %), and $m/e = 152$ (8 %) have been attributed[101] to the manifestation of such events. The trialkyl phosphates, on the other hand, fragment more predictably, with hydrogen transfer processes predominating.



(165)

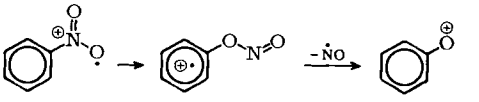
m/e = 228

m/e = 170 m/e = 152

[100] *H. Budzikiewicz* and *Z. Pelah*, Mh. Chem. *96*, 1739 (1965).

[101] *A. Quayle*, Advances Mass Spectrometry *1*, 365 (1959).

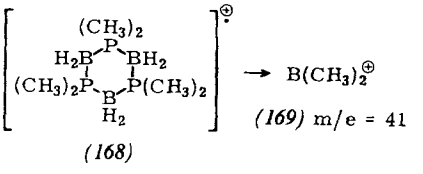
A significant peak (10 % relative abundance) at $m/e = 93$ (M – 30) in the mass spectrum of nitrobenzene *(166)* has been rationalized by the assumption[102] that prior isomerization of the molecular ion to that



(166) *(167)* m/e = 93

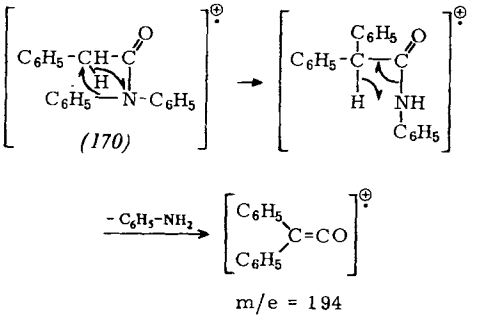
of phenyl nitrite *(167)* occurs. No complementary rearrangement is apparent with aliphatic nitro-compounds[103].

In the spectrum of the triphosphatriboracyclohexane[104] *(168)*, the base peak appears at $m/e = 41$, which has been attributed to the formation of dimethylboron ion *(169)*. Interestingly, the appearance potential for this species is greater than 20 eV.



(168) *(169)* m/e = 41

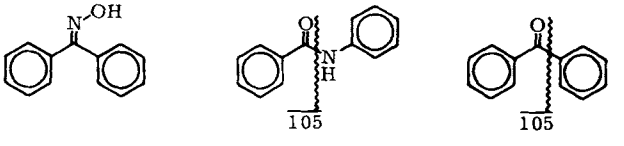
A small peak (0.2 % Σ_{40}) at $m/e = 149$ detected[105] in the spectrum of *N,N*-diphenyl phenylacetamide *(170)* has been interpreted by invoking a phenyl migration, and substituent and deuterium labeling results (but no exact mass measurements) are cited as corroborative evidence.



(170)

m/e = 194

In the same paper[105], an electron impact induced "Beckmann rearrangement" was claimed to operate in the fragmentation of benzophenone oxime *(158)*, due to the presence



(158) *(171)* *(172)*

of an otherwise anomalous peak at $m/e = 105$ (4 % Σ_{40}), which would be expected to result from cleavage in the Beckmann product benzanilide *(171)*. However, repetition of this

[102] *J. H. Beynon*, *R. A. Saunders*, and *A. E. Williams*, Ind. chim. belg. *1964*, 311.

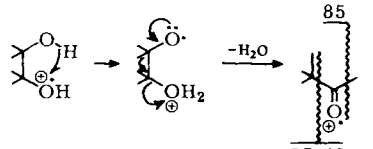
[103] *R.T. Aplin*, *M. Fischer*, *D. Becher*, *H. Budzikiewicz*, and *C. Djerassi*, J. Amer. chem. Soc. *87*, 4888 (1965).

[104] *R. E. Florin*, *L. A. Wall*, *F. L. Mohler*, and *E. Quinn*, J. Amer. chem. Soc. *76*, 3344 (1954).

[105] *P.T. Funke*, *K. G. Das*, and *A. K. Bose*, J. Amer. chem. Soc. *86*, 2527 (1964).

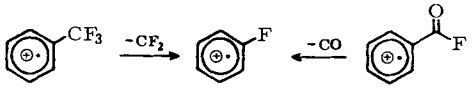
work [18] suggests that the $m/e = 105$ peak probably originates from benzophenone *(172)* present as impurity in the oxime sample used.

The more mechanistically feasible claim is also made [105] that pinacol *(173)* (and related 1,2-diols) may suffer an electron impact induced pinacol rearrangement. Thus peaks at M − 18, $m/e = 85$ (1.6 % Σ_{40}), $m/e = 57$ (2.5 %), and $m/e = 43$ (0.8 %) are observed in the spectrum of pinacol *(173)*, but apparently no precise mass determinations have been carried out.



(173) *(138)*

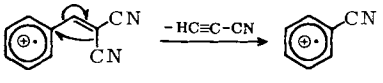
Migration of fluorine accompanied by skeletal rearrangement gives rise to major peaks in the mass spectra of perfluoroxylenes [106], trifluoromethyl substituted benzenes [107] [*e.g.*, *(174)*], and aroyl fluorides [107] [*e.g.*, *(175)*]. The enormous difference in



(174) *(175)*

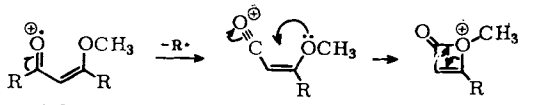
ease of elimination of CF_2 compared with CH_2 from organic compounds under electron impact has already been noted [108]. This trend is further illustrated by the rearrangement with CF_2 elimination which is suffered [109] by simple perfluorohydrocarbons.

A large peak (25 % relative abundance) in the spectrum of benzylidene malononitrile *(176)* at $m/e = 103$ has been attributed [110], on the basis of precise mass measurements, to the formal loss of the elements of cyanoacetylene from the molecular ion, accompanied by migration of a nitrile group.



(176) m/e = 103

The base peak for a series of acyclic 1,3-diketone enol ethers *(177)* occurs [111] at $m/e = 59$, and is due to an ion of composition $C_2H_3O_2^{\oplus}$. Such a species requires formal migration of the methoxy function, and the presence of appropriate metastable peaks betray its origin as M − R fragments. The contribution of $C_2H_3O_2^{\oplus}$ to the total ion current decreases as the size of R increases.

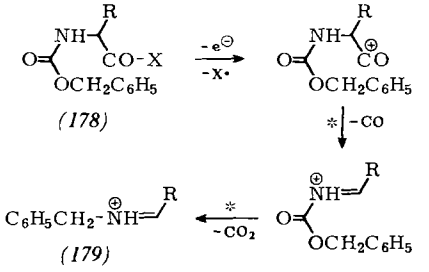


(177)

R	Σ_{30}
CH_3	11.1
C_2H_5	4.5
n-C_3H_7	3.6
n-C_4H_9	1.5

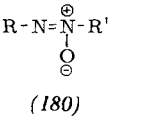
$CH_3O\overset{\oplus}{C}O$
m/e = 59

The occurrence of benzyl migrations in the mass spectra of benzyloxycarbonyl derivatives of certain amino-acid esters has been reported [112]. Important peaks (4–52 % relative abundance) were recorded for a series of mainly dipeptide methyl (X = CH_3), ethyl (X = C_2H_5), and phenylthio (X = C_6H_5S) esters, corresponding to rearrangement ions *(179)*. It seems very likely that the rearrangement step (loss of carbon dioxide) is closely related mechanistically to that occurring in ethyl carbamate derivatives [75,76].



(178) *(179)*

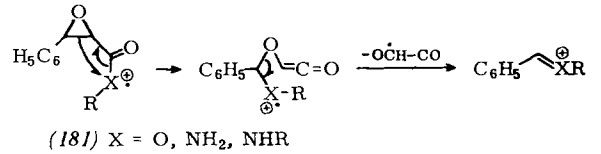
Extensive rearrangement in the molecular ion of a series of aromatic azoxy compounds *(180)* is indicated [113] by their proclivity to eliminate carbon monoxide followed by loss of nitrogen on electron impact. The rearranged ion in the case of *(180)* R = R′ = phenyl seems to be different from the molecular ion of *o*-hydroxyazobenzene, since this species expels nitrogen followed by carbon monoxide.



(180)

R = R′ = Phenyl
R = Phenyl, R′ = β-Naphthyl
R = β-Naphthyl, R′ = Phenyl
R = 2,4,6-Trimethylphenyl, R′ = Phenyl

An important rearrangement process, often generating the base peak of the spectrum, in glycidic esters and amides *(181)* has been noted [114], involving loss of C_2HO_2 from the molecular ion. As might be expected from the proposed mechanism, this rearrangement was not encountered [115] in 1,2-epoxyketones [*e.g.*, *(181)* X–R = alkyl).



(181) X = O, NH_2, NHR

[106] *J. R. Majer*, J. appl. Chem. *11*, 141 (1961).

[107] *J. R. Majer*, Symposium on "Newer Physical Methods in Structural Chemistry", Oxford 1966.

[108] Cf. [44], p. 330.

[109] *J. H. Beynon*: Mass Spectrometry and Its Applications to Organic Chemistry. Elsevier Publishing Co., Amsterdam 1960, p. 416.

[110] *D. H. Williams*, Symposium on "Newer Physical Methods in Structural Chemistry", Oxford 1966.

[111] *M. Vandewalle, N. Schamp*, and *M. Francque*, Bull. Soc. chim. Belge, in press.

[112] *R. T. Aplin, J. H. Jones*, and *B. Liberek*, Chem. Commun. *1966*, 794.

[113] *J. H. Bowie, R. G. Cooks*, and *G. E. Lewis*, Chem. Commun. *1967*, 284.

[114] *J. Baldas* and *Q. N. Porter*, Chem. Commun. *1966*, 571.

[115] *W. Reusch* and *C. Djerassi*, Tetrahedron, in press.

4. Summary

In view of the relatively high incidence of electron impact induced skeletal rearrangements recognized during the past year, it seems highly probable that many additional examples await discovery in the near future. All such instances will be of intrinsic mechanistic interest, irrespective of the probability of the process, but only the more abundant peaks will be of serious consequence to the interpretation of "element maps".

Elimination of stable, neutral species (*e.g.* CO, CO_2, SO_2, HCN, CH_2O, *etc.*) from a non-terminal position in aromatic or other unsaturated molecules presently provides the largest collection of reorganization processes. In many cases, the migrating group may be visualized as a nucleophilic species, moving preferentially to the most positive site available. Operation of the same rearrangement in the molecular ion of the corresponding saturated analogues is usually markedly reduced, or even absent. Prior cleavage, in order to develop a full positive charge, is often necessary to induce a subsequent group migration. The most effective migrating groups appear to be those which have little tendency to suffer fragmentation, such as methyl and phenyl.

From a consideration of trends already apparent, it seems likely that thermal, photochemical, and acid catalysed rearrangements will act as important guides in the design of electron impact induced parallels. To date, it is a fairly safe assertion that good fortune has been involved in the detection of most, if not all, recorded mass spectral skeletal rearrangements. Critical comparison of such processes with free-radical and carbonium ion chemistry is required, and one avenue which may prove to be profitable in this connection, presently under active investigation, involves the study of relative migratory aptitudes.

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Reactions with Molecular Oxygen

BY S. FALLAB [*]

Molecular oxygen is an important oxidizing agent both in industrial and in biological processes. In many of these processes, the O_2 molecule reacts preferentially with free radicals, which are frequently paramagnetic metal ions. Homogeneous systems of this type that are described in the literature are discussed, and an attempt is made to establish the factors that determine the course and mechanism of the reaction.

1. Introduction

According to its position in the electrochemical series, molecular oxygen is a powerful oxidizing agent. The calculated standard potential for the redox equilibrium (1) is +1.23 V [**]. However, reactions with molecular

$$O_2 + 4\,H^+ + 4e^- \rightarrow 2\,H_2O \qquad (1)$$

oxygen at room temperature generally proceed very slowly in the gas phase as well as in homogeneous solution. This is even more surprising in view of the fact that, in the ground state, the oxygen molecule possesses two unpaired electrons.

The stepwise course of the reduction (1) accounts in part for the slowness of reaction. The full redox potential is realized only when the oxidation can be carried out in a more or less synchronous four-electron step of the type that is assumed to play a part in enzymatic oxidations [1]. Such processes require a substrate with a specifically fixed steric position, and this is presumably possible only in a macromolecular environment.

If these conditions are not satisfied, the reduction of the oxygen molecule must take place in two-electron steps (2) and (3), or even in one-electron steps (4) to (7). Since the standard potential of reaction (2) is only +0.68 V [2], the O_2 molecule is a much weaker oxidizing agent when the structure of the substrate, or the medium, compels the oxidation to proceed in two-electron steps. The standard potentials assigned to the four one-electron steps (4) to (7) are −0.32, +1.68,

[*] Prof. Dr. S. Fallab
Institut für Anorganische Chemie der Universität Basel
Spitalstr. 51
Basel (Switzerland)

[**] The standard potentials of the following redox systems are of the same order of magnitude: Pb^{2+}/PbO_2: +1.46 V; Cl^-/Cl_2: +1.36 V; $Cr^{3+}/Cr_2O_7^{2-}$: +1.33 V; I_2/IO_3^-: +1.20 V; Br^-/Br_2: +1.07 V; VO^{2+}/VO_2^+: 1.00 V.

[1] *J. H. Wang* and *W. S. Brinigar*, Proc. nat. Acad. Sci. *46*, 958 (1960); *T. Nakamura*, Biochim. Biophysica Acta *42*, 499 (1960).

[2] *P. George*: Oxidases and Related Redox Systems. Wiley, New York 1965, p. 3.

$$O_2 + 2\,H^+ + 2\,e^- \rightarrow H_2O_2 \quad (2)$$

$$H_2O_2 + 2\,e^- + 2\,H^+ \rightarrow 2\,H_2O \quad (3)$$

$$O_2 + H^+ + e^- \rightarrow HO_2\cdot \quad (4)$$

$$HO_2\cdot + H^+ + e^- \rightarrow H_2O_2 \quad (5)$$

$$H_2O_2 + e^- \rightarrow OH\cdot + OH^- \quad (6)$$

$$OH\cdot + H^+ + e^- \rightarrow H_2O \quad (7)$$

+0.80, and 2.74 V respectively [2]. Thus the first step (4), which primarily determines the reactivity of the O_2 molecule, is thermodynamically very difficult in a mechanism divided into four steps. Consequently, before the energetically favorable later steps can take place, the energy threshold of the radical $HO_2\cdot$ must be crossed.

The unreactive nature is also partly due to the electronic structure of the molecule. The homonuclear diatomic structure leads to degeneracy of the molecular orbitals with π symmetry formed from the atomic orbitals $2p_x$ and $2p_y$ (z = molecular axis) [3]. Since the oxidizing action of the molecule is based on the tendency to complete the half filled antibonding orbitals π^*2p_x and π^*2p_y, the configuration of the transition state for such an electron transfer is fixed by the geometry of these orbitals, and the reactivity is restricted accordingly.

In a complete reduction of the O_2 molecule in accordance with equation (1), the O–O bond must be cleaved at some stage of the reaction. Since the energy required for the cleavage of the single bond is much lower in the peroxo group O_2^{2-} than in O_2, it may generally be assumed that the cleavage of the O–O bond takes place only after an electron transfer.

2. Oxidation Mechanisms

The autoxidation [4] of hydrated transition-metal ions is strongly dependent on the reaction medium. In a series of reactions of the type (8), the kinetics of which have been extensively studied, equation (8a) is valid at

$$4\,M^{\lambda+} + O_2 + 4\,H^+ \rightarrow 4\,M^{(\lambda+1)+} + 2\,H_2O \quad (8)$$

constant oxygen concentration. In weakly acidic solution, metal ions $M^{\lambda+}$ are hydrolysed to a greater or

$$d[M^{(\lambda+1)+}]/dt = k'[M^{\lambda+}]/[H^+] \quad (8a)$$

lesser degree in accordance with equation (8b). Replacement of $[M^{\lambda+}]$ in equation (8a) by the mass-action expression found from equation (8b) gives

$$M^{\lambda+} + H_2O \rightleftharpoons MOH^{(\lambda-1)+} + H^+ \quad (8b)$$

equation (8c). The apparent rate constant k'' now includes the hydrolysis constant of equation (8b), and

$$d[M^{(\lambda+1)+}]/dt = k''[MOH^{(\lambda+1)+}] \quad (8c)$$

it can be concluded from the empirical relationship (8a) that the actual reactive species is $MOH^{(\lambda-1)+}$, which is present in low concentrations.

This is true of the autoxidation of Fe^{2+} in weakly acidic solution [5], of U^{4+} in perchloric acid solution [6], of Ti^{3+} in hydrochloric acid solution [7], and of V^{3+} in perchloric acid

$$4\,MOH^{(\lambda-1)+} + O_2 + 4\,H^+ \rightarrow 4\,MOH^{\lambda+} + 2\,H_2O \quad (9)$$

solution [8]. The reaction kinetics found in all these cases correspond to a mechanism in which the first step, *i.e.* the reaction with the O_2 molecule itself (10), is rate-determining.

$$MOH^{(\lambda-1)+} + O_2 + H^+ \rightarrow MOH^{\lambda+} + HO_2\cdot \quad (10)$$

$$M^{\lambda+} + HO_2\cdot + H_2O \rightarrow MOH^{\lambda+} + H_2O_2 \quad (11)$$

$$M^{\lambda+} + H_2O_2 \rightarrow MOH^{\lambda+} + OH^- + OH\cdot \quad (12)$$

$$M^{\lambda+} + OH\cdot \rightarrow MOH^{\lambda+} \quad (13)$$

In any series of reaction steps, the rate of formation of the end product is determined mainly by the slowest step. Steps (11) to (13), which are reactions with H_2O_2 and with the reactive radicals $HO_2\cdot$ and $OH\cdot$, are relatively fast, and so influence the experimental kinetics only in that the concentration of $M^{\lambda+}$ is decreased fourfold per unit of time.

The scheme (10) to (13), which was first proposed by *Haber* and *Weiss* [9], provides a satisfactory explanation of the experimental findings. However, conclusive proof of the validity of this four-step mechanism for the reduction of O_2 is not yet available.

The results of kinetic studies on the autoxidation of Fe^{2+} and Pu^{3+} in strongly acidic solution suggest other reaction mechanisms. Under conditions that eliminate the formation of $FeOH^+$ or $PuOH^{2+}$, oxidation can evidently proceed by an alternative path (*via* a relative energy minimum). In addition to the linear dependence on the O_2 concentration exhibited by all the systems mentioned above, the reaction rate also depends on the square of the metal ion concentration [equations (14) and (15)]. *George* interprets this [10] as evidence

$$-d[Fe^{2+}]/dt = k[Fe^{2+}]^2[O_2] \quad (14)$$

$$-d[Pu^{3+}]/dt = k[Pu^{3+}]^2[O_2] \quad (15)$$

$$Fe^{2+} + O_2 \rightleftharpoons Fe^{II}O_2^{2+} \quad (16)$$

$$Fe^{II}O_2^{2+} + Fe^{2+} \rightarrow Fe^{III}O_2^{+} + Fe^{3+} \quad (17)$$

$$Fe^{III}O_2^{+} + 2\,H^+ \rightarrow Fe^{3+} + H_2O_2 \quad (18)$$

for the rate-determining reaction (17), which is preceded by the formation (16) of a presumably very unstable iron(II)-O_2 adduct. Reaction (17) leads first to electron transfer and formation of the iron(III)-peroxo

[3] *C. A. Coulson*: Valence. Oxford University Press, Oxford 1961, p. 71.

[4] Autoxidation is "spontaneous" oxidation by free oxygen at room temperature. Cf. *M. Traube*, "Über Aktivierung des Sauerstoffs", Ber. dtsch. chem. Ges. *15*, 659 (1882).

[5] *Th. Kaden*, *D. Walz*, and *S. Fallab*, Helv. chim. Acta *43*, 1639 (1960).

[6] *J. Halpern* and *J. G. Smith*, Canad. J. Chem. *34*, 1419 (1956).

[7] *H. A. Mackenzie* and *F. C. Tompkins*, Trans. Faraday Soc. *38*, 465 (1942).

[8] *J. B. Ramsey*, *R. Sugimoto*, and *H. J. DeVorkin*, J. Amer. chem. Soc. *63*, 3480 (1941).

[9] *F. Haber* and *J. Weiss*, Proc. Roy. Soc. (London) Ser. A *147*, 332 (1934).

[10] *P. George*, J. chem. Soc. (London) *1954*, 4349.

complex $Fe^{III}O_2^{2+}$, which then undergoes dissociation and protonation, to give H_2O_2 in accordance with equation (18). An analogous mechanism can be formulated for the oxidation $Pu^{3+} \rightharpoonup Pu^{4+}$ [11].

Thus in contrast to the Haber-Weiss mechanism (equations (10) to (13)) the reaction involves a two-electron step, which bypasses the energetically unfavorable step (4). This very plausible explanation is supported by information gained from autoxidation studies of V^{2+} and Cr^{2+}. In both cases it was possible to detect a binuclear oxidation product VOV^{4+} or $CrOCr^{4+}$, the formation of which is open to various interpretations, but which makes the Haber-Weiss mechanism appear unlikely.

According to *Swinehart* [12], the autoxidation begins with a two-electron step (19), which yields a vanadium(IV) species as an intermediate. VO^{2+} then reacts

$$V^{2+} + O_2 + H_2O \rightarrow VO^{2+} + H_2O_2 \quad (19)$$

$$V^{2+} + VO^{2+} \rightarrow VOV^{4+} \quad (20)$$

with unreacted V^{2+} to form VOV^{4+}, see equation (20). The formation of this binuclear product in accordance with equation (20) has been confirmed in an independent investigation [13]. VOV^{4+} absorbs at 425 nm, and can be unambiguously detected spectrometrically.

Thus the energetically unfavorable formation of the HO_2 radical is again avoided. A similar mechanism can be formulated for the autoxidation of Cr^{2+} [14]. However, the intermediate CrO^{2+} is much less stable than the corresponding vanadium compound. The reduction of the O_2 molecule (21) to (23) could conceivably take place in two successive two-electron steps, in which an adduct of O_2 with Cr^{2+}, formed in accordance with equation (21), reacts as shown in equation (22) with intermediate formation of a binuclear peroxo complex; this complex then undergoes homolytic decomposition in accordance with equation (23). ^{18}O-Tracer studies by *Gordon* and

$$Cr^{2+} + O_2 \rightleftharpoons Cr^{II}O_2^{2+} \quad (21)$$

$$Cr^{II}O_2^{2+} + Cr^{2+} \rightarrow Cr^{III}OOCr^{III4+} \quad (22)$$

$$Cr^{III}OOCr^{III4+} \rightarrow 2\,Cr^{IV}O^{2+} \quad (23)$$

Taube [15] have cast doubt on the Haber-Weiss mechanism proposed by *Halpern* and *Smith* [6] for the autoxidation of uranium(IV) salts. According to these studies, only one of the oxygen atoms in the final product UO_2^{2+} is derived from the O_2. On the other hand, when the reaction is complete, nearly all the labeled oxygen from the oxidizing agent O_2 is found in the bound form in UO_2^{2+}. This distribution would be incompatible with a mechanism (10) to (14) involving four one-electron steps. Thus two-electron steps are also more likely in this case: UOH^{3+} would react in the rate-determining step (24) to give a uranium(VI)-peroxo compound, which would then undergo a rapid secondary reaction with further UOH^{3+}.

$$UOH^{3+} + O_2 \rightarrow U(O_2)OH^{3+} \quad (24)$$

$$U(O_2)OH^{3+} + UOH^{3+} \rightarrow 2\,UO_2^{2+} + 2\,H^+ \quad (25)$$

Experiments with a chelate of vanadium(IV) with picolinic acid showed that partially hydrolysed metal ions are particularly readily autoxidized. The chelate bis(picolinato)oxovanadium(IV), VOZ_2 (Z = picolinate), which is formed in weakly acidic solution, is autoxidized only extremely slowly. In neutral solution, the chelate is hydrolysed to $V(OH)OZ_2^-$, with the hydroxo group *trans* to the vanadyl oxygen [16]. The autoxidation of this hexacoordinated species also proceeds very slowly, since the coordination sphere is fully occupied. Fast autoxidation takes place only on further hydrolysis to $V(OH)_2OZ^-$, with elimination of a picolinic acid ligand [17].

There now arises the question of the relationship between hydrolysis and autoxidizability. Since the more highly oxidized species of a redox pair $M^{\lambda+}/M^{(\lambda+1)+}$ will always be the more strongly hydrolysed, the redox potential must decrease with increasing OH^- concentration, *i.e.* $M^{\lambda+}$ apparently becomes a stronger reducing agent. Though the reactivity, which is determined by kinetic quantities, is in principle independent of the thermodynamic equilibrium position, various workers have found linear relationships between the free energy of activation $\Delta F^{\neq}$ and the total change in free energy ΔF° [18]. For a redox reaction of the type (8), the redox potential of $M^{\lambda+}/M^{(\lambda+1)+}$ is a relative measure of ΔF°. Under comparable conditions, the rates of autoxidation of V^{3+} and U^{4+} in acidic solution are 7×10^{-10} and 2.5×10^{-4} mole l^{-1} min^{-1} respectively. If the autoxidation reactions are assumed to proceed by the general mechanism (10) to (13), these experimental values give the rates of the bimolecular reaction steps (26) and (27). The standard potentials

$$VOH^{2+} + O_2 \rightarrow VO^{2+} + H^+ \quad (26)$$

$$UOH^{3+} + O_2 \xrightarrow{H_2O} UO_2^{2+} + H_2O_2 + H^+ \quad (27)$$

of the systems V^{3+}/VO^{2+} and U^{4+}/UO_2^{2+} (0.33 and 0.36 V, respectively) provide a relative measure of the equilibrium position for the redox steps (26) and (27). Comparison of the two pairs of figures shows immediately that the two potentials, which lie relatively close together, do not explain the enormous difference in the rates of reaction [19].

[11] *F. B. Baker* and *T. W. Newton*, J. physic. Chem. *60*, 1417 (1956).

[12] *J. H. Swinehart*, Inorg. Chem. *4*, 1069 (1965).

[13] *T. W. Newton* and *F. B. Baker*, Inorg. Chem. *3*, 569 (1964).

[14] *M. Ardon* and *R. A. Plane*, J. Amer. chem. Soc. *81*, 3197 (1959).

[15] *G. Gordon* and *H. Taube*, Inorg. Chem. *1*, 69 (1962).

[16] *Th. Kaden* and *S. Fallab*, Chimia *20*, 51 (1966).

[17] *Th. Kaden* and *S. Fallab*, Chimia *19*, 176 (1965); *Th. Kaden*, Helv. chim. Acta *49*, 1915 (1966).

[18] *J. O. Edwards*: Inorganic Reaction Mechanism. Benjamin, New York 1964, p. 31.

[19] The hydrolysis constants of V^{3+} and U^{4+} that enter into the calculation have only a small effect on this comparison.

A second comparison of this type can be carried out for the systems Fe^{2+}/Fe^{3+} and Pu^{3+}/Pu^{4+}, which have the standard potentials $E^\circ = 0.77$ and 0.97 V respectively. The rate constants for the autoxidation [cf. equations (14) and (15)] measured under comparable conditions are 0.2 and 10^4 mole^{-1} l min^{-1} respectively; thus the autoxidation of the weaker reducing agent, Pu^{3+}, is 10^5 times as fast.

These two examples show that there is no parallelism between the reaction rate and the equilibrium position, and that the accelerating influence of the coordinately-bound hydroxo group must therefore be explained by specific kinetic factors.

The stereochemistry of reaction (26) is indicative of hydrogen transfer (Fig. 1a). This would readily explain

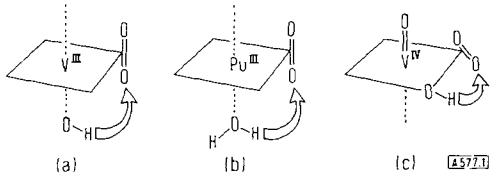


Fig. 1. Schematic representation of hydrogen-transfer mechanisms.

the influence of the hydroxo group on the reactivity toward O_2. The reaction of hydrated Pu^{3+} [11] could, in principle, also proceed by a hydrogen-transfer mechanism (Fig. 1b). The reaction step requiring the main part of the activation energy would then be the cleavage of an O–H bond, and since a monomolecular decomposition is strongly dependent on the vibration energy of the system, the reaction rates measured in H_2O and in D_2O should show a kinetic isotope effect. The theoretical ratio of the rate constants for the cleavage of O–H and O–D bonds at 25 °C is $k_H/k_D \approx 10$ [20]. Corresponding measurements on the autoxidation of $VO(OH)_2Z^-$ (Fig. 1c) gave $k_H/k_D = 0.92$. Values of between 1.2 and 1.3 were found for the autoxidation of Pu^{3+} [11]. Since the ratio k_H/k_D for both of these systems is only insignificantly different from 1, a hydrogen-transfer mechanism can be definitely ruled out.

Thus the reasonable and unrefuted mechanism for the general redox reaction (10) with molecular oxygen is electron transfer from the valence shell of the metal ion to the O_2 molecule. No definite information is available at present regarding the geometry of the transition state of such a reaction, but certain possibilities can be advanced on a purely theoretical basis. Thus from the electronic configuration of the O_2 molecule [3], it can be concluded that the reduction involves the transfer of an electron into an antibonding orbital having π symmetry. This is possible only if the corresponding atomic orbital of the electron donor has a matching symmetry.

Figure 2a shows a situation that favors the electron transfer [21]. The increase in the positive charge on the metal ion brought about by the redox reaction leads to

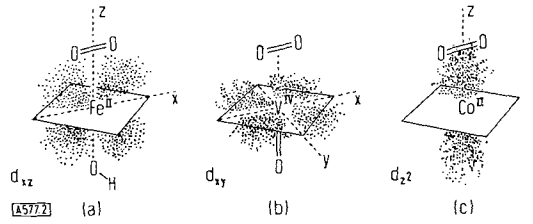


Fig. 2. Schematic representation of the orbitals of the central metal atom that might be used in electron-transfer mechanisms.

considerable reorganization of the coordination sphere: the lengths of the coordinate bonds become smaller, and the hydration sphere becomes larger. The electron transfer is very fast compared with these displacements of atomic nuclei, and after the activation energy for the reorganization has been supplied, an "energyless" electron transfer takes place from the high-spin d^6 configuration (from d_{xz} in Fig. 2a) to the O_2 molecule, which must also be favorably "prepared" by nuclear vibrations.

This hypothesis is confirmed by autoxidation experiments with VO^{2+} chelates [17]. According to calculations by *Ballhausen* [22], the one d electron of the vanadyl ion is localized in d_{xy} (Fig. 2b). Since bis(picolinato)oxovanadium(IV) must be assumed to have a square-pyramidal configuration [16], the attack by the O_2 molecule must take place exclusively in the *trans* position with respect to the vanadyl oxygen.

In the position shown in Figure 2b, the electron would have to enter a π^*2p_z or π^*2p_y antibonding orbital of the O_2 molecule. The maximum values of the function π^*2p_z lie in the xz plane, and coincide with a nodal plane of the d_{xy} orbital of vanadium. On the other hand, the overlap of d_{xy} with π^*2p_y should become important only when the O_2 molecule moves very close to the vanadium ion. An "energyless" electron transfer, such as occurs in the autoxidation of Fe^{3+} (Fig. 2a), is therefore impossible in this case.

The electron-transfer hypothesis is further confirmed by investigations on the influence of ligands on the rate of autoxidation. It was found in the autoxidation $Fe^{2+} \rightarrow Fe^{3+}$ that the transfer of the electron from Fe^{2+} to the O_2 molecule can be influenced by coordination of further ligands with Fe^{2+}, and that the nature of the coordinate linkage is evidently of decisive importance. Strongly basic ligand atoms, such as amino nitrogen, are σ bonded to the metal ion through their lone pair of electrons. σ-Donor properties predominate, so that the pair of bonding electrons that enters the position *trans* to the O_2 molecule in Figure 2a can directly influence only those d electrons of Fe^{2+} that have a high probability density along the z axis. However, it can be seen from Figure 2a that this is not the case for the d_{xz} electron. We have found [23] that N ligand atoms generally have little influence on the redox process, whereas O ligand atoms, particularly in the hydroxide and phenoxide anions, accelerate the electron transfer. In these cases the ligand atom has an additional non-bonding electron pair, which gives the base π-donor properties and exerts a direct repulsion on the d_{xz} electron of iron.

[20] *R. P. Bell*: The Proton in Chemistry. New York 1959, p. 184.

[21] The assumed arrangement of the O_2 molecule transverse to the z axis is justified below.

[22] *C. J. Ballhausen* and *H. B. Gray*, Inorg. Chem. *1*, 111 (1962).

[23] *Th. Kaden* and *S. Fallab*, Helv. chim. Acta *44*, 714 (1961); *Th. Kaden* and *S. Fallab*: Advances in the Chemistry of Coordination Compounds. MacMillan, New York 1961, p. 654; S. *Fallab*, Chimia *16*, 189 (1962).

The above observations on the medium-dependence and kinetics of autoxidation relate exclusively to metal ions with an incomplete d or f shell. The mode of reaction of these metal ions contrasts in some respects with the behavior of Sn^{2+} and Cu^{+} [24]. The pH-dependence observed in these cases shows that the hydroxo group does not act in the same way as in the reactions discussed earlier. The rate of the reaction is not significantly affected by the hydrogen ion concentration. An increase in the acidity of the solution is accompanied by a small increase in reaction rate, the latter being relatively high for Cu^{+} and Sn^{2+} when compared with the rates of oxidation of metal ions having partially filled d and f shells. The influence of ligands Z on the rate of the reaction (28) has been studied for Cu^{+}. In contrast to the findings for Fe^{2+}, reaction (28) is only

$$4\,ZCu^{+} + O_2 + 4\,H^{+} \rightarrow 4\,ZCu^{2+} + 2\,H_2O \qquad (28)$$

slightly dependent on the nature of the ligand [25]. Cu^{+} and Sn^{2+} are spherically symmetrical ions having the configurations d^{10} and $d^{10}s^2$ respectively, and whose reactivities are evidently little affected by coordinately bound groups.

A recent kinetic study of autoxidation in accordance with equation (28) has revealed some interesting peculiarities [25a]. Cu^{I} is used in the form of $Cu(CH_3CN)_4ClO_4$, and solutions containing O_2 at definite concentrations are added; the rate $d[O_2]/dt$ or $d[Cu^{2+}]/dt$ is measured as a function of the concentrations of Cu^{I}, O_2, and complexing agents Z with the aid of an electrochemical oxygen analyser and a "stopped-flow" spectrophotometer, which is used to follow absorption changes in the millisecond range. For solutions in which the Cu^{I} is almost entirely in the form of the complexes $Cu(NH_3)_2^{+}$ and $Cu(Im)_2^{+}$, and which contain an excess of the buffer ammonia or imidazole, the kinetic equation (28a) is obtained. The rate constant k is of the order of 10^4 l^2 mole^{-2} sec^{-1}, and is approximately three times as great for NH_3 as for imidazole. Moreover, since the rate is independent of the pH, a partially hydrolysed species can be ruled out as the reactive species. The linear relationship with the

$$d[Cu^{2+}]/dt = k[Cu(NH_3)_2^{+}][O_2][NH_3] \qquad (28a)$$

concentration of the buffer base must be interpreted as indicating that the actual electron transfer takes place within a species $Cu(NH_3)_3 \cdot O_2^{+}$ or $Cu(Im)_3 \cdot O_2^{+}$, in accordance with Scheme (28b).

$$Cu(NH_3)_2^{+} \underset{\leftarrow}{\overset{NH_3}{\rightleftharpoons}} Cu(NH_3)_3^{+} \underset{\leftarrow}{\overset{O_2}{\rightleftharpoons}} Cu(NH_3)_3O_2^{+} \overset{NH_3}{\rightarrow} Cu(NH_3)_4^{2+} + O_2^{-} \qquad (28b)$$

The linear complexes $Cu(NH_3)_2^{+}$ and $Cu(Im)_2^{+}$ are evidently extremely unreactive toward O_2, and the system becomes redox-active only after the introduction of a third ligand which causes a change in steric configuration.

Special mention should be made of the autoxidation $Co^{2+} \rightarrow Co^{3+}$. Owing to the high standard potential of the system Co^{2+}/Co^{3+}, autoxidation of Co^{2+} in acidic aqueous solution is thermodynamically impossible.

$$Co(H_2O)_6^{2+} \rightleftharpoons Co(H_2O)_6^{3+} + e^{-} \quad E^{\circ} = 1.8\ V\ [26] \qquad (29)$$

$$Co(NH_3)_5H_2O^{2+} \rightleftharpoons Co(NH_3)_5H_2O^{3+} + e^{-} \quad E^{\circ} = 0.33\ V\ [27] \qquad (30)$$

$$Co(NH_3)_6^{2+} \rightleftharpoons Co(NH_3)_6^{3+} + e^{-} \quad E^{\circ} = 0.1\ V\ [28] \qquad (31)$$

The hydrated Co^{3+} is such a strong oxidizing agent ($E^{\circ} = 1.8$ V) that it can oxidize H_2O to O_2. However, in coordination compounds, particularly with nitrogen as the ligand atom, the Co^{III} stage is stabilized to such an extent, *i.e.* the standard potential is lowered to such an extent (see equations (30) and (31)), that reaction (32) becomes thermodynamically possible in the presence of complex formers such as NH_3.

Nevertheless, reaction (32) does not take place spontaneously (as *e.g.* in the case of Fe^{2+}), but only when the medium satisfies certain conditions. The coordination compound to be formed must be formed beforehand in the Co^{II} stage. With amines as the complexing

$$4\,Co^{2+} + 6\,NH_3 + O_2 + 4\,H^{+} \rightarrow 4\,Co(NH_3)_6^{3+} + 2\,H_2O \qquad (32)$$

agents, therefore, this is possible only at a relatively high pH; however, even in this basic medium, the rate of oxidation is very low. The activation step consists in a rearrangement of the starting complex, *i.e.* the electron transfer from Co^{2+} to the O_2 molecule can take place only when the Co^{II}-N bond lengths are reduced by nuclear vibrations to the length required for the final complex. Since all Co^{III}-amine complexes have the diamagnetic d^6 configuration, the rearrangement energy, and hence the activation energy, is relatively high [29]. Moreover, the rearrangement preceding the electron transfer imposes a charge distribution on the d^7 ion (Co^{II}) that corresponds to the low spin $d_\varepsilon^6 d_\gamma$ configuration. It follows that the electron undergoing transfer occupies a $d_{x^2-y^2}$ or d_{z^2} orbital in the initial state; this is again unfavorable to the electron transfer, on grounds of symmetry (cf. Fig. 2c).

These considerations are valid for an unperturbed octahedral ligand field. However, if the six coordination sites are not uniformly occupied by strong σ donors, the charge distribution in the starting complex undergoes a deformation that favors the electron transfer. Such a ligand effect has been observed in the autoxidation of 3-azapentylene-1,5-diaminecobalt(II) complex ions $Co^{II}Z^{\lambda+}$ [29], in which additional ligands having π-donor properties, such as PO_4^{3-}, $P_2O_7^{4-}$, and CO_3^{2-}, considerably favor the reaction with O_2.

[24] *H. Nord*, Acta chem. scand. *9*, 430 (1955); *G. W. Filson* and *J. H. Walton*, J. physic. Chem. *36*, 740 (1932).

[25] *L. Graf* and *S. Fallab*, Experientia *20*, 46 (1964).

[25a] *A. Zuberbühler*, Helv. chim. Acta *50*, 466 (1967).

[26] *A. A. Noyes* and *T. J. Deahl*, J. Amer. chem. Soc. *59*, 1337 (1937).

[27] *R. G. Yalman*, Inorg. Chem. *1*, 16 (1962).

[28] *K. L. Cheng*, Analyt. Chem. *30*, 1035 (1958).

[29] *B. Erdem* and *S. Fallab*, Chimia *19*, 463 (1965).

In this case the actual oxidation step (34) takes place in a binuclear complex, as is shown by the dependence of the reaction rate on the square of the cobalt concentration. The structure and composition of this oxygen complex, which is formed in accordance with equation (33), have also been established by numerous spectrophotometric investigations (see Section 3). It must be concluded from the reaction kinetics that a relatively stable cobalt(III)-peroxo complex is formed as a second intermediate. *Haim* and *Wilmarth* found a similar course for the autoxidation of $Co^{II}(CN)_5^{3-}$ [30].

$$2\,Co^{II}Z^{\lambda+} + O_2 \rightleftharpoons ZCo^{II}O_2Co^{II}Z^{2\lambda+} \quad (33)$$

$$ZCo^{II}O_2Co^{II}Z^{2\lambda+} \rightleftharpoons ZCo^{III}\text{–}O\text{–}O\text{–}Co^{III}Z^{2\lambda+} \xrightarrow{2H^+} 2\,Co^{III}Z^{(\lambda+1)+} + H_2O_2 \quad (34)$$

An unambiguous mechanistic interpretation of the autoxidation of organic substances is generally difficult [31], and a uniform reaction course can be observed only in exceptional cases, since the substance being oxidized generally offers several possible points of attack.

The behavior of most organic substances toward O_2 is similar in two respects: 1) the rate of oxidation increases as the reaction proceeds; 2) the course, yield, and rate are very sensitive to impurities, particularly traces of metals [32]. This behavior is typical of free-radical chain-reactions. The following reaction scheme is generally accepted for the autoxidation of hydrocarbons, alcohols, or aldehydes (RH)· Since a direct reaction (35) with O_2 is very improbable, a radical X· must be assumed, which may be produced by radiation or by added peroxide. X· reacts with RH in accordance with

$$RH + O_2 \rightarrow R\cdot + HO_2\cdot \quad (35)$$

$$X\cdot + RH \rightarrow R\cdot + XH \quad (36)$$

equation (36), with homolysis of the weakest C–H bond, and so initiates the chain reaction indicated in equations (37) and (38).

$$R\cdot + O_2 \rightarrow RO_2\cdot \quad (37)$$

$$RO_2\cdot + RH \rightarrow ROOH + R\cdot \quad (38)$$

The radical RO_2· and the peroxide ROOH can react further in various ways. For example, if RH is a secondary alcohol [33], RO_2· gives the corresponding ketone and HO_2·, which then reacts with RH to form H_2O_2 and another radical R·. The peroxide formed in accordance with equation (38) may decompose into new radicals [eq. (39)], which can then help to propagate the radical chain. The rate is determined mainly by the reaction leading to the radicals X·, *i.e.* the reaction that initiates the autoxidation. The rates of reactions (38) and (39), which provide new radicals, are also important. Thus if this general scheme is valid, the reactivity of the O_2 molecule itself is only of minor importance to the oxidation kinetics, since the direct attack (35) of O_2 on RH is so slow that it may be ignored [34], whereas the free-radical reaction (37) is extremely fast.

$$ROOH \rightarrow RO\cdot + OH\cdot \quad (39)$$

3. The Formation of Stable and Unstable O_2 Adducts

In the autoxidations described above, it is often assumed that the actual electron transfer is preceded by the reversible formation of an O_2 adduct. In most cases there is no direct evidence [36] for the existence of such adducts, which are not transition states, but true intermediates with a (relative) minimum in the energy-reaction coordinate diagram [35].

Thus there is only uncertain kinetic evidence of the occurrence of the species $Fe(OH)\cdot O_2^+$ (Fig. 1a) as an intermediate in the autoxidation in weakly acidic solution [cf. reaction (16)] [23]. Calculation of the activation energy from the temperature-dependence of the rate of reaction gives a surprisingly low value of about 5 to 6 kcal/mole. If one assumes a normal frequency factor of 10^{11} l mole^{-1} sec^{-1} [37], this gives an activation entropy of about -30 cal deg^{-1} mole^{-1}. This strongly negative activation entropy is not very plausible for a bimolecular reaction in which one of the reactants is uncharged [38]. The kinetic parameters are more in agreement with the intramolecular electron transfer (40) as the rate-determining step, and so indicate that the oxidation is preceded by the reversible formation of $Fe(OH)\cdot O_2^+$.

$$Fe(OH)O_2^+ \rightarrow FeOH^{2+} + O_2^- \quad (40)$$

The reversible formation of an O_2 adduct is also postulated for the autoxidation of NO. *Bodenstein* had already observed that the rate of oxidation depends on the square of the nitric oxide concentration, and had explained this observation by a two-step mechanism as shown in equations (41) and (42) [39]. This mechanism has been confirmed by more recent investigations [40]. The reversibly formed, unstable intermediate

$$NO + O_2 \rightarrow ON\cdot O_2 \quad (41)$$

$$ON\cdot O_2 + NO \rightarrow 2\,NO_2 \quad (42)$$

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[30] *A. Haim* and *W. K. Wilmarth*, J. Amer. chem. Soc. *83*, 509 (1961). Cf. mechanism of the autoxidation of ethylenediaminetetraacetatocobalt(II) *R. G. Yalman*, J. physic. Chem. *65*, 556 (1961).

[31] *G. H. Twigg*, Chem. and Ind. *1962*, 4.

[32] The dependence on impurities is particularly noticeable in the autoxidation of acetaldehyde. The first observations on the aerobic oxidation of acetaldehyde were reported by *J. v. Liebig*, Liebigs Ann. Chem. *14*, 139 (1835). Doubts were later raised about whether very pure acetaldehyde is in fact autoxidizable: *H. Wieland* and *D. Richter*, Liebigs Ann. Chem. *495*, 284 (1932).

[33] In this case the free radical attacks the C atom carrying the hydroxyl group [31].

[34] In the autoxidation of n-decanal, *H. R. Cooper* and *H. W. Melville*, J. chem. Soc. (London) *1951*, 1994, obtained the bimolecular rate constant $k = 2.6 \times 10^{-7}$ mole l^{-1} sec^{-1} for equation (34). The activation energy was 15.6 kcal/mole.

[35] *S. Fallab*, Z. naturwiss. med. Grundlagenforsch. *1*, 366 (1963).

[36] In some cases it also follows from coordination-chemical considerations that the O_2 molecule must occupy a fixed position in the coordination sphere during the oxidation process.

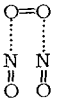
[37] *A. A. Frost* and *R. G. Pearson*: Kinetics and Mechanism. Wiley, New York 1953, p. 92.

[38] *W. C. E. Higginson, D. R. Rosseinsky, J. B. Stead*, and *A. G. Sykes*, Discuss. Faraday Soc. *29*, 49 (1960).

[39] *M. Bodenstein*, Z. physik. Chem. *100*, 88 (1922).

[40] *P. G. Ashmore, M. G. Burnett*, and *B. J. Tyler*, Trans. Faraday Soc. *58*, 685 (1962).

$ON{\cdot}O_2$ is not identical with a species NO_3 that exists in the "nitrate form". Certain conclusions about the geometry of the activated complex can be drawn on the basis of calculations carried out by *Gerschinowitz* and *Eyring*[41]. These authors found good agreement between the rate of autoxidation of NO as obtained by purely theoretical calculations and the experimental values obtained by *Bodenstein* when they assumed that the activation energy for the combination (41) of the free radicals is negligible and that the transition state of (42) has the structure *(42a)*. The N.....O distance (5 Å),



(42a)

which is large in relation to the other interatomic distances, rules out the nitrate form for the intermediate NO_3.

Analogous intermediates $Cl{\cdot}O_2$ and $SO_3{\cdot}O_2^-$ have been postulated for the photoactivated autoxidation of chlorine[42] and for the autoxidation of sulfite[43].

An adduct of O_2 with the radical R· also plays an important part in the mechanism of the autoxidation of organic compounds [see eq. (37)]. No detailed information is available concerning the structure and stability of RO_2· and the reversibility of its formation. Investigations by *Cooper* and *Melville*[34] on the autoxidation of n-decanal have shown that the further reactions of RO_2· are extremely fast.

The suppression of fluorescence by O_2, *e.g.* in substituted anthracenes and more highly condensed aromatic hydrocarbons, is due to the tendency of the O_2 molecule to combine with particles possessing unpaired electrons[44]. A photoactivated molecule X* reacts reversibly in the triplet state with O_2 (43); the radiation quantum is converted into heat in the O_2 complex. Reaction (43) also forms the basis of the photosensitization discussed in Section 4.

$$X^* + O_2 \rightarrow X{\cdot}O_2^* \qquad (43)$$

The combination of the O_2 molecule with paramagnetic particles or with molecules in the triplet state is readily understandable in view of the free-radical character of both reactants. Rather surprisingly, however, O_2 can evidently also combine with otherwise inert components to form labile associates. Thus *Mulliken* interprets the small UV absorptions observed in basic organic solvents containing O_2 as charge-transfer bands of O_2-solvent complexes[45]. Similarly, *Heidt*[46] found that O_2 in aqueous solution forms hydrates in accordance with equation (44). Though from the

$$H_2O + O_2 \rightleftharpoons H_2O{\cdot}O_2 \qquad (44)$$

kinetic point of view these are undoubtedly only very labile collision complexes, their lifetime is still several orders of magnitude longer than the contact time in an elastic collision, since excitation to a charge-transfer transition is possible.

However, many extremely stable oxygen complexes are also known. A very limited number of paramagnetic metal complexes $ZM^{\lambda+}$, which are known as "oxygen carriers"[47], react reversibly with O_2 [see equation (45)] with partial or complete spin saturation. $ZM{\cdot}O_2^{\lambda+}$ undergoes practically no further reactions, or at most reacts only very slowly, and decomposes completely into the starting components in a different medium. It has not so far been possible to establish definitely

$$ZM^{\lambda+} + O_2 \rightleftharpoons ZM{\cdot}O_2^{\lambda+} \qquad (45)$$

the factors responsible for such substantial displacement of the equilibrium (45) in favor of the adduct. The electronic configuration of the metal ion is evidently of decisive importance, since only a few metals exhibit this complex formation[47].

Fe^{II} and Co^{II} are outstanding oxygen carriers when used in conjunction with certain polydentate complexing agents. A spectrophotometric study has shown[48] that O_2 is reversibly bound by Fe^{II} as a chelate with phthalocyaninetetrasulfonic acid. Cobalt(II) bis(salicylaldehyde imine) chelates were the first synthetic oxygen carriers. Extensive studies by *M. Calvin* (cf.[47]) have shown that the molar ratio of metal to oxygen is $Co^{II}:O_2$ or $Co_2^{II}:O_2$, depending on the structure of the ligand. The reversible formation of O_2 can be observed in the solid as well as in solution.

A plane-tetragonal Ir^{1+} complex[49] that reversibly binds O_2[50] in benzene solution in accordance with equation (46) was discovered in 1963. The entry of the

$$IrCO(P(C_6H_5)_3)_2Cl + O_2 \rightarrow Ir(O_2)CO(P(C_6H_5)_3)_2Cl \qquad (46)$$

O_2 molecule into the coordination sphere leads to rearrangement of the complex to an approximately trigonal-bipyramidal structure (see Fig. 3)[51]. On the basis of X-ray analysis, it was possible to confirm

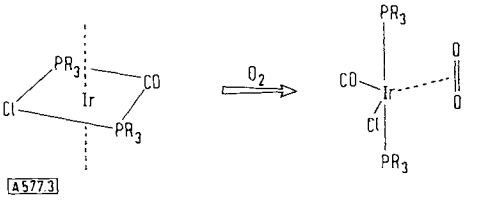


Fig. 3. Schematic steric representation of the formation of an iridium-oxygen complex.

[41] *H. Gerschinowitz* and *H. Eyring*, J. Amer. chem. Soc. *57*, 985 (1935).

[42] *G. Porter* and *F. J. Wright*, Discuss. Faraday Soc. *14*, 23 (1953).

[43] *W. A. Waters*, Rep. Progr. Chem. *1945*, 152.

[44] *C. Reid*: Excited States in Chemistry and Biology. Butterworths, London 1957, p. 100.

[45] *H. Tsubomura* and *R. S. Mulliken*, J. Amer. chem. Soc. *82*, 5966 (1960).

[46] *L. J. Heidt* and *L. Ekstrom*, J. Amer. chem. Soc. *79*, 1260, 5587 (1957).

[47] The biologically important oxygen carriers cannot be discussed here. The first synthetic system in which this reaction was detected was *N,N*-ethylene-bis(salicylideneiminato)cobalt(II): *P. Pfeiffer*, *E. Breith*, *E. Lubbe*, and *T. Tsumaki*, Liebigs Ann. Chem. *503*, 84 (1933). Cf. the review: *L. H. Vogt*, *H. M. Faigenbaum*, and *E. S. Wiberley*, Chem. Reviews *63*, 269 (1963).

[48] *S. Fallab*, Z. naturwiss. med. Grundlagenforsch. *2*, 220 (1965); *D. Vonderschmitt*, *K. Bernauer*, and *S. Fallab*, Helv. chim. Acta *48*, 951 (1965).

[49] The oxidation number 1+ is only of formal significance here, and gives no information about the true charge distribution.

[50] *L. Vaska*, Science (Washington) *140*, 809 (1963).

[51] *S. J. Placa* and *J. A. Ibers*, J. Amer. chem. Soc. *87*, 2581 (1965).

what had formerly been assumed [52], *i.e.* that the O_2 dumbbell lies transverse to the bond axis. As a result of the coordinate bonding, the distance between the O atoms in the O_2 molecule is increased from 1.21 to 1.30 Å; it may be concluded from this that a charge transfer from the metal to O_2 has taken place.

A striking feature of the iridium-oxygen complex is that the ligands, with the exception of Cl^-, belong to the class of readily polarizable "soft" Lewis bases. According to *Pearson* [53], CO and phosphines PR_3 are typical "soft", weak proton acceptors, which tend to form coordinate bonds with d-metal ions having highly occupied valence shells in a low oxidation state. Their "softness" is due to the ability to accept electrons in low unoccupied π-orbitals. The oxygen molecule, which *Jørgensen* [54] includes among the "non innocent ligands", is also "soft" owing to its π-acceptor properties.

As was shown by *Jørgensen* [55], a certain similarity in the nature of the ligands is of decisive importance to the stability of a coordination compound. Thus a complex containing only "soft" ligands will be stabilized by a "symbiotic" effect. These considerations are in excellent agreement with observations on the iridium-oxygen complex. The oxygen-carrier properties of the Fe^{II} and Co^{II} chelates are also plausible on this basis. The hydrated Fe^{2+} and Co^{2+} ions cannot bind measurable quantities of O_2. However, a macrocyclic unsaturated ligand such as porphyrin or phthalocyanine changes the coordinative properties of the metal ion to such an extent, *i.e.* apparently makes it so "soft", that O_2 can be bound in measurable quantities.

In the case of Co^{II}, the metal ion can be caused to bind O_2, not only by polydentate unsaturated complex formers such as bis(salicylaldehyde imine), but also by monodentate ligands such as CN^- or NH_3 [56]. *Haim* and *Wilmarth* [30] found that $Co(CN)_5^{3-}$ reacts with O_2 in accordance with equation (47) to form a binuclear complex. The binuclear O_2 complex formed from bis(histidinato)cobalt(II) [57] was obtained in the crystalline form by *Sano* and *Tanabe* [58].

$$2\,Co(CN)_5^{3-} + O_2 \rightleftharpoons (CN)_5CoO_2Co(CN)_5^{6-} \qquad (47)$$

Chelates of cobalt(II) with the aliphatic polyamines 3,6-diazaoctylene-1,8-diamine (DODA), 3-azapentylene-1,5-diamine (APDA), and ethylenediamine (EDA) react in the same way [59]. In aqueous solution and in the absence of oxygen, these amines form the normal chelates $Co(DODA)^{2+}$, $Co(APDA)^{2+}$, and $Co(EDA)_2^{2+}$. The corresponding complex equilibria can be readily followed by pH measurements, since the free amines are partially protonated up to pH = 9, and protons are liberated by chelation. The absorption bands of these particles are very weak ($\varepsilon < 10^2$). Air-saturated solutions of these systems, on the other hand, give strong absorption bands in the region 300 to 500 mμ ($\varepsilon > 10^3$). Like chelation in the absence of air, this reaction is reversible. The absorption bands disappear on addition of strong acids or on flushing with N_2, and reappear when a suitable change is made in the medium. On the basis of quantitative evaluation of the dependence of the absorptions on concentration and on the medium, the reaction must proceed in accordance with (48) and (48a). The ratio of bound oxygen to cobalt(II) chelate was determined by colorimetric titration of 10^{-4} M solutions of $Co(DODA)^{2+}$ and $Co(EDA)_2^{2+}$

$$2\,Co(DODA)^{2+} + O_2 \rightleftharpoons Co_2(DODA)_2{\cdot}O_2^{4+} \qquad (48)$$

$$2\,Co(EDA)_2^{2+} + O_2 \rightleftharpoons Co_2(EDA)_4{\cdot}O_2^{4+} \qquad (48a)$$

$$2\,Co(APDA)^{2+} + APDA + O_2 \rightleftharpoons Co_2(APDA)_3{\cdot}O_2^{4+} \qquad (48b)$$

with air-saturated H_2O. For the ligand APDA, spectrophotometric investigation gives the stoichiometric composition $Co_2(APDA)_3{\cdot}O_2^{4+}$ [see eq. (48b)].

The reactions are fast. When the solution is saturated with O_2, the formation of the oxygen adducts in accordance with equations (48), (48a), and (48b) is complete after one minute. After a longer period of time (several hours in the cases of DODA and EDA, and about 10 minutes in the case of APDA) the reactions are followed by autoxidation to give the corresponding cobalt(III) chelates as indicated in reaction (34). These chelates were identified by synthesis and spectrophotometric comparison [60].

The ability of Co^{II} to bind O_2 as shown in equation (48) depends greatly on the structure of the complex ligands. If the polyamine is replaced by aminopolycarboxylic acids, *e.g.* nitrilotriacetic acid, ethylenediaminetetraacetic acid, or ethylenediamine-*N*,*N*-diacetic acid, the ability to bind O_2 is completely lost. On the other hand, the tridentate complexing agent iminodiacetic acid (IDA) in conjunction with EDA permits the formation of a species $Co(IDA)(EDA){\cdot}O_2$.

It appears from these experiments that at least three N-ligand atoms must be present in the coordination compound if the binding of O_2 is to be possible. In conjunction with other bidentate ligands such as glycine, EDA, or oxalate, $Co(APDA)^{2+}$ can react with O_2 to give $Co(APDA)(GLY){\cdot}O_2^{+}$, $Co(APDA)(EDA){\cdot}O_2^{2+}$, and $Co(APDA)(C_2O_4){\cdot}O_2$. On the other hand, the binding of O_2 again becomes impossible when the six coordination sites of Co^{II} are fully occupied. Thus Co(APDA)(IDA) no longer gives an O_2 complex. Similarly, no fixation of oxygen as indicated in equation (48b) is observed with $Co(APDA)_2^{2+}$. These experiments confirm that the O_2 molecule is directly bonded to Co^{II} in the innermost coordination sphere, and that there is a pronounced tendency toward the formation of binuclear complexes (cf. Fig. 4a. – the representation of $Co_2(APDA)_2{\cdot}O_2^{4+}$ is to be regarded as schematic; nothing is known as yet about the spatial arrangement of the ligands in the coordination octahedron). Ligand exchange experiments show that in the binuclear species $Co_2(APDA)_3{\cdot}O_2^{4+}$, two

[52] On the basis of stereochemistry and bonding theory, *A. A. Vlcek* postulated a similar structure for binuclear O_2 complexes of cobalt: Trans. Faraday Soc. *56*, 1137 (1960).

[53] *R. G. Pearson*, J. Amer. chem. Soc. *85*, 3533 (1963).

[54] *C. K. Jørgensen*, Z. naturwiss. med. Grundlagenforsch. *2*, 248 (1965).

[55] *C. K. Jørgensen*, Inorg. Chem. *3*, 1201 (1964).

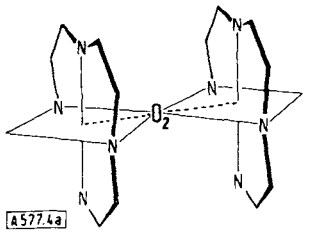
[56] *L. Michaelis*, Arch. Biochemistry *17*, 201 (1948).

[57] *L. Michaelis*, Arch. Biochemistry *14*, 17 (1942).

[58] *Y. Sano* and *H. Tanabe*, J. inorg. nuclear Chem. *25*, 11 (1963).

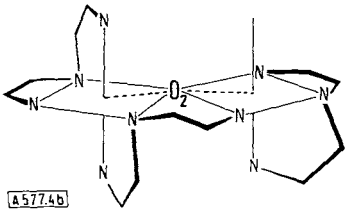
[59] *O. Bekâroglu* and *S. Fallab*, Helv. chim. Acta *46*, 2120 (1963).

[60] *S. Fallab*, unpublished.



A 577.4a

$Co(APDA)^{2+}$ units must be linked by O_2 as a bridge ligand, and that the third molecule of APDA, which is very much more labile than the other two is also bound in the form of a bridge. A conjectural structure is shown in Figure 4b.



A 577.4b

The spatial position of the O_2 dumbbell in these oxygen complexes is not yet known [61]. However, experiments with cobalt-polyamine chelates show that the O_2 adducts, which have been well characterized by spectrophotometry, are not identical with corresponding cobalt(III)-peroxo complexes. This supports the theoretical considerations of *Vlceck* [52], according to which π bonding predominates, so that the O_2 group is transverse to the bond axis. The oxygen complexes formed in accordance with equations (48), (48a), and (48b) are kinetically stable, *i.e.* in contrast to normal cobalt(II) chelates, decomposition and ligand exchange reactions are slow enough to be measured. This observation suggests a low spin (d^6) configuration of the cobalt, which would be compatible only with a charge distribution $Co^{3+}O_2^{2-}Co^{3+}$. On the basis of the above mentioned reversibility of the reactions with O_2, however, the assignment of the Co^{II} valence state seems more correct.

4. Activation of the Oxygen Molecule

A possible mode of reaction that has not yet been discussed involves the low excited singlet states of molecular oxygen $^1\Delta$ or $^1\Sigma$ with paired electron spins. [see equation (49)], which differ from the triplet ground

$$^3O_2 + h\nu \rightarrow {}^1O_2 \qquad (49)$$

state by 0.977 and 1.63 eV respectively [62]. *Wexler* was able to show that in the oxidation of unsaturated hydrocarbons by singlet oxygen, which may be produced in a discharge tube or by reaction of H_2O_2 with sodium hypochlorite, the same products are formed as in the photosensitized autoxidation [63].

Investigations carried out by *Schenk* [64] have shown that the autoxidation of olefins is accelerated in the presence of dyes such as eosin, fluorescein, or anthracene. Excitation of the dye Y and reaction with $^3O_2$ [equation (50)] leads to the formation of the biradical $\cdot YO_2\cdot$, which then reacts with a substrate RH in accordance with equation (51).

$$Y^* + {}^3O_2 \rightarrow \cdot YO_2\cdot \qquad (50)$$

According to *Schenck* [64], the existence of a biradical $\cdot YO_2\cdot$ is confirmed by the facts that *e.g.* in the case of anthracene, irradiation in the absence of O_2 leads simply to dimerization, whereas in the presence of O_2, a substance having the composition YO_2 is formed; this can only be interpreted as a reaction of photochemically formed free radicals. The reaction sequence

$$\cdot YO_2\cdot + RH \rightarrow RO_2\cdot + H\cdot + Y \qquad (51)$$

(50) to (51), from which the sensitizer is recovered unchanged, is further confirmed by kinetic studies. The kinetics of corresponding unsensitized photooxidations show the typical characteristics of a chain reaction and quantum yields $\gg 1$ [48].

Wexler's experiments [63] indicate a different mechanism, in which $\cdot YO_2\cdot$ decomposes by path (52), and the resulting singlet oxygen reacts with the substrate RH in accordance with equation (53); $\cdot YO_2\cdot$ is therefore regarded as an extremely short-lived charge-transfer complex, which serves to transfer the excitation energy to the O_2 molecule.

$$\cdot YO_2\cdot \rightarrow Y + {}^1O_2 \qquad (52)$$

$$^1O_2 + RH \rightarrow RO_2\cdot + H\cdot \qquad (53)$$

Purely chemical activation of the oxygen molecule is also conceivable. The polarization of the electron sheath of O_2 as a result of a more or less labile linkage with an activator molecule A may be sufficient to facilitate reaction with an autoxidizable substrate RH.

$$A + O_2 \rightleftharpoons A^{\delta+}O_2^{\delta-} \qquad (54)$$

$$A^{\delta+}O_2^{\delta-} + RH \rightarrow A + R\cdot + HO_2\cdot \qquad (55)$$

Equations (54) and (55) show possible steps in the catalysis of autoxidation discussed in Section 5. It is also conceivable, in principle, that a strongly electropositive activator A causes heterolysis (56) of the O_2 molecule into highly reactive atomic particles [65]; however, such a reaction course has never been observed in practice.

$$A^{\delta+}O_2^{\delta-} \rightarrow A + O^+ + O^- \qquad (56)$$

[61] The X-ray analysis of $[(NH_3)_5CoO_2Co(NH_3)_5](NO_3)_5$ published some time ago, according to which the O–O axis is oblique to the line joining the Co nuclei, provides no definite indication of this, since the cobalt in this case is in a different oxidation state. *W. P. Schaefer* and *R. E. Marsh*, J. Amer. chem. Soc. *88*, 178 (1966).

[62] *J. W. Linnett*, J. Amer. chem. Soc. *83*, 2643 (1961).

[63] *C. S. Foote*, *S. Wexler*, and *W. Ando*, Tetrahedron Letters *46*, 4111 (1965).

[64] *G. O. Schenck*, Naturwissenschaften *35*, 28 (1948); *G. O. Schenck* and *E. Koch*, Z. Elektrochem., Ber. Bunsenges. physik. Chem. *64*, 170 (1960).

[65] *A. Goudot*, C. R. hebd. Séances Acad. Sci. *251*, 722 (1960).

The autoxidation of unsaturated fatty acids in the presence of metal chelates is interpreted by *Uri*[66] as activation in the sense of equations (54) and (55). Co^{II} was particularly effective in conjunction with the macrocyclic complexing agents phthalocyanine and octamethyltetrazaporphin. In this case the activation results from the coordinative bonding of the O_2 molecule to the metal. *Kropf* postulated a similar activation mechanism for the autoxidation of cumene in nonpolar solvents in the presence of copper(II) phthalocyanine[67]. The activation energy is 6.7 kcal/mole lower than in the uncatalysed reaction, providing clear evidence in favor of mechanism (55). In studies on the mechanism of the autoxidation of *o*-phenylenediamine[68] in aqueous media, it was found (contrary to the results obtained by *Kropf*[67]) that copper(II) phthalocyaninetetrasulfonic acid is completely inactive as an autoxidation catalyst. This contradiction may be due to the fact that the *Kropf* activation mechanism is impossible in a polar medium[69].

The catalytic action of iron(II) salts in the hydroxylation of aromatic compounds in aerated solutions[70] could also be regarded as activation of oxygen in the widest sense. However, this effect is presumably due to reactions of the highly reactive intermediates H_2O_2 and OH· formed in the autoxidation of Fe^{2+} (cf. the Haber-Weiss mechanism equations (10) to (13)), since the reaction course and the oxidation products are substantially the same with the two systems Fe^{2+}/O_2 and Fe^{2+}/H_2O_2[71].

Hydroxylation with the system Fe^{2+}/O_2EDTA/ascorbic acid, which was investigated by *Udenfriend*, follows a different course[72]. With the aid of $^{18}O_2$, it could be shown that the oxygen of the hydroxyl group entering the aromatic system is derived mainly from the O_2 molecule. The mechanism (57)/(58) proposed by *Mason*[73] would correspond to true activation of O_2 in the sense of equation (54).

$$(EDTA)Fe^{II} + O_2 \rightleftharpoons (EDTA)Fe^{II}\cdot O_2 \quad (57)$$

$$(EDTA)Fe^{II}\cdot O_2 + ArH \rightarrow (EDTA)Fe^{IV}O + ArOH \quad (58)$$

The large number of reactive O_2 adducts formulated in Section 2 justifies the assumption that the relatively firmly bound O_2 molecule in the cobalt-polyamine chelates is also activated and capable of smooth reaction with oxidizable substrates. In particular it is to be expected that the binuclear O_2 adduct of 3-azapentylene-1,5-diamine-cobalt(II) (Fig. 4), in which "free" coordination sites (*i.e.* sites occupied by readily replaceable H_2O molecules) are still available, would be redox-active. Surprisingly, however, all attempts to promote reaction of the oxygen bound in this way have been unsuccessful[74]. No acceleration of autoxidation has been observed even with readily oxidizable substrates such as aromatic diamines and 4,4′-diamino-3,3′-dimethoxybiphenyl. It appears that the acceptor properties of the binuclearly bound O_2 molecule are in fact weaker than those of free oxygen. An activation mechanism in the sense of equation (54) would also be inconceivable on symmetry grounds (cf. Fig. 4).

5. Metal-Catalysed Autoxidation

The autoxidation of many organic substances can be catalysed by metal salts, the transition metals manganese, iron, cobalt, and copper as redox systems M^{2+}/M^{3+} or M^{+}/M^{2+} being particularly effective catalysts[75]. Whereas the mechanism of the uncatalysed autoxidations described above has been clarified in its broad outlines, there is still great uncertainty regarding the role of the metal ion.

The redox pair Co^{2+}/Co^{3+} can participate in various ways in the oxidation mechanism described in equations (35) to (39). Reaction with the peroxide formed in reaction (38) can lead in accordance with equations (59) and (60) to the accelerated formation of a further radical, with the result that the chain reaction is accelerated[76].

According to *Twigg*[31], the average chain length, which is defined as the number of O_2 molecules consumed per initial step (35), decreases with increasing

$$ROOH + Co^{2+} \rightarrow RO\cdot + OH^- + Co^{3+} \quad (59)$$

$$ROOH + Co^{3+} \rightarrow RO_2\cdot + H^+ + Co^{2+} \quad (60)$$

$$RH + Co^{3+} \rightarrow R\cdot + Co^{2+} + H^+ \quad (61)$$

metal ion concentration. The thermal decomposition of the hydroperoxide ROOH in accordance with equation (39) with formation of two free radicals is of decisive importance to the chain length, and the ROOH concentration is in fact lowered by reactions (59) and (60).

An important feature of the course of cobalt-catalysed autoxidation is that the induction period is considerably shorter than in the uncatalysed reaction[76]. The only possible explanation for this on the basis of the postulated catalysis mechanism is that the formation of the hydroperoxide ROOH that reacts with the catalyst is also accelerated, *e.g.* by the initial reaction (61). However, the overall oxidation could be appreciably accelerated by reaction (61) only if the reoxidation of Co^{2+} by O_2 were fast, and model experiments pro-

[66] *N. Uri*, Nature (London) *177*, 1177 (1956).

[67] *H. Kropf*, Liebigs Ann. Chem. *637*, 73, 86 (1960).

[68] *K. Wüthrich* and *S. Fallab*, Helv. chim. Acta *47*, 1440 (1964).

[69] Under certain circumstances, heterogeneous catalysis also plays a part here, since the non-sulfonated copper phthalocyanine is very sparingly soluble, and since the phthalocyanines tend to associate; cf. *K. Bernauer* and *S. Fallab*, Helv. chim. Acta *44*, 1287 (1961).

[70] *C. Nofre*, *A. Cier*, and *A. Lefier*, Bull. Soc. chim. France *1961*, 530.

[71] The reactions of the mixture Fe^{2+}/H_2O_2, which is known as "Fenton's reagent" have been described in detail: *J. H. Baxendale*, Advances Catalysis related Subjects *4*, 31 (1950); *W. C. Bray* and *M. H. Gorin*, J. Amer. chem. Soc. *54*, 2124 (1932).

[72] *B. B. Brodie*, *J. Axelrod*, *J. R. Cooper*, *L. Gandette*, *B. N. La Du*, *C. Mitoma*, and *S. Udenfriend*, Science (Washington) *121*, 603 (1955); *S. Udenfriend*, *C. T. Clark*, *J. Axelrod*, and *B. B. Brodie*, J. biol. Chemistry *208*, 731 (1954).

[73] *H. S. Mason*, Advances in Enzymol. *19*, 79 (1957).

[74] *S. Fallab*, unpublished.

[75] *A. J. Chalk* and *F. Smith*, Trans. Faraday Soc. *53*, 1214 (1957).

[76] *C. E. H. Bawn* and *J. B. Williamson*, Trans. Faraday Soc. *47*, 721, 735 (1951).

vide no evidence that this is so. It must therefore be admitted that the catalysis of autoxidation by metal ions is only incompletely explained by the mechanisms proposed so far.

The condition of fast reoxidation is satisfied in various Cu-catalysed autoxidations, and in these cases the reaction follows a very simple course described as a "two-stroke mechanism" [equations (62) and (63)][77].

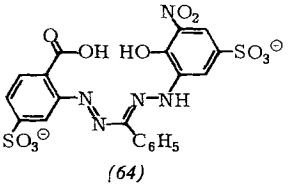
$$RH + Cu(Pyridine)^{2+} \rightarrow R\cdot + Cu(Pyridine)^{+} + H^{+} \quad (62)$$

$$4\,Cu(Pyridine)^{+} + O_2 + 4\,H^{+} \rightarrow 4\,Cu(Pyridine)^{2+} + 2\,H_2O \quad (63)$$

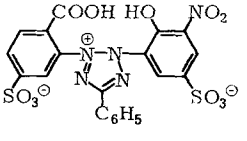
In the first step, which is rate-determining, the substrate undergoes a one-electron oxidation (62) with Cu^{2+}, and the copper ion is then rapidly reoxidized (63) to the bivalent state. The induction period is completely eliminated; however, this catalysis is limited by the relatively low redox potential of Cu^{+}/Cu^{2+}. As has been shown in the autoxidation of *o*-phenylenediamine, pyridines can displace the thermodynamic equilibrium (62) in favor of the reaction products. A similar mechanism may be involved in the oxidative coupling of phenols and amines in the presence of copper salts [78].

For our purposes, the most important feature of the "two-stroke mechanism" is the absence of any direct interaction between the substrate to be oxidized and the oxidizing agent O_2, the catalyst ion acting as an intermediary.

Another obvious and plausible catalysis mechanism is one in which the metal ion brings the two reactants together in a ternary complex. Such a mechanism has been detected in the autoxidation of the formazan dye 1-(2-carboxy-5-sulfophenyl)-5-(2-hydroxy-3-nitro-5-sulfophenyl)-3-phenylformazan *(64)* to form the corresponding tetrazolium salt *(64a)*. The dye (FORM) reacts with Fe^{2+} in accordance with equation (65) to give a stable, planar Fe^{II} chelate, which binds O_2 in accordance with equation (65a). The redox process



(64)



(64a)

$$Fe^{2+} + FORM \rightleftharpoons Fe^{II}(FORM) \quad (65)$$

$$Fe^{II}(FORM) + O_2 \rightleftharpoons Fe^{II}(FORM)\cdot O_2 \quad (65a)$$

then takes place within this ternary complex. A "two-stroke mechanism" is definitely not valid in this reaction, since the oxidation of the formazan dye by Fe^{3+} proceeds very much more slowly in the absence of oxygen.

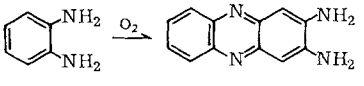
In this case the catalyst ion plays a more intimate role as an intermediary; on the one hand it fixes the reactants in a spatially favorable arrangement within its coordination sphere, and on the other it provides the redox components with a bridge for the electron transfer.

As expected, ternary complexes of this type can be detected only when the substrate to be oxidized exhibits complex-forming properties [80]. Thus it is unlikely that cobalt-substrate complexes occur in measurable concentrations in the Co-catalysed autoxidation of hydrocarbons, alcohols, and aldehydes. However, such a mechanism cannot be ruled out in advance, in view of the ability of Co^{II} particles to bind oxygen. The catalyst ion would then participate actively even in the first, radical-producing step in accordance with equation

$$Co\cdot O_2^{2+} + RH \rightarrow R\cdot + Co^{2+} + HO_2\cdot \quad (66)$$

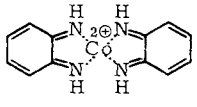
(66). This would explain the observed shortening of the induction period in the presence of cobalt salts. It has not yet been possible to decide whether a ternary complex $Co(O_2)RH^{2+}$ occurs as an intermediate in reaction (66); however, a transition state would necessarily have the composition $Co(O_2)RH^{2+}$.

Spectroscopic studies on the autoxidation of *o*-phenylenediamine to give 2,3-diaminophenazine *(67)* show that reactive intermediates of this nature must occur in Co^{2+}-catalysed autoxidations. In the absence of



(67)

catalyst ions, the reaction takes place in neutral dilute aqueous solution (approx. 10^{-3} M) within several hours; the course of the reaction, which was followed by measuring the increase in the quantity of 2,3-diaminophenazine (λ_{max} = 415 nm), is characterized by a long induction period. In the presence of cobalt(II) salts in an NH_3 buffer, the reaction rate increases by a factor of about 10. Moreover, under these conditions a violet intermediate Z *(68)* is formed, the composition of which has been determined by quantitative experiments in dimethylformamide with H_2O_2 as the oxidizing agent [74]. Each ligand molecule has undergone a two-equivalent oxidation. The spectroscopic data yield no information about the further course of the



(68)

reaction leading from the intermediate *(68)* to the end product 2,3-diaminophenazine, but the kinetics of the formation of the intermediate Z provide an insight into the mechanism of the initial reaction with O_2. Equation (69) describes the dependence of the reaction rate

$$d[Z]/dt = k[Co^{2+}][o\text{-PHEN}][O_2] \quad (69)$$

[77] *K. Wüthrich* and *S. Fallab*, Helv. chim. Acta *47*, 1609 (1964).

[78] *E. Ochiai*, Tetrahedron *20*, 1831 (1964); *Y. Ogata* and *T. Movimoto*, *ibid. 21*, 2791 (1965).

[79] *K. Trefzer* and *S. Fallab*, Helv. chim. Acta *48*, 945 (1965).

[80] Cf. the mechanism of the Fe^{2+}-catalysed autoxidation of 1-hydrazinophthalazine: *D. Walz* and *S. Fallab*, Helv. chim. Acta *44*, 13 (1961).

d[Z]/dt on the concentration for reaction solutions containing a large excess of *o*-phenylenediamine (*o*-PHEN). The rate d[Z]/dt is also strongly dependent on the medium. The autoxidation is almost completely suppressed in phosphate buffer. On the other hand, if imidazole is added to NH_3 buffer, the oxidation exhibits significant further acceleration. In conjunction with the studies on cobalt(II)-oxygen complexes described in Section 4, these observations lead to the assumption that the first step consists in the reversible bonding of O_2 to the catalyst ion [see equation (70)]. Since the irreversible oxidation to the cobalt(III) stage (71) is very slow, the *o*-phenylenediamine cannot be oxidized by an initially formed cobalt(III) particle; on the contrary, a ternary complex must be formed in accordance with equation (72), the rate-determining redox step then taking place intramolecularly. Ligands L containing nitrogen displace the equilibrium to the right,

$$CoL_x^{2+} + O_2 \rightleftharpoons CoL_x \cdot O_2^{2+} \quad (70)$$

$$CoL_x \cdot O_2^{2+} \rightarrow CoL_x^{3+} + O_2^- \quad (71)$$

$$Co(o\text{-PHEN})L_x^{2+} + O_2 \rightleftharpoons Co(o\text{-PHEN})L_x \cdot O_2^{2+} \quad (72)$$

and this accounts for the specific effects of the buffer bases. The intramolecular redox step can, in principle, be based on a hydrogen-transfer or an electron-transfer mechanism. In the latter case the electron would have to be transferred to the O_2 *via* the coordinated amino group and *via* the d-metal ion. However, all the orbitals that the coordinately bound N atom can make available for the transport of electrons have bonding character and are fully occupied. The abstraction of a bonding electron from the amino group is energetically unfavorable, and a hydrogen-transfer mechanism (Fig. 5) is therefore more probable.

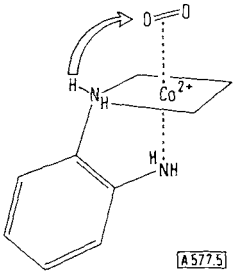


Fig. 5. Rate-determining step in the cobalt-catalysed autoxidation of *o*-phenylenediamine.

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Separation of the Isotopes of Uranium by the Separation Nozzle Process

BY E. W. BECKER, K. BIER, W. BIER, R. SCHÜTTE, AND D. SEIDEL [*]

The separation nozzle process is based on the partial spatial separation of components of different mass in an expanding supersonic jet stream. The process is of especial interest for the separation of uranium isotopes. Details of a systematic experimental determination of the most favorable operating conditions for such a separation are given and the construction and testing of a closed circulation system, the basic unit of a ten membered pilot cascade separator for uranium isotope separation, is described. The optimum values of the specific cost factors obtained experimentally for the separation nozzle process are compared with the corresponding values estimated for the gaseous diffusion process.

Introduction

The light isotope of uranium, ^{235}U, required for the production of nuclear power, is currently enriched on a large scale by means of the gaseous diffusion process [1]. This method is based on the difference between the velocities with which $^{235}UF_6$ and $^{238}UF_6$ molecules migrate through porous membranes. It is also possible to separate the isotopes of uranium with gas centrifuges [2]; however, as far as is known, no such production facilities have as yet been constructed.

In the course of the past few years we have developed a process for the separation of the isotopes of uranium which avoids both the problems of the delicate membranes required by the diffusion process and also

[*] Prof. Dr. E.W. Becker, Dr. W. Bier, Dr. R. Schütte, and Dr. D. Seidel
Institut für Kernverfahrenstechnik der Technischen Hochschule und der Kernforschungszentrum
75 Karlsruhe (Germany)
Prof. Dr. K. Bier
Thermodynamisches Institut der Technischen Hochschule
75 Karlsruhe (Germany)

[1] *E. W. Becker*, Chemie-Ing.-Techn. *29*, 365 (1957).
[2] *W. Groth*, Chemie-Ing.-Techn. *31*, 310 (1959).

those of the high mechanical stresses which occur in the centrifuge process [3–10]. This process is based on the partial spatial separation of the components of a gaseous mixture that takes place in an expanding supersonic jet. The separating effect of the jet may be explained qualitatively by the fact that the streamlines of an expanding jet are curved and, as in a centrifuge, the isotopic mixture is subjected to the action of a centrifugal acceleration, that is, to the pressure gradient which arises as a result of the centrifugal forces.

Figure 1a is a sketch of the arrangement which was used initially in the earlier experiments [3–5]. A convergent nozzle with either a circular or slit-shaped cross section was used in these experiments. A diaphragm, either conical or V-shaped, depending on the nozzle cross section, and having an aperture the same shape as that of the nozzle opening, was positioned directly in front of the nozzle. The diaphragm divided the jet emerging from the nozzle into two fractions, a core fraction and a peripheral fraction, which were then pumped off separately from the separating element. The peripheral gas fraction is enriched in the light component of the mixture when the streamlines are curved away from the axis of the jet. When a reversal in the curvature of the streamlines occurs, as is the case in the recompression region of an over-

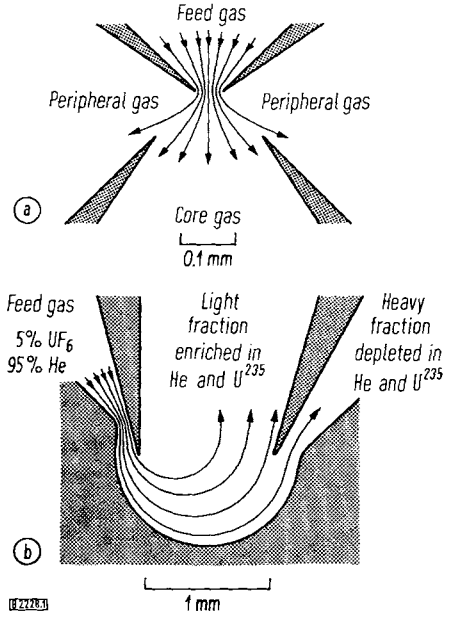


Fig. 1. Cross sections of the separation nozzle arrangements used in the earlier experiments (with a schematic representation of the streamlines):
a) a freely expanding jet from a circular or slit-shaped nozzle.
b) a UF_6 jet with helium as the auxiliary gas deflected by a curved wall.

expanded jet, the sign of the separation effect can also change [6].

Experiments with uranium hexafluoride as the process gas, using the arrangement pictured in Figure 1a, showed that the elementary separation effect for the nozzle process could, in fact, be somewhat larger than that for the gaseous diffusion process [5]. However, due to the higher expansion ratio required and to the appreciably lower absolute pressure which had to be used, the method, in this form, could only be economically competitive with the gaseous diffusion process in certain special cases.

A theoretical investigation of the separating processes taking place in supersonic jets [4, 7] indicated that the separation effect should increase if the angle through which the streamlines turn in the region between the nozzle and the diaphragm could be increased and if the Mach number of the jet could be increased.

An attempt to improve the economic potential of the process by increasing the angle through which the streamlines turn with the aid of a curved wall [8] met with little success. In the case of a mixture of argon isotopes alone, the mechanical deflection of the jet exhibited no clear economic advantages. This could be explained by the fact that, in this case, the increase in the angle of deflection of the streamlines which could be realized was relatively small, while, on the other hand, the decrease in the Mach number, caused by the entropy-producing effects associated with deflecting the jet, was relatively large.

An attempt to increase the Mach number of the isotopic mixture being separated by adding a light auxiliary gas in large molar excess was more successful [9]. The experimental arrangement used was that shown in Figure 1a. In the case of the argon isotopes, both the separation effect and the absolute pressure could be increased considerably, while the expansion ratio required could be decreased considerably. In spite of the necessity of compressing the light auxiliary gas along with the isotopic mixture, an appreciable improvement in the economic efficiency of the process was obtained.

However, when it came to the separation of the isotopes of uranium, the use of a light auxiliary gas with the experimental arrangement of Figure 1a appeared to be of questionable merit. Although the specific cost factors (defined below) which reflect the investment costs of the process could be reduced by more than a factor of four by the addition of 400 mole per cent of helium to the UF_6, the energy requirement increased by about the same factor [10]. This result could be explained by the fact that the large separation that occurred between the isotopic mixture and the light auxiliary gas caused a decrease in the angle of deflection of the streamlines of the isotopic mixture.

Thus, in the case of deflecting the jet with a curved wall, the advantage of the greater angle of deflection could only be obtained along with the accompanying disadvantage of having a smaller Mach number; while, in the case of adding a light auxiliary gas without deflecting the jet, the advantage of the larger

[3] *E. W. Becker, K. Bier*, and *H. Burghoff*, Z. Naturforschg. *10a*, 565 (1955).

[4] *E. W. Becker, W. Beyrich, K. Bier, H. Burghoff*, and *F. Zigan*, Z. Naturforschg. *12a*, 609 (1957).

[5] *E. W. Becker* and *R. Schütte*, Z. Naturforschg. *15a*, 336 (1960)

[6] *K. Bier*, Z. Naturforschg. *15a*, 714 (1960).

[7] *F. Zigan*, Z. Naturforschg. *17a*, 772 (1962).

[8] *E. W. Becker, H. Burghoff*, and *J. Gspann*, Z. Naturforschg. *16a*, 955 (1961).

[9] *E. W. Becker, K. Bier*, and *W. Bier*, Z. Naturforschg. *17a*, 778 (1962).

[10] *E. W. Becker, K. Bier, W. Bier*, and *R. Schütte*, Z. Naturforschg. *18a*, 246 (1963).

Mach number of the isotopic mixture was counteracted by the accompanying disadvantage of a smaller angle of deflection. It therefore appeared promising to combine the two types of operation. With the type of operation shown in Figure 1b, it was, in fact, possible to achieve a considerable decrease in the investment costs for separating the uranium isotopes without an appreciable increase in the operating costs [10]. Further development work was therefore concentrated on the method combining the use of a light auxiliary gas with the mechanical deflection of the jet.

In order to obtain criteria for the optimum shape of the separating system without performing time consuming separation experiments, Schlieren investigations were carried out using an experimental arrangement corresponding to that shown in Figure 1b [11]. It was assumed that a deflection of the jet as free as possible from disturbances would be the optimum for the separation process. Figure 2 shows examples of the formation of a jet, using nitrogen as a test gas, produced in one case by a convergent nozzle and in the other case by a curved Laval nozzle. It is evident from the figure that in the case of the convergent nozzle both shock waves and boundary layer separation occurred, while the curved Laval nozzle, on the other hand, produced an essentially disturbance-free, curved jet.

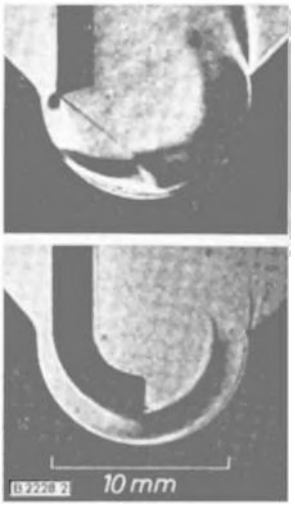


Fig. 2. Schlieren photographs of a nitrogen jet deflected through 180° produced by a convergent nozzle (above) and by a curved Laval nozzle (below). Inlet pressure, $p_0 = 258$ mm Hg; Expansion ratio, $p_0/p_M = 12.3$.

1. Determination of the Optimum Operating Conditions

On the basis of the Schlieren investigations and preliminary experiments with $He-UF_6$ mixtures, the separating elements shown in Figure 3 were selected for further experimentation. The two elements have essentially the same shape, but differ by a factor of two in the characteristic dimensions of the nozzle and of the deflecting surface (see Table 1).

[11] *K. Bier, V. Lippig*, and *K. Schlegel*, to be published.



Fig. 3. Side views of the separation nozzle arrangements, X and XIII, used in the experiments for evaluating the optimum operating conditions (see Table 1).

Table 1. The characteristic dimensions of the separating systems investigated. The effective length of the nozzle slit (perpendicular to the plane shown in Figure 3) was 10 mm for both systems.

System	Width of nozzle at throat, a (mm)	Width of nozzle at mouth (mm)	Radius of curvature of the deflecting surface (mm)
X	0.40	0.60	1.5
XIII	0.20	0.30	0.75

1.1. Apparatus and Method of Evaluation

The separation experiments for the determination of the most favorable operating conditions were carried out with the apparatus shown schematically in Figure 4.

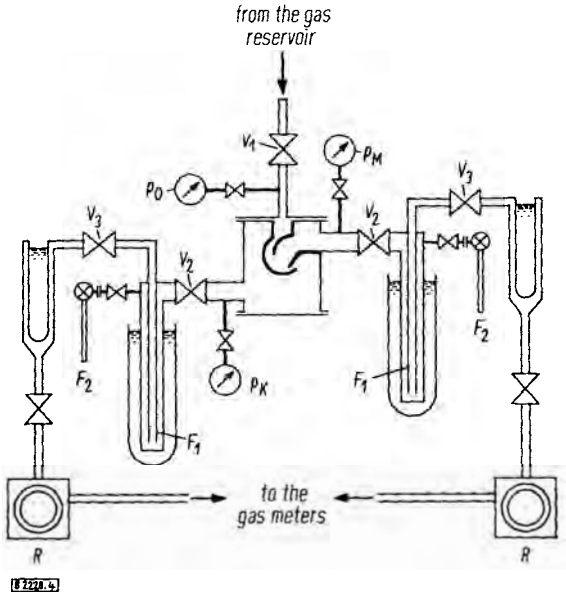


Fig. 4. Schematic diagram of the separation apparatus
F, cold traps; R, rotary pumps; V, valves.

The mixture of UF_6 and auxiliary gas which had been charged to the gas reservoir flowed through the regulating valve, V_1, to the nozzle of the separating system. The pressures, p_M and p_K, of the light and

heavy fractions, respectively, were adjusted to the desired values by means of the valves, V_2. Three diaphragm-type manometers were provided for the measurement of the pressures, p_0, p_M, and p_K. The UF_6 portions of the light and heavy gas fractions were precipitated out in the cold traps, F_1, which were cooled with liquid nitrogen. The cold traps could be isolated from the rotary pumps, R, by means of the valves, V_3.

The cut of the auxiliary gas (of the helium, for example), defined by

$$\theta_{He} = \frac{\text{flow rate of He in the light fraction}}{\text{flow rate of He in the feed gas}}, \quad (1)$$

was determined by means of gas meters installed on the high pressure side of the pumps. The cut of the UF_6 gas,

$$\theta_{UF_6} = \frac{\text{flow rate of } UF_6 \text{ in the light fraction}}{\text{flow rate of } UF_6 \text{ in the feed gas}}, \quad (2)$$

was determined by weighing the two UF_6 fractions which had been collected in the cold traps, F_1, and then reprecipitated in the pipettes, F_2.

The separation factor between the helium and the UF_6, A, was obtained from the cuts defined above by means of the relationship:

$$A = \theta_{He}(1-\theta_{UF_6})/\theta_{UF_6}(1-\theta_{He}) \quad (3)$$

The elementary separation effect for the uranium isotope separation, ε_A, is defined by

$$\varepsilon_A = [n_M(1-n_K)/n_K(1-n_M)]-1, \quad (4)$$

where n_M and n_K are the mole fractions of the light uranium isotope in the UF_6 isotopic mixture in the light and heavy fractions, respectively. The concentrations, n_M and n_K were determined mass spectrometrically [*].

1.2. Bases for the Optimization

In order to make practical use of the process, the elementary separation effect must be multiplied by connecting a large number of separating elements together to form a separation cascade. The elements should be connected in such a way that only streams with the same isotopic abundance ratio are mixed together in the cascade [12]. A separation of the auxiliary gas, accomplished, for example, by first enriching it with several stages of the separation nozzle process itself and then by freezing out the remaining UF_6, will be required only where the gas throughput changes, that is, only at the end of each square section in the cascade. The auxiliary gas which is separated at the top of a cascade section can be recycled and added to the UF_6 at the bottom of the cascade section.

Since a square cascade section consists, in practice, of many identical separating elements connected in series, the cost of separating the auxiliary gas, which needs to be done only at the top of the section, can be neglected in comparison with the other cascade costs. The economic efficiency of the process, using a light auxiliary gas, can therefore also be characterized by the previously defined "specific cost factors" [4,9].

Since, in the experimental work described in this report, the suction pressures, p_M and p_K, of the light and heavy fractions were always equal, the following simplified expressions could be used:

1) the specific ideal isothermal work of compression,

$$E_s = (1/\delta U)\, LRT \ln(p_0/p_M), \quad (5)$$

2) the specific suction volume,

$$V_s = (1/\delta U)\, LRT/p_M, \quad (6)$$

3) and the specific slit length,

$$l_s = (1/\delta U)\, l, \quad (7)$$

where δU is the separative power [12], given by

$$\delta U = \frac{L^*}{2}\varepsilon_A^2\, \theta_{UF_6}\, (1-\theta_{UF_6}), \quad (8)$$

L is the throughput of the gas mixture, L^* is the UF_6 throughput, and l is the slit length of the separating element.

The quantity, E_s, is a measure of the power requirement of the process; the quantity, V_s, is a measure of the investment costs of the compressors, piping, and valves; and the quantity, l_s, is a measure of the investment costs of the separating elements. From an investigation of the dependence of these three cost factors on the experimental parameters, the most favorable operating conditions for the process can be determined to within reasonable limits.

1.3. Experimental Results

The following parameters were varied during the experiments: the type of auxiliary gas, the mole fraction of the UF_6 in the mixture, the inlet pressure, the size of the separation system, the expansion ratio, and the distance between the knife edge and the curved wall (see Figure 1b or 3).

1.3.1. Type of Auxiliary Gas

Nitrogen, neon, and helium were tried as the auxiliary gas using separation system X (see Table 1). The UF_6 concentration was 10 mole per cent in these experiments. First, by varying the inlet pressure, p_0, with the expansion ratio, $p_0/p_M = 4$, held constant, the inlet

[*] Mass Spectrometer, Type 21–220 A, manufactured by CEC, Pasadena, California (U.S.A.).

[12] *K. Cohen*: The Theory of Isotope Separation as Applied to the Large Scale Production of U^{235}. McGraw-Hill Book Co., New York 1951.

pressure which yielded the minimum specific suction volume was determined for each of the three mixtures. The optimum values obtained for p_0 were: 16 mm Hg for the nitrogen-UF_6 mixture, 24 mm Hg for the neon-UF_6 mixture, and 32 mm Hg for the helium-UF_6 mixture. Next, the expansion ratio was varied with the inlet pressure held constant at its optimum value. From the results of the series of experiments presented in Figure 5, it can be seen that the smallest values of the specific cost factors were obtained with helium as the auxiliary gas. For this reason, only helium was used as the auxiliary gas in the experiments which followed [*].

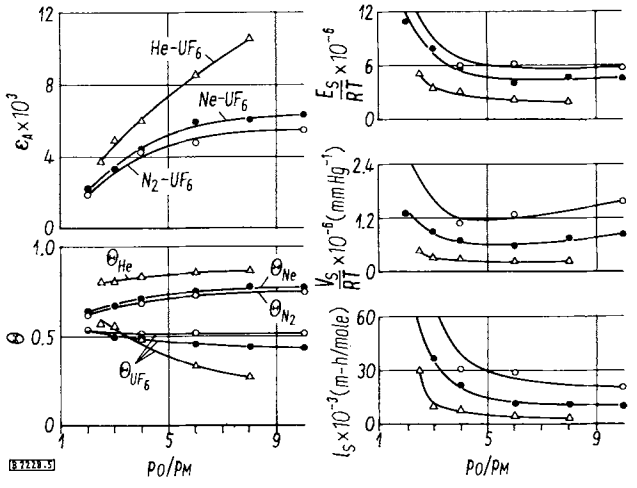


Fig. 5. The effect of different auxiliary gases on the specific cost factors. Inlet pressure: p_0 = 16 mm Hg for the N_2—UF_6 mixture, p_0 = 24 mm Hg for the Ne—UF_6 mixture, and p_0 = 32 mm Hg for the He—UF_6 mixture; Separation system X; Distance between the knife edge and the curved wall: 0.19 mm for the He—UF_6 mixture and 0.29 mm. for the N_2—UF_6 and the Ne—UF_6 mixtures; The UF_6 concentration was 10 mole per cent in all cases.

1.3.2. UF_6 Mole Fraction

Mixtures containing 3, 5, and 10 mole per cent UF_6 were investigated using separation system X. The optimum inlet pressure for each of the three mixtures was again determined first by varying the inlet pressure, p_0, with the expansion ratio, p_0/p_M = 4, held constant. The optimum values obtained for p_0 in these cases were: 60 mm Hg for the 3 % UF_6 mixture, 48 mm Hg for the 5 % UF_6 mixture, and 32 mm Hg for the 10 % UF_6 mixture. Next the expansion ratio was again varied with the inlet pressure held constant at its optimum value. It is evident from the results shown in Figure 6 that the specific suction volume, V_s, and the specific slit length, l_s, decrease monotonically with decreasing UF_6 content in the region investigated. However, as can be seen, the gain in going from the 5 % mixture to the 3 % mixture is rather slight. Therefore, since the 5 % mixture exhibits a somewhat smaller specific work of compression, E_s, the subsequent experiments were carried out using a 5 % UF_6 mixture.

[*] More favorable results can be obtained with hydrogen as the auxiliary gas. However, since H_2 and UF_6 can react chemically with each other, the advisability of using hydrogen as the auxiliary gas is questionable.

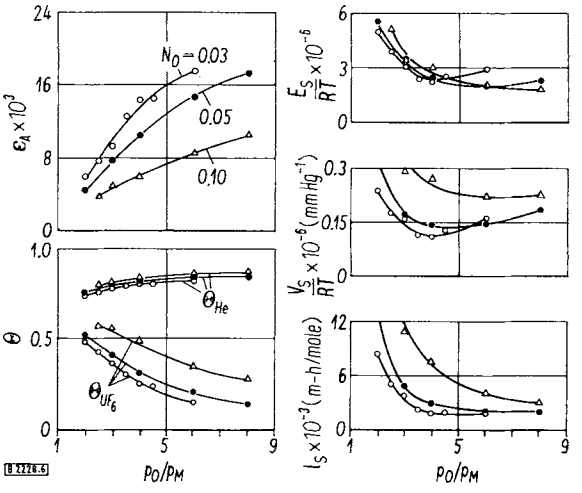


Fig. 6. The effect of the UF_6 mole fraction, N_0, on the specific cost factors.

Helium-UF_6 mixtures; Inlet pressure: p_0 = 60 mm Hg for the 3 % UF_6 mixture, p_0 = 48 mm Hg for the 5 % UF_6 mixture, and p_0 = 32 mm Hg for the 10 % UF_6 mixture; Separation system X; Distance between the knife edge and the curved wall: 0.19 mm.

1.3.3. Inlet Pressure and Size of the Separation System

The effect of the inlet pressure was investigated using separation systems X and XIII with the expansion ratio, p_0/p_M = 4, held constant. It can be seen from Figure 7, where the abscissa is the product of the inlet pressure, p_0, and the nozzle width, a, that both separation systems attain their optimum separating properties at about the same value of the p_0a product. The minimum values of E_s and l_s for both systems are

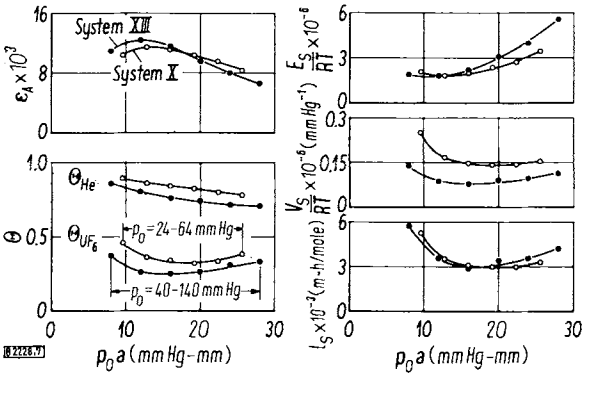


Fig. 7. Effect of the inlet pressure, p_0, and the size of the separation system on the specific cost factors.

Separation system X: width of nozzle at throat, a = 0.4 mm, distance between the knife edge and the curved wall = 0.19 mm.

Separation system XIII: width of nozzle at throat, a = 0.2 mm, distance between the knife edge and the curved wall = 0.11 mm.

Expansion ratio: p_0/p_M = 4; Helium-UF_6 mixture containing 5 mole % UF_6.

essentially the same. However, the minimum specific suction volume for the smaller system, which occurs at a higher value of p_0, is only about one half as large as it is for the larger system. For this reason further work was carried on with the smaller separation system.

1.3.4. Expansion Ratio

The effect of varying the expansion ratio with the inlet pressure held constant at the value which yielded the minimum specific suction volume, p_0 = 80 mm Hg, is shown in Figure 8. It can be seen that the minimum

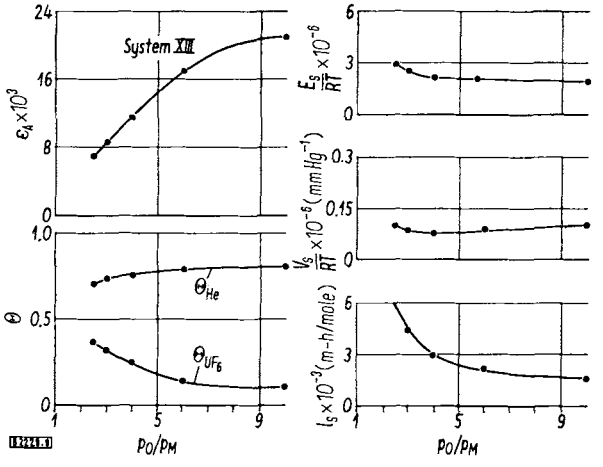


Fig. 8. The effect of the expansion ratio, p_0/p_M, on the specific cost factors.
Inlet pressure: p_0 = 80 mm Hg; Separation system XIII; Distance between the knife edge and the curved wall: 0.11 mm; Helium—UF_6 mixture containing 5 mole% UF_6.

values of E_S and V_S are obtained at an expansion ratio equal to about four. The specific slit length, l_S, continues to decrease with further increases in p_0/p_M. However, since the contribution which l_S makes to the cost of product seems to be of less importance than the contributions of the other two specific cost factors, the expansion ratio, $p_0/p_M \approx 4$, can be regarded as an optimum value.

1.3.5. Distance between the Knife Edge and the Curved Wall

It has already been mentioned that in an isotope separation cascade only streams with the same isotopic concentration should mix. In order for this condition to be satisfied, a different type of cascade connection is required for each different value of the UF_6 cut [1]. Economically satisfactory cascade arrangements are to be expected only when θ_{UF_6} can be expressed as the ratio of two small integers. The value, $\theta_{UF_6} = 1/2$, is a particularly good one as it is associated with the simplest type of cascade connection.

In the experiments described above, the minimum values of the specific cost factors were determined without regard to the θ_{UF_6} value which occurred. The cut, $\theta_{UF_6} = 1/2$, was obtained, if at all, only with relatively unsatisfactory values of the specific cost factors. In order to obtain the minimum values of the specific cost factors in conjunction with practical values of the cut, the effect of the expansion ratio was once again investigated, with the inlet pressure, p_0 = 80 mm Hg, again held constant, but with the distance between the knife edge and the curved wall a variable. The curves for constant values of θ_{UF_6}, shown in

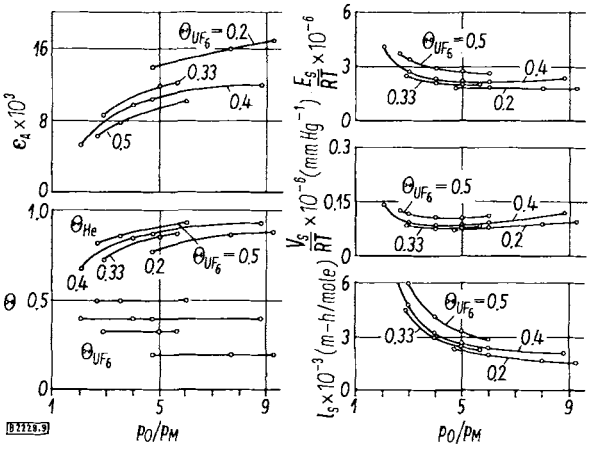


Fig. 9. The effect of the UF_6 cut, θ_{UF_6}, on the specific cost factors. The curves were obtained by varying the distance between the knife edge and the curved wall and interpolating between the measured results. Inlet pressure: p_0 = 80 mm Hg; Separation system XIII; Helium—UF_6 mixture containing 5 mole% UF_6.

Figure 9, were obtained by interpolating between the measured values. It can be seen that the smallest values of the specific cost factors were obtained at the smallest value of the cut which was investigated (θ_{UF_6} = 0.2). Between θ_{UF_6} = 0.2 and θ_{UF_6} = 0.33, the cost factors increase only slightly; on the other hand, between θ_{UF_6} = 0.33 and θ_{UF_6} = 0.5, they increase by a factor of about 1.4. Since the cost of piping and valves should be only slightly greater for a cascade operating with the cut, θ_{UF_6} = 0.33, than for a cascade operating with a cut of one half, the value, θ_{UF_6} = 0.33, will be assumed to be the optimum value of the cut for the separation nozzle process.

The optimum values of the specific cost factors resulting from the investigations described above and the associated operating conditions are compared in Table 2 with the corresponding, previously published values [10]. It can be seen that the specific work of compression and the specific suction volume have been reduced by almost a factor of two by the improvement of the separating element. The decrease in the optimum value of the compression ratio from 10 to 4 is also advantageous since it reduces the number of stages required in the compressors. The increase in the optimum suction pressure, $p_M = p_K$, from 12 to 20 mm Hg should also serve to reduce the relative pressure losses in the cascade piping.

Table 2. Comparison of the optimum values of the specific cost factors and associated operating conditions obtained with the improved separating system with the corresponding values from the previous investigation [10]. In both cases the UF_6 content of the He—UF_6 mixture was 5 mole per cent and the radius of the curved deflecting wall 0.75 mm. A temperature of 295 °K was assumed for the calculation of E_S and V_S.

	Present results	Previous results [10]
Specific work of compression, E_S (kWh/mole)	14.4×10^2	26.6×10^2
Specific suction volume, V_S (m³/mole)	1.40×10^6	2.61×10^6
Specific slit length, l_S (m-h/mole)	3.0×10^3	3.2×10^3
Compression ratio, p_0/p_M	4	10
Suction pressure, $p_M = p_K$ (mm Hg)	20	12
Elementary separation effect, ε_A	10.6×10^{-3}	10.6×10^{-3}
UF_6 cut, θ_{UF_6}	0.33	0.31

2. Testing the Process in a Closed Test Loop

In a separation cascade, the process gas containing the UF_6 which is expanded in one separating element must be recompressed by UF_6-resistant compressors before entering the neighboring elements. It must be demonstrated that such a cascade will be gas dynamically stable. Since a theoretical treatment of this problem is not sufficient for the design of large installations, a ten stage pilot plant is currently under construction in our institute. The construction and testing of the prototype unit for this pilot plant are described below.

2.1. Separating Element

Figure 10 shows a cross section of the separation nozzle system used and gives the nominal values of the pressures, p_0, p_M, and p_K, for these experiments. L moles per hour of a gaseous mixture consisting of 5 mole per

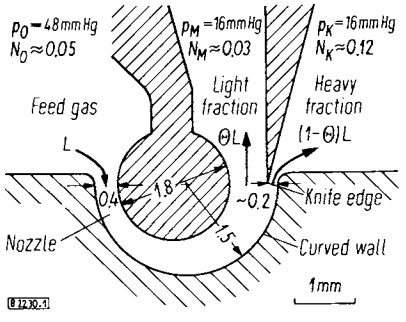


Fig. 10. Cross section of the separation nozzle system used in the closed test loop.

N_0, N_M, and N_K are the mole fractions of the UF_6 in the helium-UF_6 mixture used as the process gas; L is the molar flow rate of the process gas; Θ is the process gas cut.

cent UF_6 and 95 mole per cent helium were expanded through the curved Laval nozzle. The nozzle inlet pressure, p_0, was 48 mm Hg. The nozzle consisted of a curved wall with a radius of curvature, r = 1.5 mm, and a solid cylinder, eccentric to the wall, 1.8 mm in diameter. This model of the curved Laval nozzle has the advantage, compared with the nozzles investigated in detail in Section 1, of a simpler fabrication process for producing the longer separating systems. The width of the nozzle at its narrowest point, or throat, was 0.40 mm. The gas mixture expanded in the nozzle to the pressure, p_M = 16 mm Hg. These dimensions and operating conditions were fixed on the basis of the experiments described in Section 1 and from a consideration of the capability of the compressors which were available. The nozzle had a length of 100 mm in the direction perpendicular to the plane shown and was therefore ten times as long as the nozzles used in the earlier investigations.

The details of the assembly of the individual parts can be seen from Figure 11. In order to carry out all the testing desired, a scheme of construction was chosen which offered extensive possibilities for adjusting and changing all of the parameters affecting the geometry of the jet. The plate (b) bearing the nozzle cylinder (c) and the plate (f) terminating in

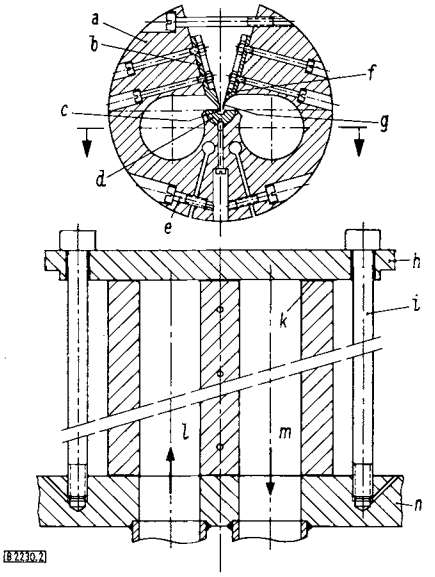


Fig. 11. Details of the separating element assembly. The separation nozzle system consisting of the curved wall (d), the cylinder (c), and the knife edge (g), are shown enlarged in Fig. 10.

(a) mounting block
(b) nozzle cylinder holder
(c) nozzle cylinder
(d) curved wall assembly
(e) adjusting screws
(f) knife edge holder
(g) knife edge
(h) blind flange
(i) bolts
(k) teflon film
(l) feed gas inlet
(m) heavy fraction outlet
(n) separation chamber cover

the knife edge were bolted securely to the machined surfaces of the brass cylinder (a). The plates (b) and (f) were fabricated from hardened tool steel (90 MnV8) and were, as was the brass cylinder (a), nickel-plated after the final machining. The positions of the nozzle cylinder (c) and of the knife edge (g) with respect to the curved wall (d) could be changed either by shifting the plates on their supporting surfaces or by extending the slotted brass cylinder (a) by means of the screws (e) provided for this purpose[*].

The separating element was bolted, by means of a blank flange (h) and the bolts (i), to the cover flange (n) of a cylindrical chamber, not shown, which surrounded the separating element. The sealing between the plane ground surfaces was accomplished with 0.1 mm thick teflon film (k). The light fraction passed between the nozzle plate (b) and the knife edge plate (f) into the chamber surrounding the element and was pumped off from there.

2.2. Compressor

In the construction of a plant utilizing the separation nozzle process, only compressors of the axial or centrifugal type ought to be considered. However, in making the choice of the type of compressor for the pilot plant, it had to be kept in mind that the plant should operate at the lowest practicable throughput in order to keep the cost of the installation low. A reasonable compromise was achieved with the use of Roots compressors. They can be constructed to have the desired, relatively small gas flow rate of about 100 m^3/h without much additional development work being required, and the dependence of their operating characteristics on the composition and physical prop-

[*] In practice, separating systems in which the critical dimensions are fixed at sufficiently close intervals along the length of the system would be used.

erties of the process gas is similar to that for centrifugal and axial compressors.

The Roots compressor used in these investigations has vacuum-tight shaft seals in the form of sealing chambers which are closed off by mechanical, radial-face seals at each end and through which flows a UF_6-resistant sealing oil. The compressor is provided with a built-in gas cooler. Additional internal cooling of the impellers is also possible. The compressor was developed in cooperation with the firm, E. Leybolds Nachfolger, Köln-Bayental, from the commercial Roots compressors designated "Ruvac E 126" [*]. All special elements in the construction were tested in our institute under process conditions and brought step by step to their final form.

The welded compressor housing is closed off on both sides by two face plates which contain four individual bearing assemblies which support the two impellers of the compressor. In each of the four bearing assemblies are a pair of the radial-face seals. They form four sealing chambers through which flows a sealing agent (KEL-F oil) which is maintained at a pressure higher than the surroundings. A water-cooled, spiral-tube cooler is built into the square-cornered gas outlet. If needed, the sealing oil can be conducted from one face plate to the other through the cooling chambers of the impellers to provide additional cooling. The compressor is driven by a three phase electric motor which turns at 2900 rpm. At this speed the compressor has a geometrical suction volume of 380 m^3/h.

The impellers are of stainless steel No. 4571. The face plates, the welded compressor housing, and all of the other parts which come into contact with the process gas were fabricated from stainless steel No. 4541. The sealing between the metal parts exposed to the process gas was accomplished with O-rings of Viton, a fluoroelastomer, which were inserted into slots provided for that purpose.

The radial-face seals have a layer of Stellite on their sliding surfaces. During the life testing of the compressor, values between 0.5 and 1.8 cm^3/d per compressor were obtained for the amount of sealing oil entering the process gas space. This inleakage is drawn off into a water-cooled oil collector. A vapor seal is used to prevent entry of the sealing oil vapor into the process gas region of the compressor.

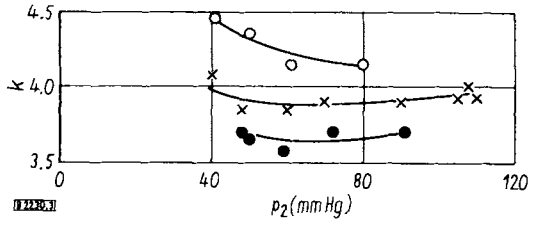


Fig. 12. The dependence of the compression ratio, $k = p_2/p_1$ of the Roots compressor on the discharge pressure, p_2, with the molar throughput, L, as a parameter.

Gas cooler with a cooling water flow rate of 2 l/min;
○ ○ L = 28 mole/h; × × L = 43 mole/h; ● ● L = 60 mole/h;
Helium-UF_6 mixture containing 5 mole% UF_6.

In order to evaluate the performance of the process compressors, the dependence of the throughput, L (moles/h), and of the compression ratio, $k = p_2/p_1$, on the discharge pressure, p_2, was measured using a UF_6-helium mixture containing 5 mole per cent UF_6. The measurements were made after the steady state temperature distribution was attained throughout the compressor. It can be seen from Figure 12 that at the specified operating point, that is, at a throughput of 60 moles/h and at 48 mm Hg discharge pressure, the compression ratio exceeds the required value of 3 by more than 20 per cent.

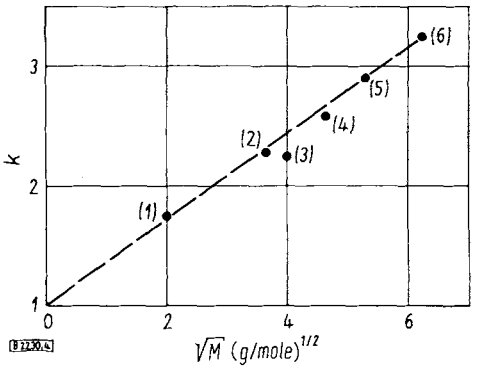


Fig. 13. The dependence of the compression ratio, k, on the square root of the molecular weight, M, of the process gas. Roots compressor without gas cooler;

Discharge pressure: p_2 = 50 mm Hg;
Molar throughput: L = 60 mole/h;
Data points: (1) He, M = 4
(2) 2.7 mole %UF_6—97.3 mole % He, M = 13.5,
(3) CH_4, M = 16,
(4) 5 mole % UF_6—95 mole % He, M = 21.4,
(5) N_2, M = 28,
(6) 10 mole % UF_6—90 mole % He, M = 38.8

Measurements of the throughput, made with an earlier model compressor without a gas cooler, for various process gases of different densities, showed a linear relationship between the square root of the average molecular weight of the gas and the compression ratio, k, which the compressor achieved at a given molar throughput, L, and discharge pressure, p_2. The measured results for L = 60 moles/h and p_2 = 50 mm Hg are shown in Figure 13.

2.3. Process Test Loop

The construction of the process test loop can be seen from Figure 14. The heavy and light fractions are removed from the separation chamber through separate lines and are pumped off simultaneously through the valves (c) and (b), respectively, by the Roots compressor (h). The compressed gas is returned to the separating element (i) through valve (e). Sample withdrawal reservoirs (k) are connected in parallel with the process gas lines. Their volumes were so determined that they contain, under operating conditions, a sufficient amount of UF_6 (about 0.1 g) for isotopic analysis with a mass spectrometer. During an experiment, they were swept out with process gas and then isolated from the system before the withdrawal of the sample. The samples were pumped from these reservoirs through cold traps (not shown) in which the UF_6 was frozen out. The UF_6, after being weighed, was then subjected to isotopic analysis. The UF_6 concentration in the UF_6-helium mixture was determined from the weight of the UF_6, the pressure, and the volume of the sample withdrawal reservoirs.

In order to facilitate a longer period of operation with frequent sample withdrawal, a 1000 l reservoir (l) can be connected to the system to increase its volume. Without the

[*] We wish to thank *W. Röllinger* and *H. Bode* of the firm, E. Leybolds Nachfolger, Köln-Bayental, for their valuable cooperation.

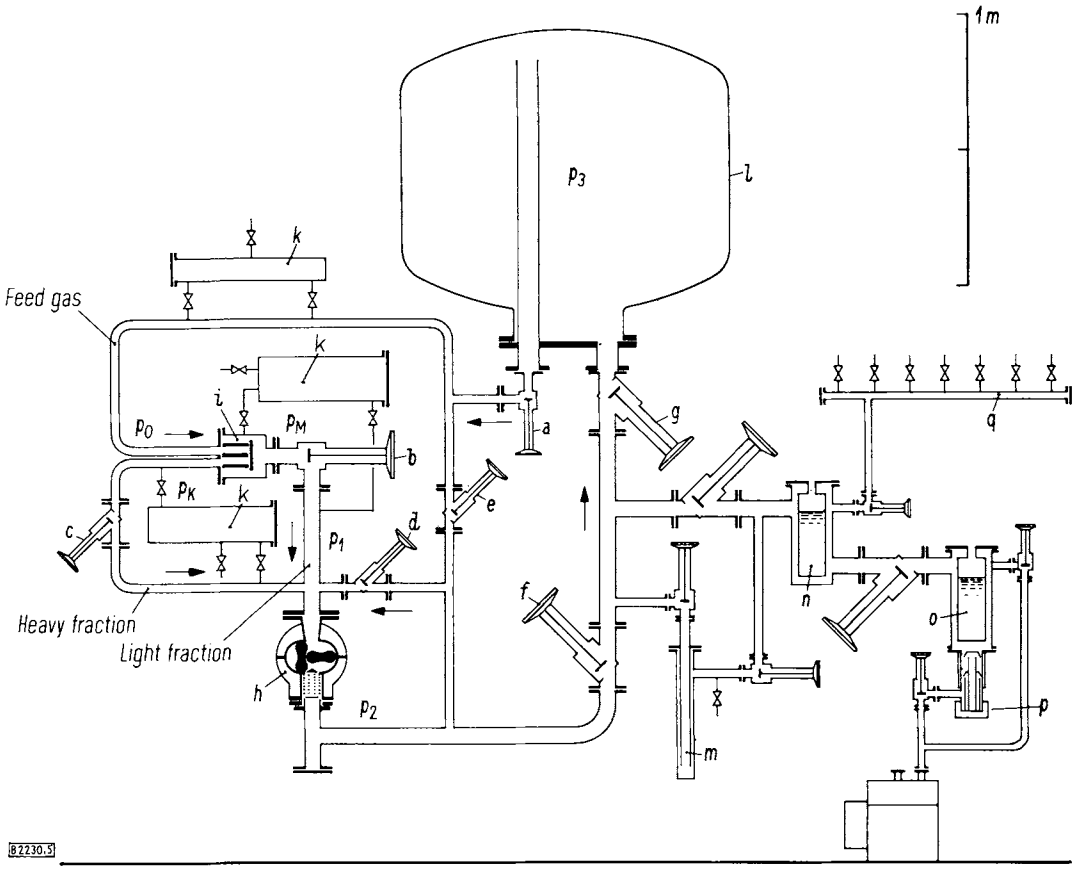


Fig. 14. Schematic drawing of the process test loop.

(a) through (g) valves; (h) Roots compressor; (i) separating element; (k) sample withdrawal reservoirs; (l) gas reservoir; (m) UF_6 trap; (n,o) cold traps; (p) vacuum pumps; (q) vacuum header.

reservoir, the volume of the test loop was 20 l. The reservoir also makes it possible to change the operating pressure without removing or adding process gas. When valve (e) is closed, the compressor pumps gas through the open valves (f) and (g) against the reservoir pressure, p_3. The nozzle fore-pressure, p_0, can then be regulated to values between the reservoir pressure, p_3, and the suction pressure of the compressor, p_1, by throttling the flow with valve (a). The pressures of the light and heavy fractions, p_M and p_K, can be adjusted by means of valves (b) and (c) to values between p_0 and p_1. The suction pressure, p_1, is regulated by means of the by-pass valve (d). The discharge pressure, p_2, of the compressor is normally identical to the reservoir pressure, p_3, and changes only slightly when the operating pressures of the separating element are changed due to the large volume ratio between the reservoir and the test loop. The pressures were measured with direct reading aneroid type and membrane type manometers as well as with electrical pressure transducers[*]. A self-stabilizing electromagnetic pressure balance with a linear response in the region from 0 to 760 mm Hg served as a standard[**]. For measurements in the region below 1 mm Hg, an electrostatic membrane micromanometer with a maximum sensitivity of 10^{-3} mm Hg per scale division was used. All of these instruments are suitable for direct measurements in UF_6 or in other fluorinating gases at room temperature. In addition, thermal conductivity and ionization pressure gauges were used for the control of the evacuation processes and for the measurement of the final vacuum in the different parts of the installation. These instruments were separated from the process gas space during operation with UF_6.

The test loop can be emptied by means of the liquid nitrogen-cooled UF_6 condenser (m). The helium can be pumped off with a rotary pump. A mercury diffusion pump is provided for the production of a high vacuum. It is protected against corrosive gas residues by two liquid nitrogen-cooled traps (n, o).

Austenitic steels, Nos. 4541, 4550, and 4571, were used for the construction of the test loop. All valves have a bellows or membrane type seal around the valve stem. Viton or, in special cases, teflon was used as gasket material. The maximum inleakage rate permitted was 5×10^{-6} mm Hg-l/s for the entire test loop, including the instrumentation and compressor, but excluding the 1000 liter reservoir. Before filling with UF_6, the entire test loop was baked out under high vacuum and passivated with a mixture of chlorine trifluoride (ClF_3) and nitrogen.

2.4. Isotope Separation Experiments

Although, according to the results of the experiments described in Section 1, a value of the UF_6 cut, θ_{UF_6}, equal to 0.33 would be expected to lead to the economically most favorable cascade arrangement, the ten stage pilot plant, because of the simpler interstage connections required, was designed to operate with a value of θ_{UF_6} equal to 0.5.

In practice, the value of θ_{UF_6} can only be set within a certain limit of error by the choice of a particular distance between the knife edge and the curved wall of the Laval nozzle. Since providing a means for

[*] Manufacturer: Appleby & Ireland, Basingstoke (England), Type 101 and 533.
Manufacturer: Heraeus GmbH., Hanau (Germany) Type VM–M.
Manufacturer: CEC, Pasadena, California (U.S.A.), Type 4-353-0001.
Manufacturer: Ateliers de Construction de Bagneux, Bagneux/Seine (France), Type 437 Gd 25121 and 25221.

[**] Manufacturer: CEC, Pasadena, California (U.S.A.), Type 4-336-0102.

adjusting the position of the knife edge during operation would be quite expensive, it seemed reasonable to utilize the dependence of θ_{UF_6} on the expansion ratio as a method for making fine adjustments in the value of the UF_6 cut.

For this reason, several series of isotope separation experiments were carried out with the test loop in which the variation of the separation effect and of the cut as a function of the expansion ratio, p_0/p_M, were of particular interest. At the same time these experiments served the purpose of life-testing the entire installation.

The compressor operated against the reservoir pressure, p_3, which was somewhat greater than the nozzle fore-pressure, p_0 = 48 mm Hg, so that a sufficiently large excess of gas was available in the installation for the withdrawal of samples. The expansion ratio was regulated with the by-pass valve (d) and the nozzle fore-pressure, p_0, with valve (a) (see Figure 14). The pressures of the light and heavy fractions, p_M and p_K, were always equal.

The dependence of the UF_6 mole fractions, N_0, N_M, and N_K in the feed gas, the light fraction, and the heavy fraction, respectively (obtained from the gas analysis), as well as that of the elementary separation effect, ε_A, for the uranium isotopes (defined by equation (4)) on the expansion ratio, p_0/p_M, is shown in Figure 15. The cuts, θ and θ_{UF_6}, were calculated from the relationships:

$$\text{Total cut, } \theta = (N_0 - N_K)/(N_M - N_K) \tag{9}$$

$$UF_6 \text{ cut, } \theta_{UF_6} = N_M\theta/N_0 \tag{10}$$

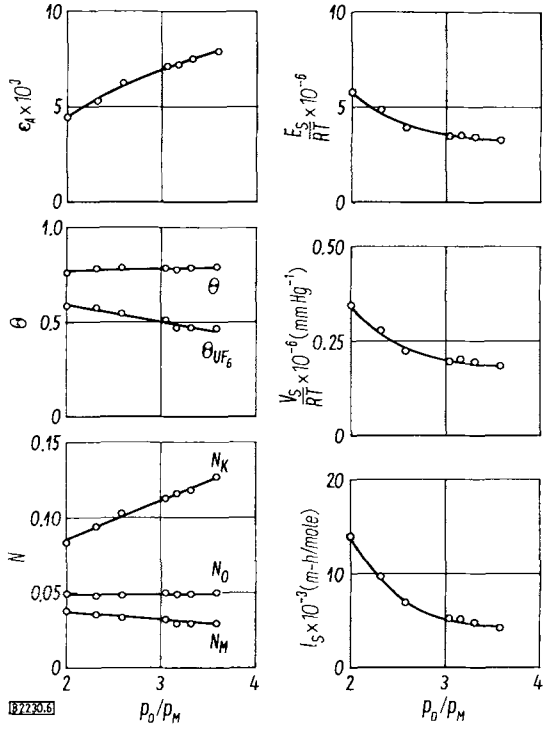


Fig. 15. The effect of the expansion ratio, p_0/p_M, on the elementary separation effect, ε_A; the total cut, θ; the UF_6 cut, θ_{UF_6}; the UF_6 mole fraction in the feed gas, N_0, in the light fraction, N_M, and in the heavy fraction, N_K; the specific work of compression, E_S; the specific suction volume, V_S; and the specific slit length, l_S.
Inlet pressure: p_3 = 48 mm Hg; $p_K = p_M$;
Helium-UF_6 mixture containing 5 mole % UF_6.

The dependence of the specific cost factors, defined by equations (5) through (7), on the expansion ratio is also shown in Figure 15.

The values for the separation effect and for the specific cost factors obtained in the test loop with the separation nozzle system 100 mm in length agree within the limits of error with those obtained in the corresponding earlier experiments with the 10 mm long nozzle system.

All of the experimental results presented in Figure 15 were obtained with the distance between the knife edge and the curved wall of the nozzle equal to 0.20 mm. Within the limit of error of the measurements, the curve for θ_{UF_6} as a function of the expansion ratio passes through the specified operating point (θ_{UF_6} = 0.5 at p_0/p_M = 3). From a different series of measurements, it was observed that, at this value of the expansion ratio, a decrease in the distance between the knife edge and the nozzle wall of 0.01 mm caused the UF_6 cut to increase from 0.50 to 0.54. The θ_{UF_6} curve presented in Figure 15 shows that a deviation from the design point of this magnitude can be compensated for by an increase of about 10 per cent in the expansion ratio.

One of the series of measurements was repeated after an interval of more than four months. In the interim, suction volume measurements were made and the endurance-testing of the Roots compressor was undertaken. During the entire time the installation was filled with the helium-UF_6 mixture, and for about 1100 hours it was maintained under operating conditions. The results from both experiments were in agreement. This signified that the properties of the separating element did not change measurably during the many months of experimental operation.

3. Comparison of the Specific Cost Factors of the Separation Nozzle Process and the Gaseous Diffusion Process

For the purpose of judging the economic potential of the separation nozzle process, one can compare the optimum values obtained for the specific cost factors with the corresponding values for the gaseous diffusion process. Since the operating conditions employed in the gaseous diffusion process and the value of the elementary separation effect which has been attained in practice are not known, the values of the specific cost factors for the diffusion process can only be estimated.

According to theory, the upper limit for the elementary separation effect for the gaseous diffusion process for uranium isotope separation, using UF_6 as the process gas, is given by

$$\varepsilon_A(\max) = 0.00429\,(1-p_M/p_0)\,\frac{1}{\theta}\ln\frac{1}{1-\theta}, \tag{11}$$

where again p_0 is the pressure in the gas entering the separating element and p_M is the pressure in the light fraction. The cut, θ, is the fraction of the feed stream which is pumped from the separating element as the light fraction at the pressure, p_M. One can safely

assume that in the gaseous diffusion process θ is equal to 0.5. The optimum value of the pressure ratio, p_0/p_M, for the gaseous diffusion process, will be assumed to lie in the neighborhood of four, as is the case for the separation nozzle process.

Thus one obtains:

$$\varepsilon_A \text{ (max)} = 4.45\times10^{-3}.$$

This maximum value for the elementary separation effect can only be attained in practice when the mean free path of the UF_6 molecules is large compared to the diameters of the pores in the membrane and when no local depletion of the light isotope occurs on the high pressure side of the membrane. However, in order to decrease the investment costs of the diffusion process, one would choose a gas pressure as high as practicable and thereby accept in the bargain a certain decrease in ε_A due to the smaller ratio of the mean free path to the pore diameter. Moreover, in practice, the mixing in the gas on the high pressure side of the membrane in the direction perpendicular to the membrane surface is not complete. If it is assumed that in practice only 60 per cent of the theoretical maximum value of ε_A is attained, one obtains for the effective elementary separation effect:

$$\varepsilon_A(\text{eff}) = 2.67\times10^{-3}.$$

The specific ideal isothermal work of compression is given by the ratio of the ideal isothermal work of compression performed per unit time to the separative power, δU, defined by equation (8). The resulting expression is

$$E_s = \frac{1}{\delta U}\,\frac{L^*}{2}\,RT\,(\ln\frac{p_o}{p_M} + \ln\frac{p_o}{p_K}). \qquad (12)$$

With $\varepsilon_A = 2.67\times10^{-3}$, $p_0/p_M = 4$, an estimated pressure drop for the heavy fraction, $p_0/p_K = 1.2$, and an estimated operating temperature, $T = 330\,^\circ\text{K}$ (see below), it follows that

$$E_s \text{ (diffusion)} = 6.8 \times 10^2 \text{ kWh/mole}.$$

The optimum value, $E_s = 14.4\times10^2$ kWh/mole, obtained for the separation nozzle process with the improved separating system and with $\theta_{UF_6} = 0.33$, is therefore still higher by a factor of 2.1 than that estimated for the diffusion process. In addition, it should be kept in mind that the compressor efficiency to be expected with the $He-UF_6$ mixture is somewhat lower than that with pure UF_6 because of the smaller molar heat capacity of the mixture.

In the estimate for the diffusion process it was assumed that the heavy fraction is pumped off at an appreciably higher pressure than the light fraction. This implies that each separation stage is provided either with two compressors or with a single compressor of a special type which pumps gas simultaneously at the pressures, p_M and p_K. It could be of advantage, at least when processing the higher ^{235}U concentrations, to avoid this complication by expanding the heavy fraction to the pressure, p_M [13]. In this case the difference between the specific work of compression for the gaseous diffusion process and for the separation nozzle process would almost disappear.

In order to estimate the specific suction volume, one must make an assumption regarding the absolute pressure at which the diffusion process operates. An upper limit, assuming that sufficiently fine-pored membranes are available, is given by the vapor pressure of UF_6. At room temperature the vapor pressure of UF_6 is about 100 mm Hg, and at 53 °C it reaches 1 atm. Since the operating temperature of the plant is probably not much above 50 °C, and since it must be maintained at a safe distance from the condensation point, one can take 0.5 atm to be a reasonable value for the operating pressure. With this value for p_0 and the values for the other variables as given above, one obtains from the equation for the specific suction volume,

$$V_s = \frac{1}{\delta U}\,\frac{L^*}{2}\,RT\left(\frac{1}{p_M} + \frac{1}{p_K}\right), \qquad (13)$$

that for the diffusion process:

$$V_s \text{ (diffusion)} = 1.59\times10^5 \text{ m}^3\text{/mole}.$$

The optimum value, $V_s = 1.40\times10^6$ m³/mole, obtained for the separation nozzle process with the improved separating system, is therefore higher by a factor of 8.8 than that estimated for the gaseous diffusion process.

When judging the economic consequences of the larger specific suction volume, one must bear in mind that the separation nozzle process, operating with a UF_6 cut of 0.33, requires only about 1/2.7 times as many stages as the diffusion process [*]. For a given separation job the suction volume per stage will therefore be greater than that for the gaseous diffusion process by the factor, 8.8 times 2.7, *i.e. ca.* 24. Results obtained in the French gaseous diffusion plant studies indicate that the variation of the investment costs per stage with the size of the stage is given by a constant times $L^{0.38}$, where L represents the throughput of the stage [14]. If one assumes the same dependence and the same constant for the separation nozzle process, and postulates that changes in the volume throughput due to changing the pressure affect the investment costs in exactly the same way as changes in the molar throughput, one obtains the result:

[13] *H. Kronberger* and *G. R. H. Geoghegan*: Proceedings of the International Symposium on Isotope Separation, Amsterdam 1957. North Holland Publ. Co., Amsterdam 1958, p. 517.

[*] The concentration change between adjacent stages in a cascade is equal to $^1/_3$ of the elementary separation effect, ε_A, defined by equation (4), when $\theta_{UF_6} = 0.33$, and is equal to $\varepsilon_A/2$ when $\theta_{UF_6} = 0.5$.

[14] *C. Frejacques* and *R. Galley*, Third International Conference on the Peaceful Uses of Atomic Energy, Geneva 1964, Paper 28/P/89.

$$\left.\begin{matrix}\text{Investment Costs for the}\\ \text{Separation Nozzle Process}\end{matrix}\right\} = \frac{24^{0.38}}{2.7} (= 1.2) \left\{\begin{matrix}\text{Investment Costs for the}\\ \text{Gaseous Diffusion Process.}\end{matrix}\right.$$

Thus, in spite of the fact that, according to the estimate above, the specific suction volume is greater by a factor of 8.8 one would not expect an appreciably greater investment cost for the separation nozzle process than for the gaseous diffusion process.

It is expected that the separation nozzle process will have a real advantage compared to the gaseous diffusion process with respect to the equilibrium time of a separation cascade. By the term, equilibrium time, one refers to the time required between the start-up of a cascade and the attainment of the product concentration, *i.e.* the time during which no product can be withdrawn. The equilibrium time for cascades which enrich ^{235}U to medium or high concentrations can be so long that they may not be neglected in the economic considerations. For a given separation job, the equilibrium time is directly proportional to the average residence time of a UF_6 molecule in a stage and inversely proportional to the square of the elementary separation effect [12]. Since the average residence time will be at least no greater, and probably appreciably less, in the separation nozzle process than in the diffusion process, one can expect that the equilibrium time will be shorter by at least an order of magnitude in the former owing to the larger elementary separation effect.

We wish to thank G. Frey for his assistance in the development of the Roots compressor and the test loop as well as Miss B. Gebauer and J. Dröge, W. Mannherz, and G. Schüler for their help in carrying out the experiments. We also wish to thank Dr. von Halle for valuable discussions and for the translation of this report.

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German version: Chemie-Ing.-Techn. *39*, 1, 80 (1967)

Hexamethyl(Dewar Benzene) (Hexamethylbicyclo[2.2.0]hexa-2,5-diene)

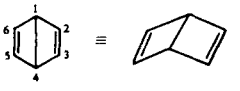
BY W. SCHÄFER AND H. HELLMANN [*]

Dedicated to Professor Friedrich Asinger on the occasion of his 60th birthday

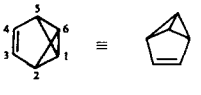
Hexamethyl(Dewar benzene) was first obtained by bicyclotrimerization of 2-butyne in the presence of aluminum chloride. This preparation provided a basis for a comprehensive study of the chemical reactivity of Dewar benzene derivatives. Interesting information concerning the reactivity of the permethylated Dewar benzene system can be deduced from its behavior on hydrogenation and oxidation, and, in particular, from the addition of H-acidic compounds and from the substitution and elimination reactions of the resulting adducts.

1. Introduction

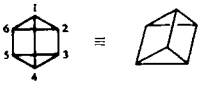
Dewar benzenes, benzvalenes, and prismanes, derivatives of the three non-planar "valence isomers" of benzene, are now, 100 years after Kekulé's conception of his benzene formula, emerging from the ranks of the esoteric organic compounds (see also [1, 2]). Fears that the unstable valence-isomeric forms would readily isomerize into benzene derivatives, because of their steric strain, are now recognized as being almost groundless. Derivatives of all three "valence isomers" have been prepared in recent years; these compounds can be handled without difficulty in the absence of



Dewar benzene (*Dewar*, 1867)[**]
Bicyclo[2.2.0]hexa-2,5-diene [3]



Benzvalene (*Hückel*, 1937)
Tricyclo[3.1.0.0^{2,6}]hex-3-ene [3]



Prismane (*Ladenburg*, 1869)
Tetracyclo[2.2.0.0^{2,6}0^{3,5}]hexane [3]

rearrangement catalysts. It still remains to be seen whether this is also true of the three parent compounds. Of these, the only one synthesized so far is the un-

[*] Dr. W. Schäfer and Prof. Dr. H. Hellmann
Forschungslaboratorien der Chemische Werke Hüls AG.
4370 Marl (Germany)

[1] *E. E. van Tamelen*, Angew. Chem. *77*, 759 (1965); Angew. Chem. internat. Edit. *4*, 738 (1965).

[2] *H. G. Viehe*, Angew. Chem. *77*, 768 (1965); Angew. Chem. internat. Edit. *4*, 746 (1965).

[**] The name "Dewar benzene" rather suggests a resonance structure of benzene. A trivial name, similar to benzvalene and prismane, has not been assigned to this compound although the structure and unsaturated character are well described by the name "tectadiene" (latin, tectum = roof).

[3] Concerning nomenclature, cf. *J. Meinwald* and *J. K. Crandall*, J. Amer. chem. Soc. *88*, 1300 (1966).

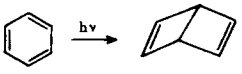
substituted Dewar benzene [4, 4a], which is less stable than its derivatives (half-life 2 days at 20 °C).

From the point of view of preparation, the Dewar benzene derivatives occupy a special place among the derivatives of the valence isomers of benzene, since all the preparations of prismanes yet accomplished are based on the photochemical excitation of Dewar benzene derivatives.

Dewar benzenes can be synthesized by the following five methods.

1.1. Photoisomerization of Benzene Derivatives

A benzene derivative is irradiated with high frequency UV light.



(a)

The first Dewar benzene derivative was synthesized by *van Tamelen* and *Pappas* [5], who obtained 1,2,5-tri-t-butyl(Dewar benzene) by photoisomerization of 1,2,4-tri-t-butylbenzene in ether. 1,2,3,5-Tetra-t-butyl(Dewar benzene) was obtained, together with the corresponding benzene derivative, by irradiation of 1,2,4,5-tetra-t-butylbenzene [6]. The photochemical rearrangement of hexafluorobenzene to hexafluoro(Dewar benzene) proceeds particularly smoothly (60 % yield) [7, 8]; octafluorotoluene, on the other hand, gives a mixture of 1- and 2-trifluoromethylpentafluoro(Dewar benzenes) [8].

Van Tamelen and *Pappas* chose 1,2,4-tri-t-butylbenzene as starting material because they deduced that the steric interaction of the bulky t-butyl groups situated *ortho* to each other ("aromatic destabilization", cf. *e.g.* [9]) would favor the Dewar form, in which these groups are farther apart.

However, the success of the photoisomerization is not tied to steric conditions of this nature [10], as is shown by the photoisomerizations of hexafluorobenzene and octafluorotoluene, as well as by a number of reactions in which the intermediate formation of Dewar benzenes has been postulated in order to explain the structure of the products. An example of such a reaction was described by *Kaplan et al.* [11], who obtained [1,2,4-$^{14}C_3$]trimethylbenzene *via* Dewar benzenes on photolysis of [1,3,5-$^{14}C_3$]trimethylbenzene; the course of this reaction also shows that the migration of the methyl groups does not involve free radicals.

The irradiation of a 20 vol.-% solution of cyclobutene in benzene with UV light (λ = 2537 Å) at room temperature gave rise to a novel cycloaddition. The reaction afforded the tetracyclic hydrocarbon $C_{10}H_{12}$ (50 % yield), the formation of which can be explained by the addition of cyclobutene to the Dewar benzene that is formed as an intermediate [12] (eq. (b)).

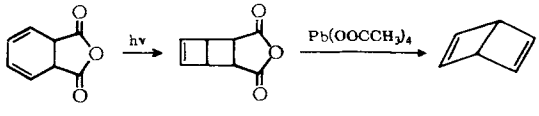


(b)

On the other hand, no Dewar benzene derivative can be isolated on irradiation of the "aromatically destabilized" *o*-di-t-butylbenzene; the product is in fact a mixture of *m*- and *p*-di-t-butylbenzenes in a ratio that depends on the irradiation time [13, 14], a result that can again be explained by the formation of Dewar benzene and prismane intermediates.

1.2. Degradation of Bicyclo[2.2.0]hex-5-ene-2,3-dicarboxylic Anhydride with Lead Tetraacetate

UV irradiation of *cis*-1,2-dihydrophthalic anhydride in ether yields bicyclo[2.2.0]hex-5-ene-2,3-dicarboxylic anhydride, which has been converted into the unstable Dewar benzene in 20 % yield by degradation with lead tetraacetate under mild conditions [4].



(c)

1.3. Addition of Cyclobutadiene *in situ* to Dihalogenomaleic Anhydride, Esterification, and Dehalogenation

Criegee and *Zanker* [15] have obtained dimethyl tetramethyl(Dewar phthalate) *(1)* in accordance with equation (d). The last step is reminiscent of a method used for the preparation of a Dewar anthracene derivative [16] [*].

(1) can be converted into another Dewar benzene derivative, namely, octamethylbicyclo[2.2.0]hexa-2,5-diene-2,3-dimethanol, by reaction with an excess of methylmagnesium iodide [17].

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[4] *E. E. van Tamelen* and *S. P. Pappas*, J. Amer. chem. Soc. *85*, 3297 (1963).

[4a] Note added in proof: *K. E. Wilzbach*, *J. S. Ritscher*, and *L. Kaplan*, J. Amer. chem. Soc. *89*, 1031 (1967), were able to separate benzvalene from the photoisomerization products (λ = 2537 Å) of benzene in the liquid phase by gas chromatography. Benzvalene rearomatizes slowly at room temperature.

[5] *E. E. van Tamelen* and *S. P. Pappas*, J. Amer. chem. Soc. *84*, 3789 (1962).

[6] *E. M. Arnett* and *J. M. Bollinger*, Tetrahedron Letters *1964*, 3803.

[7] *I. Haller*, J. Amer. chem. Soc. *88*, 2070 (1966).

[8] *G. Camaggi*, *F. Gozzo*, and *G. Cevidalli*, Chem. Commun. *1966*, 313.

[9] *A. W. Burgstahler*, *P.-L. Chien*, and *M. O. Abdel-Rahman*, J. Amer. chem. Soc. *86*, 5281 (1964).

[10] Cf., however, *D. Seebach*, Angew. Chem. *77*, 119 (1965), especially p. 122; Angew. Chem. internat. Edit. *4*, 121 (1965).

[11] *L. Kaplan*, *K. E. Wilzbach*, *W. G. Brown*, and *S. S. Yang*, J. Amer. chem. Soc. *87*, 675 (1965).

[12] *R. Srinivasan* and *K. A. Hill*, J. Amer. chem. Soc. *87*, 4653 (1965); cf., however, *K. E. Wilzbach* and *L. Kaplan*, *ibid.* *88*, 2066 (1966).

[13] *K. Kirk*, Dissertation, University of Wisconsin (1963).

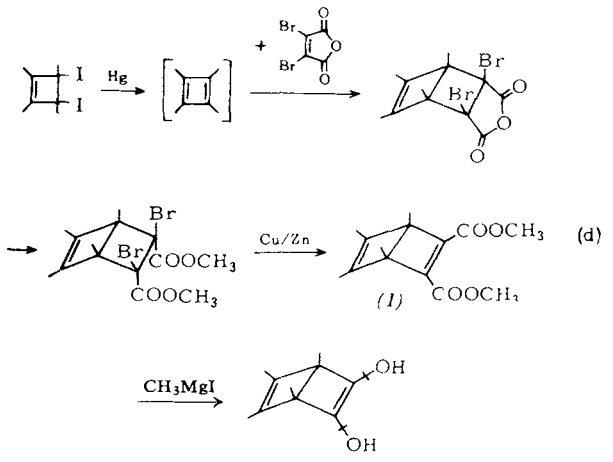
[14] *A. W. Burgstahler* and *P.-L. Chien*, J. Amer. chem. Soc. *86*, 2940 (1964).

[15] *R. Criegee* and *F. Zanker*, Chem. Ber. *98*, 3838 (1965); Angew. Chem. *76*, 716 (1964); Angew. Chem. internat. Edit. *3*, 695 (1964).

[16] *D. E. Applequist* and *R. Searle*, J. Amer. chem. Soc. *86*, 1389 (1964).

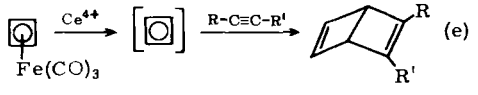
[*] In all the following formulae, lines attached to the ring denote methyl groups, and crosses denote t-butyl groups.

[17] *R. Criegee* and *R. Askani*, Angew. Chem. *78*, 494 (1966); Angew. Chem. internat. Edit. *5*, 519 (1966).



1.4. Addition of Cyclobutadiene *in situ* to Acetylenes

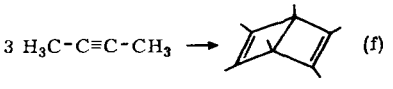
All attempts to isolate cyclobutadiene or its derivatives as such have so far been unsuccessful. However, there are a number of stable cyclobutadienemetal complexes [18] of which tricarbonylcyclobutadieneiron, which can be prepared [19] in 40% yield by the reaction of *cis*-3,4-dichlorocyclobutene with $Fe_2(CO)_9$, can be used for the synthesis of Dewar benzenes [20]. When the complex is decomposed by oxidation with salts of Ce(IV) in the presence of acetylene derivatives, the resulting cyclobutadiene is intercepted to form the Dewar benzene system (eq. (e)).



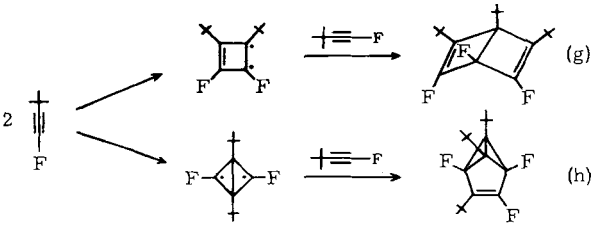
R	R'	Ref.
H	$COOCH_3$	[21]
$COOCH_3$	$COOCH_3$	[21]
H	C_6H_5	[22]

1.5. Bicyclotrimerization of Acetylenes

The formally most simple method for the preparation of Dewar benzenes is the bicyclotrimerization of acetylenes in accordance with equation (f).



In 1964, *Viehe et al.* [2,23] reported a spontaneous trimerization of the extremely reactive compound t-butylfluoroacetylene. 1,2,6-Tri-t-butyl-3,4,5-trifluoro-(Dewar benzene) and 1,3,6-tri-t-butyl-2,4,5-trifluorobenzvalene were formed in a yield of 33 % each. The trimerization of t-butylfluoroacetylene proceeds *via* dimeric intermediates, which can be intercepted with an excess of acrylonitrile or styrene. The origin of small quantities of tetramers observed in the oligomerization of t-butylfluoroacetylene can also be traced back to the dimerization of the dimeric intermediates. *Viehe* explained the reaction as proceeding formally *via* biradicals (eq. (g) and (h)) [24].



2. Synthesis of Hexamethyl(Dewar Benzene) *(3)*

It can be seen from the above survey that the preparation of Dewar benzenes requires the use of processes involving several steps. In the photochemically induced valence isomerizations, the yields and the uniformity of the reaction course generally leave much to be desired.

Early in 1966, we discovered a new synthesis that is free from these disadvantages, *i.e.* the bicyclotrimerization of 2-butyne in the presence of aluminum chloride to form hexamethyl(Dewar benzene) *(3)* [25]; the reaction proceeds formally in accordance with equation (f).

Optimization experiments showed that the synthesis is best carried out at 35–40 °C in benzene or methylene chloride. The catalyst is added in the proportion of about 5 wt-% (based on the 2-butyne), and the reaction time at 35 °C is 5–7 hours. The brown reaction mixture is poured onto ice and washed with dilute alkali, and *(3)* is isolated in a very pure state by fractional distillation of the organic phase. The conversion of 2-butyne is about 80 %, and the yield is 60 to 70 %, based on the reacted 2-butyne. Hexamethylbenzene and an approximately equal quantity of a dark oil are formed as by-products. Longer reaction times give higher conversions, but the yield of *(3)* decreases in favor of hexamethylbenzene *(5)*. This suggests that *(3)* is an intermediate and that *(5)* is the true stable end product of the $AlCl_3$-catalysed trimerization of 2-butyne. *(5)* can be obtained in yields of up to 85 % by trimerization of 2-butyne with $AlCl_3$ in boiling benzene. Even at low temperatures, the reaction leads exclusively to *(5)* when the reaction time is sufficiently long.

The course of the reaction is formally as shown in equation (i).

[18] *P. M. Maitlis*, Advances organometallic Chem. *4*, 95 (1966).

[19] *G. F. Emerson, L. Watts*, and *R. Pettit*, J. Amer. chem. Soc. *87*, 131 (1965).

[20] Chem. Engng. News *43*, No. 34, p. 38 (1965).

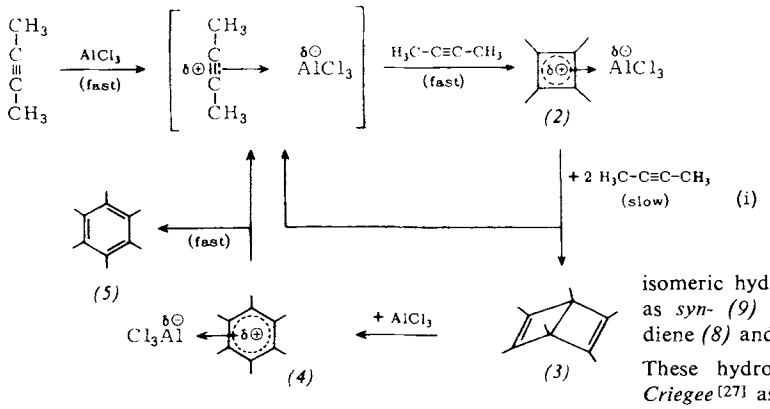
[21] *L. Watts, J. D. Fitzpatrick*, and *R. Pettit*, J. Amer. chem. Soc. *87*, 3253 (1965).

[22] *G. D. Burt* u. *R. Pettit*, Chem. Commun. *1965*, 517.

[23] *H. G. Viehe, R. Merényi, J. F. M. Oth, J. R. Senders*, and *P. Valange*, Angew. Chem. *76*, 922 (1964); Angew. Chem. internat. Edit. *3*, 755 (1964).

[24] Cf. [2], p. 771 und 772.

[25] *W. Schäfer*, Angew. Chem. *78*, 716 (1966); Angew. Chem. internat. Edit. *5*, 669 (1966).



(i)

When *(3)* is brought into contact with $AlCl_3$, it reacts extremely vigorously to form *(5)*. Quantitative exothermic rearrangement into *(5)* takes place when *(3)* is added dropwise to a slurry of $AlCl_3$ in benzene. It must therefore be concluded that in the bicyclotrimerization of 2-butyne the reaction mixture does not contain free $AlCl_3$, at least so long as the concentration of 2-butyne is sufficiently high.

2-Butyne reacts immediately with $AlCl_3$ to form a brown complex, which is readily soluble in methylene chloride but only slightly soluble in benzene. The UV, IR, and NMR spectra of *(2)* are very similar to the spectra of the 4-chloro-1,2,3,4-tetramethylcyclobutenyl cation *(6)*, which was prepared by *Gold* and *Katz* [26] by the action of $AlCl_3$ on 3,4-dichloro-1,2,3,4-tetramethylcyclobutene in methylene chloride.

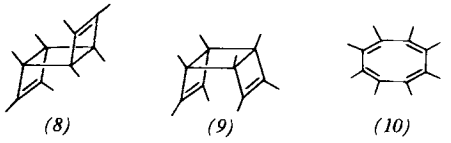


(6) *(7)*

By analogy, therefore, the cationic part of the solvated polar complex intermediate *(2)* can be formulated as *(7)*. Thus *(2)* is not comparable to the stable cyclobutadiene complexes, which have a central d^8 ion of Fe^0, Co, Ni^{II}, or Pd^{II} [18].

Since the reaction mixture contains an excess of 2-butyne, $AlCl_3$ is slowly displaced from *(2)*, with immediate formation of fresh *(2)* and liberation of the unstable tetramethylcyclobutadiene, which is also instantaneously intercepted in a diene synthesis with 2-butyne to form hexamethyl(Dewar benzene).

In addition to hexamethyl(Dewar benzene) *(3)* (60–70 %) and hexamethylbenzene *(5)* (12–18 %) (yields based on reacted 2-butyne in both cases), the trimerization of 2-butyne also yields about 2 % of a crystalline mixture, which separates out (contaminated with hexamethylbenzene) from the very non-homogeneous residual oil (10–15 %) on cooling. Repeated fractional crystallization of this mixture gives three isomeric hydrocarbons $C_{16}H_{24}$, which have been identified as *syn- (9)* and *anti*-octamethyltricyclo[4.2.0.$0^{2,5}$]octa-3,7-diene *(8)* and octamethylcyclooctatetraene *(10)*.



(8) *(9)* *(10)*

M.p. 127 °C M.p. 196 °C M.p. 113 °C

These hydrocarbons had previously been obtained by *Criegee* [27] as dimeric products formed by secondary reaction of the unstable tetramethylcyclobutadiene. We regard their formation in the $AlCl_3$-catalysed bicyclotrimerization of 2-butyne as important evidence of the occurrence of tetramethylcyclobutadiene as an intermediate.

Finally, reaction scheme (i) raises the question of how the course of the reaction is affected by the presence of hexamethylbenzene, which also forms an addition complex *(4)* with $AlCl_3$. To solve this problem an excess of hexamethylbenzene was added to the slurry of aluminum chloride in benzene, and 2-butyne was then introduced. The reaction proceeded normally, showing that 2-butyne decomposes the complex *(4)* with formation of *(5)* and *(2)*.

The bicyclotrimerization of 2-butyne is catalysed not only by $AlCl_3$, but also by other aluminum compounds particularly alkylaluminum dichlorides (alkyl = ethyl, n-propyl, n-hexyl, s-butyl). The reaction time required is several times as long, and the amount of catalyst used must be increased to correspond to the increased molecular weight. $AlBr_3$ and alkylaluminum dibromides also gave positive results. On the other hand, dialkylaluminum chlorides are catalytically inactive, as are other Lewis acids (*e.g.* $FeCl_3$, $TiCl_4$, $SnCl_4$, $ZnCl_2$, or BF_3).

3. Reactions with Hexamethyl(Dewar Benzene)

The bicyclotrimerization of 2-butyne made it possible for the first time to prepare a Dewar benzene derivative on the kg scale by a simple one-step reaction. Apart from its ready availability, hexamethyl(Dewar benzene) has two properties that favor an investigation of its chemical reactivity: its appreciable thermal stability (when heated for 48 hours at 100 °C, the hexamethylbenzene content is less than 1 %) and the fact that it carries only methyl substituents. Consequently, in chemical changes in the Dewar benzene system, there is no need to take into account the effects of different substituents. On the other hand, the chemical reactivity of hexamethyl(Dewar benzene) cannot be regarded *a priori* as typical of Dewar benzenes carrying fewer substituents.

The physical constants of hexamethyl(Dewar benzene) are listed in Table 1.

[26] *E. H. Gold* and *Th. J. Katz*, J. org. Chemistry *31*, 372 (1966); see also *D. E. Applequist* and *J. D. Roberts*, J. Amer. chem. Soc. *78*, 4012 (1956).

[27] *R. Criegee*, Angew. Chem. *74*, 703 (1962); Angew. Chem. internat. Edit. *1*, 519 (1962).

Table 1. Physical constants of hexamethyl(Dewar benzene) *(3)*.

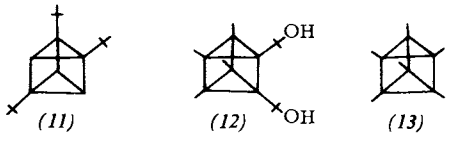
B.p.	60 °C/20mm (≈152 °C/760mm)
n_D^{20}	1.4479
M.p.	7.5 °C
d_4^{20}	0.8125
Flash point (*Pensky-Martens*)	42 °C
Ignition point	238 °C
Viscosity 20 °C	1.47 cP; 1.81 cSt
Heat of combustion	1765 ± 1.1 kcal mole^{-1}
UV spectrum (end absorption only)	250 nm, E = 0.76 l g^{-1} cm^{-1}
	240 nm, E = 2.9 l g^{-1} cm^{-1}
	230 nm, E = 7.3 l g^{-1} cm^{-1}
	220 nm, E = 13.7 l g^{-1} cm^{-1}
IR spectrum	1680, 1370, 1280, 1220, 1060
	735, 660 cm^{-1}
NMR spectrum	τ = 8.45 and 8.95 (2:1)
	(in CCl_4; internal standard: TMS)
Thermal stability:	
half-life *(3)* → *(5)*	105 h at 120 °C
	5.5 h at 140 °C
	2.1 h at 150 °C

3.1. Valence Isomerization

Hexamethyl(Dewar benzene) *(3)* can be quantitatively isomerized to hexamethylbenzene *(5)* by $AlCl_3$ (cf. Section 2). This isomerization can also be brought about by other Lewis acids, such as $FeCl_3$, $SbCl_5$, $TiCl_4$, or, on gentle heating, by $SbCl_3$, $SnCl_4$, and $ZnCl_2$.

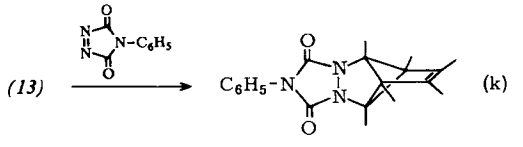
Irradiation of hexamethyl(Dewar benzene) with a low pressure UV lamp again leads mainly to hexamethylbenzene; however, in this case, the main product is accompanied by a 20–25 % yield [based on reacted *(3)*] of a second valence isomer, hexamethylprismane *(13)*, m.p. 91 °C [28,29].

Thus three prismane derivatives are now known [30,31], though *(11)* has so far been obtained only in a purity of 82 %. They were all obtained by irradiation of the corresponding Dewar benzenes with UV light of wavelength ≈ 254 nm.



(11) *(12)* *(13)*

When heated, *(13)* is converted into hexamethyl(Dewar benzene) *(3)* and hexamethylbenzene *(5)* [28,29]. It reacts with the strong dienophile 4-phenyl-1,2,4-triazoline-3,5-dione in strongly polar solvents to give *(14)* (*e.g.* (k)) [28].



(13) *(14)*

[28] *D. M. Lemal* and *J. P. Lokensgard*, J. Amer. chem. Soc. *88*, 5934 (1966).

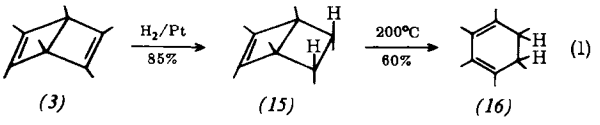
[29] *W. Schäfer*, *R. Criegee*, *R. Askani*, and *H. Grüner*, Angew. Chem. *79*, 54 (1967); Angew. Chem. internat. Edit. *6*, 78 (1967).

[30] *K. E. Wilzbach* and *L. Kaplan*, J. Amer. chem. Soc. *87*, 4004 (1965).

[31] *R. Criegee* and *R. Askani*, Angew. Chem. *78*, 494 (1966); Angew. Chem. internat. Edit. *4*, 519 (1966).

3.2. *endo*-1,2,3,4,5,6-Hexamethylbicyclo[2.2.0]hex-2-ene [32]

Hydrogenation of hexamethyl(Dewar benzene) *(3)* to form *endo*-1,2,3,4,5,6-hexamethylbicyclo[2.2.0]hex-2-ene *(15)* proceeds smoothly under normal pressure on Pt/active charcoal at room temperature, or in an autoclave at 50 °C and 20 atm with Raney nickel as the catalyst when ethyl acetate is used as the solvent. When the reaction is carried out without solvent, the temperature and pressure must be increased (60–100 °C/100 atm).



(3) *(15)* *(16)* (1)

The physical constants of the compounds *(15)* to *(45)* are listed in Table 2.

Small quantities of *(15)* had already been obtained by another route by *Criegee et al.* [33]. The thermal rearrangement of *(15)* into hexamethylcyclohexa-1,3-diene *(16)* had also been studied in the course of kinetic investigations on the valence isomerization of cyclobutenes [34], though the compound was not isolated. The rearrangement of *(15)* into *(16)* in a stainless steel (V4A) autoclave at 200 °C takes 3 hours; at 250 °C, hexamethylbenzene *(5)* is also formed.

When the pyrolysis of *(15)* is carried out at 250 °C in a sealed glass tube, pentamethylbenzene and methane are formed as well as *(16)*. Thus the course of the pyrolysis is influenced by metal ions.

Table 2. Physical constants of the products formed by secondary reactions of hexamethyl(Dewar benzene) *(3)*.

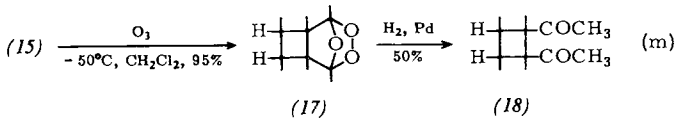
Compound	B.p. (°C/mm)	n_D^{20}	M.p. (°C)
(15)	64/20	1.4498	3.5
(16)	91–92/11		
(17)	54–55/0.13		
(18)	132–134/12		40–42
(19)	73/12	1.4471	
(20)	94/10		
(21)	63–64/14	1.4475	
(22)			87
(23)			155–157
(24)	88–92/11		50–52
(25)			53–54
(26)			184–186
(27)			57
(28)			72–73
(29)	110–112/19	1.4979	−3
(30)	76–77/9		62–64
(31)	63–64/1	1.5183	3–5
(32)	118/19	1.4809	
(33)			43–44
(34)	120/0.6		36–40
(35)	128/0.2	1.4986	
(36)	87–90/13	1.4761	
(37)	143–145/8	1.4962	
(38)	72–73/9	1.4570	10
(39)			70
(40)	90–92/18	1.5054	
(41)	64/11	1.4670	
(42)	71/11	1.4665	
(43)	70–71/12	1.4898	
(44)			194
(45)			268–269

[32] *H.-N. Junker*, *W. Schäfer*, and *H. Niedenbrück*, unpublished.

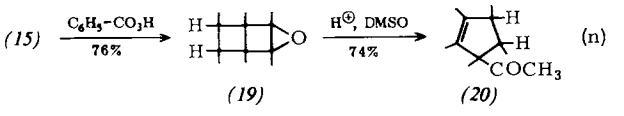
[33] *R. Criegee*, *H. Kristinsson*, *D. Seebach*, and *F. Zanker*, Chem. Ber. *98*, 2331 (1965).

[34] *R. Criegee*, *D. Seebach*, *R. E. Winter*, *B. Börretzen*, and *H.-A. Brune*, Chem. Ber. *98*, 2339 (1965).

Ozonization of *(15)* in methylene chloride at 50 °C leads quantitatively to the distillable ozonide *(17)*, reductive cleavage of which gives 1,2,3,4-tetramethyl-1,2-diacetylcyclobutane *(18)*. *(18)* is also formed directly from *(15)* in low yields by oxidation with $KMnO_4$.



(15) can be epoxidized with perbenzoic acid in benzene (76 % yield) or with peracetic acid in methylene chloride in the presence of anhydrous sodium carbonate (65 % yield).



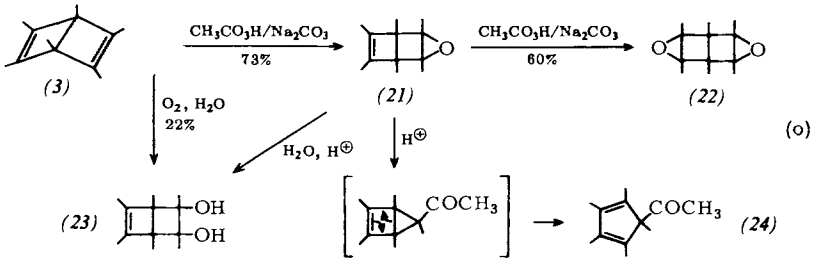
Treatment of the epoxide *(19)* with 1 % sulfuric acid in dimethyl sulfoxide leads, not to hydrolysis, but to isomerization to 1,2,3,4,5-pentamethyl-3-acetylcyclopentene *(20)*.

3.3. Oxidation Reactions with Hexamethyl(Dewar Benzene) *(3)* [35]

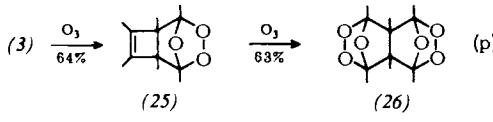
Hexamethyl(Dewar benzene) *(3)* is autoxidizable, and is therefore best stored under an inert gas. Old, partially oxidized samples, which give an acidic reaction, are washed with aqueous alkali before distillation, since rearrangement into hexamethylbenzene *(5)* may otherwise take place, sometimes very violently. When *(3)* is allowed to stand in air, colorless crystals of hexamethylbicyclo[2.2.0]hex-2-ene-5,6-diol *(23)* separate after only 1–2 days (yield ≈ 20 %). *(23)* is also formed from hexamethyl-5,6-epoxy-bicyclo[2.2.0]hex-2-ene *(21)* by hydrolysis *e.g.* with an ether-water mixture in the presence of $H^{\oplus}$ ions. The formation of *(23)* on autoxidation of *(3)* presumably also proceeds *via* the monoepoxide.

The epoxide *(21)* is obtained by the action of perbenzoic acid on an equimolar quantity of *(3)*. Peracetic acid (in the presence of anhydrous sodium carbonate) may also be used.

The epoxidation is accompanied by a side reaction, in which proton-catalysed ring contraction followed by valence isomerization leads to the formation of pentamethyl-5-acetylcyclopentadiene *(24)*. Similar acid-catalysed rearrangements to form three-membered rings have been observed with epoxycyclobutanes [36, 37]. *(21)* gives good yields of hexamethyl-2,3;5,6-bisepoxybicyclo[2.2.0]hexane *(22)* on reaction with perbenzoic or peracetic acid. *(22)* is stable under the conditions used for the hydrolysis of the monoepoxide *(21)*.

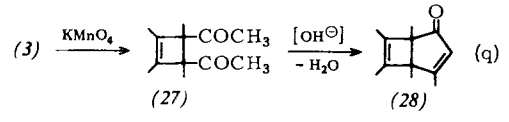


When the stoichiometric quantity of ozone is passed into a solution of *(3)* in CH_2Cl_2 at −50 °C, the monozonide *(25)* is formed, while a further mole of O_3 gives the diozonide *(26)*.



Unlike *(25)*, *(26)* is insoluble in methanol (separation method), and is so stable thermally that it melts without decomposing. The hydrogenative cleavage of *(26)* proceeds non-uniformly, and leads mainly to tetramethylfuran and acetic acid.

On oxidation of *(3)* with $KMnO_4$ in aqueous alkaline butanol at 0 °C, the main product was the steam-volatile 1,4,5,6,7-pentamethylbicyclo[3.2.0]hepta-3,6-dien-2-one *(28)* (yield 50 %), which is formed by intramolecular aldol condensation of the primary product, tetramethyl-3,4-diacetylcyclobutene *(27)*, in the alkaline solution.



If the oxidation of *(3)* is carried out with $KMnO_4$ in aqueous acetone and with the addition of $MgSO_4$ to intercept the $OH^{\ominus}$ ions, *(27)* can be isolated in good yield in the form of colorless crystals (m.p. 57 °C).

3.4. The Action of H-Acidic Compounds on Hexamethyl(Dewar Benzene) *(3)* [38]

The literature contains several references to the sensitivity of Dewar benzenes to acids. In fact this lability does exist, but the Dewar benzenes should not be expected to isomerize exclusively to the benzene derivatives.

The action of HCl on hexamethyl(Dewar benzene) *(3)* in methylene chloride at −30, 0, or +40 °C leads to a

[35] *H.-N. Junker*, *W. Schäfer*, and *H. Niedenbrück*, Chem.Ber., in press.

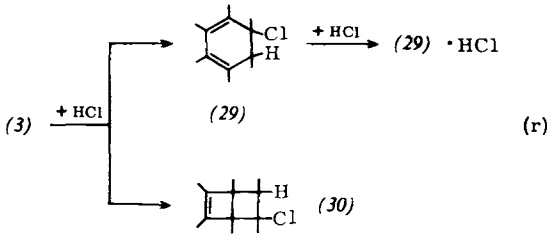
[36] *R. Criegee* and *K. Noll*, Liebigs Ann. Chem. *627*, 1 (1959).

[37] *J.-L. Ripoll* and *J.M. Conia*, Bull. Soc. chim. France *1965*, 2755.

[38] *H. Meister*, *W. Schäfer*, and *U. Sage*, unpublished.

new vacuum-distillable compound (yield 80–85 %; b.p. 110–112 °C/19 mm), elementary analysis of which shows that *(3)* has taken up 1 mole of HCl. The products also include a lower-boiling isomer having m.p. 62–64 °C, which is formed in a yield of 0–15 %, depending on the reaction conditions. Only a small amount of hexamethylbenzene is formed. The addition of HCl to *(3)* can also be carried out with concentrated HCl, though the yields obtained are lower.

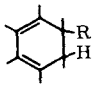
The lower-boiling HCl adduct is hexamethyl-5-chloro-6*H*-bicyclo[2.2.0]hex-2-ene *(30)*, while the higher-boiling adduct is hexamethyl-5-chloro-6*H*-cyclohexa-1,3-diene *(29)*. The course of the reaction is as indicated in equation (r).



(r)

(29) can add a further mole of HCl to form a colorless, salt-like compound, which is moderately stable at low temperatures only, and which readily decomposes into HCl and *(29)*.

Addition in accordance with equation (r) is not confined to hydrogen chloride, though it proceeds particularly uniformly and smoothly in this case. We were even able to add carboxylic acids to *(3)*.

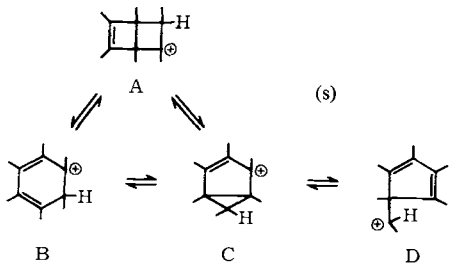
	Compound	R	Yield (%)
	*(31)*	Br	65
	(32)	OOCH	50
	(33)	$OOCCH_3$	26
	(34)	$OOCCH_2Cl$	64
	(35)	$OOCCHCl_2$	65
(31)-(36)	*(36)*	OCH_3	45

The addition of acids is always accompanied by a deep violet coloration of the reaction mixture, indicating an ionic mechanism. It is interesting to note that even methanol reacts with hexamethyl(Dewar benzene) *(3)* when the reactants are refluxed for several days in an atmosphere of nitrogen. After 48 hours, 45 % of *(36)* and 15 % of *(5)* could be isolated. *(3)* also reacts with methanol at room temperature, but the reaction is much slower. The reaction is completely suppressed by a few drops of sodium hydroxide solution.

3.5. Elimination and Substitution Reactions with Hexamethyl-5-chloro-6*H*-cyclohexa-1,3-diene *(29)* [39]

In our attempts to find chemical proof of the structure of the readily obtainable compound *(29)*, we obtained a series of unexpected reaction products. The formation of these products can be explained by the equilibrium of the carbonium ions A, B, C, and D as shown in equation (s). These ions can be formed either by protonation of *(3)* or by elimination of $Cl^{\ominus}$ from *(29)*.

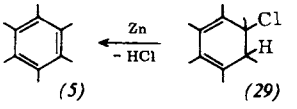
The questions of whether stabilization takes place by substitution or by deprotonation and whether the product is a derivative of A, B, C, or D depend on the



reaction conditions and on the nature of the attacking reagent.

3.5.1. Hexamethylbenzene

The structure of *(29)* can be deduced not only from spectral data, but also from the dehydrochlorination by Lewis acids such as $ZnCl_2$ or $AlCl_3$. Hexamethylbenzene *(5)* is obtained in quantitative yield even under very mild conditions. Gentle heating with zinc dust or iron powder leads to the same result.

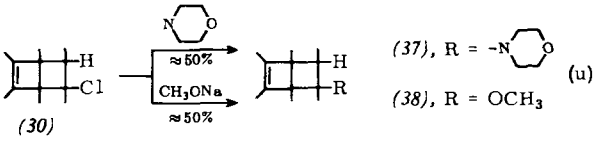


(t)

(29) can take part in diene syntheses, *e.g.* with maleic anhydride or tetracyanoethylene; the reactions proceed at temperatures up to 40 °C.

3.5.2. Bicyclo[2.2.0]hex-2-ene Derivatives

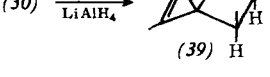
When *(30)* is refluxed for several hours with morpholine, the substitution product hexamethyl-5-morpholino-6*H*-bicyclo[2.2.0]hex-2-ene *(37)* and a mixture of elimination products, including hexamethylbenzene, are obtained in a yield of about 50 % each.



(u)

(30) behaves in a similar manner on treatment with methanolic sodium methoxide solution; hexamethyl-5-methoxy-6*H*-bicyclo[2.2.0]hex-2-ene *(38)* is formed in a yield of about 50 %, while the remainder of the products includes hexamethylbenzene.

Treatment of *(30)* with $LiAlH_4$ results in replacement of the chlorine atom by H to give *exo*-1,2,3,4,5,6-hexamethylbicyclo[2.2.0]hex-2-ene *(39)*.



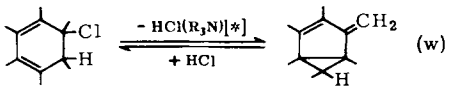
(v)

3.5.3. Bicyclo[3.1.0]hex-2-ene Derivatives

The action of amines on *(29)* leads to dehydrochlorination. Two isomeric hydrocarbons $C_{12}H_{18}$ may be formed, depending on the pK_b value of the amine.

[39] *H. Meister* and *W. Schäfer*, unpublished.

Primary, secondary, and tertiary amines having pK_b values lower than 8 give only pentamethyl-4-methylene-6*H*-bicyclo[3.1.0]hex-2-ene *(40)*. Examples of suitable strongly basic amines are [yields of *(40)* in brackets]: morpholine (86 %), cyclohexylamine (76 %), piperidine (80 %), diethylamine (77 %), *N*-methylmorpholine (72 %), triethylenediamine (1,4-diazabicyclo[2.2.2]-octane) (75 %), and ethylenediamine (79 %). To obtain *(40)*, *(29)* is heated with the amine for several hours at 60–200 °C, if necessary with the addition of an inert solvent (dioxane).

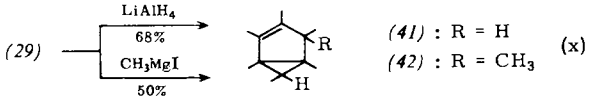


(29) *(40)* (w)

[*] R_3N = strongly basic amine.

It should be noted that this elimination can be reversed by the introduction of HCl gas into a solution of *(40)* in CH_2Cl_2 at 0 °C. *(29)* is formed in 80 % yield.

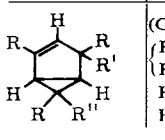
Substituted bicyclo[3.1.0]hex-2-ene derivatives are obtained when *(29)* is refluxed for several hours with $LiAlH_4$ or CH_3MgI in ether.



(41) : R = H
(42) : R = CH_3 (x)

A reaction product of analogous structure is obtained by reaction of sodium methylate on (*29*) in methanol. By reaction of silver oxide with (*29*) a bicyclo[3.1.0]hex-2-ene derivative is obtained which readily dehydrates to give (*40*).

The addition of alcohols and acids to benzene or tri-t-butylbenzene on photochemical excitation with a low-pressure UV lamp has recently been reported[40,41]. The reaction products were assigned a bicyclo[3.1.0] structure.

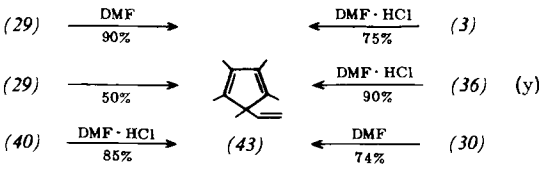


	R	R′	R″	Ref.
	$(CH_3)_3C$	OCH_3	H	[40]
	H	OCH_2CF_3	H	[40]
	H	H	OCH_2CF_3	[40]
	H	$OOCCH_3$	H	[41]
	H	OH	H	[41]

The authors assumed that the H-acidic compounds added to benzvalene, which was formed as an intermediate, with opening of the three-membered ring. Our results suggest that the photochemical excitation leads preferably to the Dewar benzene, the protonation of which would also lead, *via* the carbonium ion equilibrium (s), to the observed results.

3.5.4. Cyclopentadiene Derivatives

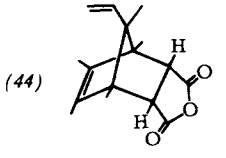
Stable derivatives of carbonium ion D (eq. (s)) are to be expected only under reaction conditions that offer the ions a "chance of survival". Such conditions prevail *e.g.* during the action of weak amines on *(29)*. A suitable amine is dimethylformamide; when the components are refluxed for about 8–10 hours, possibly in the presence of an inert solvent (toluene), the dehydrochlorination product pentamethyl-5-vinyl-cyclopentadiene *(43)* is formed in 85–90 % yield.



The dehydrochlorination can also be effected, though in lower yields, by *e.g.* formamide, quinoline, pyridine, or urea. The purely thermal dehydrochlorination of *(29)* (3 hours at 180–205 °C) in an atmosphere of N_2 proceeds in the same direction, but less uniformly. About 50 % of *(43)* and about 40 % of hexamethylbenzene *(5)* are obtained.

(43) can be also obtained in almost quantitative yield from the methyl ester *(36)* by refluxing with DMF hydrochloride (cf. eq. (y)).

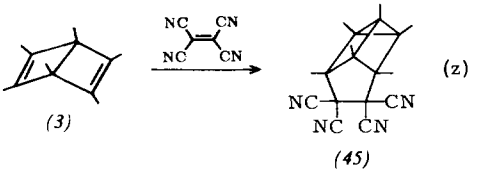
Further possibilities can be predicted from the equilibrium (s) and confirmed by experiment. Thus *(43)* is obtained in very good yields when the bicyclic compounds *(30)* and *(40)* are heated with DMF or DMF·HCl. Even *(3)* can be isomerized to *(43)* in a single-vessel reaction by heating with DMF·HCl in DMF, the product then being extracted with ligroin. The structure of *(43)* is established *e.g.* by the very smooth diene synthesis with maleic anhydride, in which the adduct *(44)* is formed in 90 % yield.



No substitution product derived from D (eq. (s)) has so far been isolated.

3.6. Action of Dienophiles on Hexamethyl(Dewar Benzene) *(3)*

The reactions of *(3)* discussed in the foregoing sections are only selected examples. It should finally be mentioned that *(3)*, by analogy with norbornadiene, may be able to add to strong dienophiles. *Lemal* and *Lokensgard*[28] reported that *(14)* could be obtained, not only from the prismane derivative *(13)* (cf. Section 3.1), but also directly from *(3)*.



(3) *(45)* (z)

We obtained the compound *(45)* (m.p. 268–269 °C) by reaction of *(3)* with tetracyanoethylene.

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[40] *L. Kaplan, J. S. Ritscher*, and *K. E. Wilzbach*, J. Amer. chem. Soc. *88*, 2881 (1966).

[41] *E. Farenhorst* and *A. F. Bickel*, Tetrahedron Letters *1966*, 5911.

Polymerization of Trioxane[**]

BY K. WEISSERMEL, E. FISCHER, K. GUTWEILER, H. D. HERMANN, AND H. CHERDRON[*]

A survey of the possible modes of polymerization of trioxane is followed by a discussion of current ideas concerning the course of the polymerization. The polymerization, which involves ring cleavage, is characterized by a number of side reactions of the growing polyoxymethylene cations, such as chain transfer, transacetalization, and hydride shift. These reactions not only determine the nature of the end groups and the molecular weight of the resulting polyoxymethylenes, but are also responsible for their chemical and molecular uniformity. Special emphasis is placed on the role of the monomeric formaldehyde formed during the polymerization of trioxane.

1. Polymerization of Trioxane

Polyoxymethylenes, *i.e.* macromolecules consisting of CH_2O structural units, were intensively studied during the 1920's by *Staudinger* and *Kern*[1]. They can be prepared either from formaldehyde or from its cyclic oligomers, such as trioxane (1,3,5-trioxacyclohexane) or tetroxane (1,3,5,7-tetraoxacyclooctane). Whereas formaldehyde can be polymerized either anionically or cationically, only cationic polymerization takes place in the case of trioxane; free-radical polymerization has not so far been detected in either case. Finally, formaldehyde can undergo polycondensation in the aqueous phase to form polyoxymethylenes[***], but trioxane cannot.

The polymerization of trioxane can be initiated by cationic initiators such as protonic acids, ansolvo acids (complexes of organic acids with inorganic salts), and compounds that form cations[2,3] (for special initiators, see Sections 3.2.2. and 3.2.3). These initiators differ not only in their activity, but also in their influence on termination and side reactions. Trioxane can also be induced to polymerize by high-energy radiation, as was shown first by *Rösinger*[4] and, a little later, by *Okamura*[5] (see also Section 2.1.2.).

The polyoxymethylenes obtained by the cationic polymerization of trioxane are similar in structure to those obtained by the cationic polymerization of formaldehyde, but differ markedly in certain respects from the polyformaldehydes prepared by anionic polymerization. This is due to the introduction of special end groups, and possibly to branching, during cationic polymerization (see Section 3.4).

The ease of polymerization of trioxane also extends to copolymerization, in which compounds of many classes, such as cyclic ethers[6], cyclic acetals[6,7], cyclic esters[8], and vinyl compounds[8,9] may be used as comonomers.

The copolymerization of trioxane is of considerable industrial importance, since it offers an elegant means of suppressing the thermal and alkaline degradation (unzip depolymerization) that generally occurs in homopolyoxymethylenes with terminal hemiacetal groups (the degradation process begins at the end groups). Even random cleavage of the polymer chains (*e.g.* by oxidation or acid hydrolysis) causes much less breakdown in copolymers of trioxane than in homopolyoxymethylenes, since the degradation of the copolymer by successive removal of formaldehyde stops when the sequence of CH_2O units is interrupted by a comonomer unit, *i.e.* a C–C bond. The copolymerization of trioxane, which has already been described in detail[10–13], will be discussed in the present article only in connection with the side reactions (see Section 3.4.), which lead to deviations from the normal copolymerization kinetics.

2. Methods for the Polymerization of Trioxane

Trioxane can be polymerized in the solid state, in the melt, in the gas phase, in suspension, and in solution (precipitation polymerization). Not only do these methods differ in their execution, but some also lead to different products, since the polymerization conditions determine the importance of the side reactions.

[*] Dr. K. Weissermel, Dr. E. Fischer, Dr. K. Gutweiler, Dr. H. D. Hermann, and Dr. H. Cherdron
Farbwerke Hoechst AG.
6230 Frankfurt/Main-Höchst (Germany)

[**] Delivered in part as a lecture at the Institut für Chemie und Technologie der Plaste der Akademie der Wissenschaften, Leipzig (June 22nd, 1966), and at Kyoto University (Japan) (October 5th, 1966).

[1] *W. Kern* in *H. Staudinger*: Die hochmolekularen organischen Verbindungen. Springer-Verlag, Berlin 1932, p. 224–287.

[***] This normally yields only low molecular weight products ("paraformaldehyde"), but high molecular weight polyoxymethylenes have recently also been obtained in this way. See *M. N. Brown, P. Langsdorf, C. E. Schweitzer*, and *D. L. Funck*, Belg. Pat. 571016 (1957) du Pont; *L. Mortillaro* and *G. Galiazzo*, Chim. e Ind. (Milano) *46*, 1148 (1964).

[2] *J. F. Walker*: Formaldehyde. Reinhold Publ. Corp., New York 1964, 3. Edit., p. 185.

[3] *V. Jaacks* and *W. Kern*, Makromolekulare Chem. *62*, 1 (1963).

[4] *S. Rösinger*, German Pat. 1157783 (1960), Farbwerke Hoechst AG.

[5] *S. Okamura, K. Hayashi*, and *Y. Nakamura*, Isotopes and Radiation *3*, 416 (1960).

[6] For instance, *C. T. Walling, F. Brown, W. Bartz*, and *G. W. Polly*, French Pat. 1221148 (1958), Celanese Corp.

[7] *K. Küllmar, E. Fischer*, and *K. Weissermel*, German Pat. 1124703 (1959), Farbwerke Hoechst AG.

[8] *W. Kern, H. Cherdron*, and *V. Jaacks*, Angew. Chem. *73*, 177 (1961).

[9] *V. Jaacks*, Makromolekulare Chem. *84*, 250 (1965).

[10] *K. Weissermel, E. Fischer, K. Gutweiler*, and *H. D. Hermann*, Kunststoffe *54*, 410 (1964).

[11] *W. Kern*, Chemiker-Ztg. *88*, 623 (1964).

[12] *H. D. Hermann* and *K. Weissermel*, Makromolekulare Chem. *94*, 91 (1966).

[13] *V. Jaacks*, Makromolekulare Chem. *101*, 33 (1967).

2.1. Bulk Polymerization

2.1.1. Melt Polymerization

Trioxane polymerizes very readily in the molten state, *i.e.* above 62 °C, in the presence of cationic initiators. For example, it is completely polymerized within a few minutes at 70 °C with 10^{-4} mole of boron trifluoride per mole of monomer [14,15]. It is sometimes difficult to distribute the initiator uniformly in the melt, since the polymerization begins almost instantaneously under suitable conditions. However, initiators are also known that first dissolve very rapidly in the monomer, and only then initiate the polymerization [15,16]; these are particularly suitable for use in kinetic studies [17], *e.g.* for the investigation of transfer reactions [18].

During the bulk polymerization of trioxane above its melting point, the reaction mixture very rapidly becomes turbid, because of the insolubility of the polymer in the monomer, and the final product is a solid white block. The polymerization is accompanied by a volume contraction due to the difference between the densities of molten trioxane (d_4^{70} =1.13) and polytrioxane (d_4^{20} = 1.42).

Despite the low thermal conductivity of the polymer, the dissipation of the heat of polymerization (about 4 kcal/mole) presents no problems in small-scale experiments. With larger quantities of starting materials, on the other hand, the heat liberated is sufficient to vaporize some of the trioxane (b.p. 115 °C/760 mm) and to heat the reaction mixture almost to the ceiling temperature of 126 °C (see Section 3.1.), beyond which polymerization is no longer possible.

2.1.2. Polymerization in the Solid State

Numerous articles have been published on the polymerization of trioxane in the solid state. A simple example is polymerization in the presence of boron trifluoride [19]. The trioxane crystals are first charged with gaseous boron trifluoride at room temperature, and are then slowly heated. It can be readily established with the aid of the hot-stage microscope that polymerization becomes appreciable only at 50–55 °C, when needle-shaped polymer crystals [20] grow very rapidly from the surfaces of the trioxane crystals into the interior. The molecular weights of the resulting polytrioxanes are roughly double those of the polymers obtained under comparable conditions in the melt; viscosity numbers η_{sp}/c of up to 3.5 were obtained (0.5 g of polymer in 100 ml of γ-butyrolactone +2 % of diphenylamine at 140 °C).

Similar observations were made by *Okamura et al.* in the cationic suspension polymerization of trioxane below its melting point [21,22].

The action of high-energy radiation on crystalline trioxane also leads to polymerization [4,5,23–32a], very probably by a cationic mechanism. It is interesting to note that this radiation-induced polymerization of trioxane takes place only in the solid state, and not in the melt; the rate of polymerization reaches a maximum just below the melting point [24,25].

Particularly high yields and high molecular weights are obtained when solid trioxane is irradiated at low temperatures and is then heated to a temperature just below its melting point [26]. The polytrioxane prepared by radiation-induced polymerization is frequently obtained in the form of long filamentous crystals ("whiskers") [27–29].

It is not known why polymerization does not take place when pure trioxane is irradiated in the liquid phase. However, in the presence of an electron acceptor such as maleic anhydride [32], trioxane polymerizes even in the molten state when irradiated.

2.1.3. Polymerization During Phase Transitions

Trioxane exhibits a pronounced tendency to polymerize during gas-solid and liquid-solid phase transitions. The polymerization of trioxane on sublimation was first observed by *Hammick* and *Boeree* [33]. According to *Kohlschütter* and *Sprenger* [34], this polymerization takes place at the surface of the trioxane crystals and *Jaacks* and *Kern* [35] found that it is initiated by formaldehyde. Much higher polymerization rates are reached when trioxane vapor is allowed

[14] *D. E. Hudgin, F. M. Berardinelli, C. L. Michaud, O. H. Axtell*, and *C. M. Clarke*, German Publ. Pat. Appl. 1137215 (1957, 1958), Celanese Corp.

[15] *K. Weissermel, K. Küllmar*, and *M. Reiher*, Brit. Pat. 943684 (1958), Farbwerke Hoechst AG.

[16] *M. Kučera, J. Láníková*, and *E. Spousta*, German Publ. Pat. Appl. 1194581 (1962).

[17] *M. Kučera* and *E. Spousta*, Makromolekulare Chem. *90*, 215 (1966) and literature cited there.

[18] *H. D. Hermann, E. Fischer*, and *K. Weissermel*, Makromolekulare Chem. *90*, 1 (1966).

[19] *E. Weiss, E. Fischer, E. Benedikt, E. Paszthory, K. Küllmar*, and *K. Weissermel*, German Publ. Pat. Appl. 1182431 (1960), Farbwerke Hoechst AG.

[20] Cf. *S. E. Jamison* and *H. D. Noether*, J. Polymer Sci. *B 1*, 51 (1963).

[21] *S. Okamura, T. Higashimura*, and *K. Takeda*, Makromolekulare Chem. *51*, 217 (1962).

[22] *S. Okamura, E. Kobayashi*, and *T. Higashimura*, Makromolekulare Chem. *94*, 20 (1966) and literature cited there.

[23] *K. Hayashi* and *S. Okamura*, Makromolekulare Chem. *47*, 230 (1961).

[24] *S. Okamura*, and *K. Hayashi*, J. Chim. physique *59*, 428 (1962).

[25] *S. Okamura, K. Hayashi*, and *Y. Kitanishi*, J. Polymer Sci. *58*, 925 (1962).

[26] *K. Hayashi, H. Ochi*, and *S. Okamura*, J. Polymer Sci. *A 2*, 2929 (1964).

[27] *N. S. Marans*, Brit. Pat. 984097 (1962), W. R. Grace and Co.

[28] *H. Sack*, Belg. Pat. 612792 (1961), Houillères du Bassin du Nord.

[29] *H. B. van der Heijde*, Nature (London) *199*, 798 (1963).

[30] *N. S. Marans* and *F. Jaffe*, Belg. Pat. 610364 (1961), W. R. Grace and Co.

[31] *H. Rao* and *D. S. Ballantine*, J. Polymer Sci. *A 3*, 2579 (1965).

[32] *K. Takakura, K. Hayashi*, and *S. Okamura*, J. Polymer Sci. *A-1.4*, 1731 (1966); *H. B. van der Heijde* and *H. Nauta*, Philos. Mag. *13*, 1015 (1966).

[32a] *H. B. van der Heijde* and *H. Nauta*, Philos. Mag. *13*, 1015 (1966).

[33] *D. L. Hammick* and *A. R. Boeree*, J. chem. Soc. (London) *121*, 2738 (1922).

[34] *H. W. Kohlschütter* and *L. Sprenger*, Z. physik. Chem. *B 16*, 284 (1932).

[35] *V. Jaacks* and *W. Kern*, Makromolekulare Chem. *52*, 37 (1962).

to crystallize on a cooled surface in the presence of cationic initiators such as boron trifluoride [14] or sulfur trioxide [36]. Polymerization under the action of high-energy radiation also takes place particularly readily during the gas-solid phase transition [4].

Similarly, trioxane polymerizes on crystallization from the liquid phase, and the polymerization can again be initiated by radiation [4] or by cationic initiators. The catalytic homopolymerization and copolymerization of trioxane during the liquid-solid phase transition are particularly interesting, since high conversions can be attained even with very small quantities of initiators (10^{-6} mole/mole of trioxane) [37]; on the other hand, practically no polymerization takes place under the same conditions in the melt. Another surprising observation is the increase in conversion when 1,3-dioxolane is added as a comonomer. This increase is also observed in radiation-induced polymerization [38]. The conversion can be further increased if, after the crystallization, the reaction mixture is twice heated to 70 °C and then cooled again. Similar results were obtained by *Baccaredda et al.* in the polymerization of trioxane in suspension or in solution on liquid-solid phase transition [39–41]. No explanation for these observations has so far been found.

2.2. Suspension Polymerization

The suspension polymerization of trioxane, in which the heat of reaction can be dissipated much more easily than in bulk polymerization, and in which the polymer is obtained, not as a solid block, but in a finely divided form, can be carried out in various ways. These include the polymerization of solid or molten trioxane with cationic initiators in the presence of suspending agents [14, 22] and the radiation-induced polymerization of solid trioxane in the presence of suspending agents [42]. Suitable suspending media include hexane, cyclohexane, heptane, and high-boiling hydrocarbons; since the monomer is soluble to a limited extent in these media, the suspension polymerization of trioxane is always accompanied by solution polymerization (precipitation polymerization).

2.3. Solution Polymerization (Precipitation Polymerization)

The solution polymerization of trioxane proceeds much more slowly than polymerization in bulk or in suspension. Benzene, halogenated hydrocarbons, nitroaliphatic compounds, and nitroaromatic compounds have been suggested as solvents [14, 43–45]. Since polytrioxane is insoluble in these solvents, the polymer precipitates right at the beginning of the polymerization (precipitation polymerization).

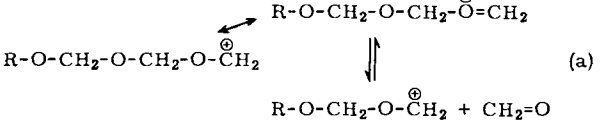
Accurate kinetic studies can be carried out on the polymerization of trioxane in solution [11], but the results are not directly applicable to bulk polymerization; this is particularly true of the copolymerization of trioxane, since the dilution effect of the solvent can prevent important reactions between the polymer molecules (transacetalization, see Section 3.4.2.), so that the copolymers obtained in solution are chemically less uniform.

3. Course of the Polymerization of Trioxane

3.1. The Role of Monomeric Formaldehyde

Monomeric formaldehyde, which is split off from the ends of the growing chains in accordance with eq. (a), plays an important part in the cationic polymerization of trioxane. It can affect the polymerization in many ways. Some of the reactions involved will therefore be considered before we proceed to discuss the course of the polymerization.

The cationic polymerization of trioxane is characterized by an induction period [46], during which no macromolecular products, but only monomeric formaldehyde and its oligomers are formed. During this period, monomeric formaldehyde is split off from the carbonium ion formed in the primary step of the polymerization until a temperature-dependent equilibrium concentration (ceiling concentration) of monomeric formaldehyde has been reached; it is only then that the polymerization begins.



(a)

In the homopolymerization of trioxane in solution, the ceiling concentration at 30 °C is 0.06 mole of CH_2O/l. As the temperature is raised, the equilibrium is displaced in favor of monomeric formaldehyde until, at the ceiling temperature of 126 °C, the polymer is no longer formed. The situation is more complicated in the case of copolymerization [47].

An induction period is no longer observed if a quantity of monomeric formaldehyde corresponding to the equilibrium concentration is introduced before the addition of the initiator. On the other hand, the induction period is lengthened if the formaldehyde formed is intercepted.

[36] *H. Richtzenhain, P. Janssen,* and *W. Vogt,* German Publ. Pat. Appl. 1198558 (1961), Dynamit Nobel AG.

[37] *K. Gutweiler, E. Fischer,* and *K. Küllmar,* Belg. Pat. 647354 (1963), Farbwerke Hoechst AG.

[38] *S. Rösinger, H. D. Hermann,* and *K. Weissermel,* J. Polymer Sci. *A-1,* 5, 183 (1967); *S. Rösinger* and *H. D. Hermann,* Belg. Pat. 667415 (1964), Farbwerke Hoechst AG.

[39] *H. Baccaredda, E. Butta,* and *P. Giusti,* J. Polymer Sci. *C 4,* 953 (1964).

[40] *F. Morelli, G. Masetti, E. Butta,* and *M. Baccaredda,* J. Polymer Sci. *A 3,* 2441 (1965).

[41] *M. Baccaredda, E. Butta, F. Morelli,* and *G. Masetti,* Makromolekulare Chem. *93,* 137 (1966).

[42] *H. Sack,* Belg. Pat. 637434, Houillères du Bassin du Nord.

[43] *K. Küllmar, K. Weissermel,* and *G. Bier,* Brit. Pat. 942745 (1958), Farbwerke Hoechst AG.

[44] *V. Jaacks,* Dissertation, Universität Mainz, 1959.

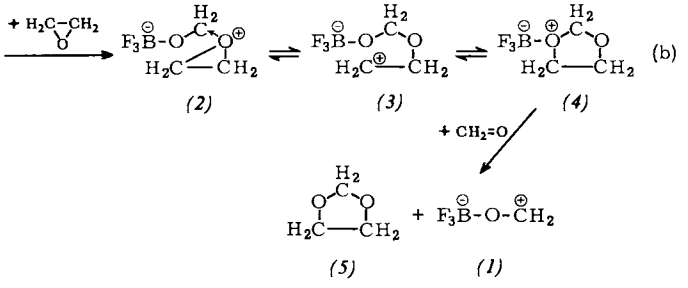
[45] *W. Wilson, R. F. Hill,* and *H. May,* Brit. Pat. 878163 (1959), British Industrial Plastics Ltd.

[46] *W. Kern* and *V. Jaacks,* J. Polymer Sci. *48,* 399 (1960).

[47] *K. Gutweiler,* unpublished.

Examples of the interception of the formaldehyde are found in the copolymerization of trioxane with ethylene oxide or of trioxane with 2-substituted 1,3-dioxolanes [48]. In the copolymerization of trioxane with ethylene oxide, the boron trifluoride-formaldehyde adduct *(1)* attacks the oxirane oxygen with formation of the cyclic oxonium salt *(2)*. The product rearranges *via* the open form *(3)* into the cyclic oxonium salt *(4)* which reacts with formaldehyde to give 1,3-dioxacyclopentane or dioxolane *(5)* [*]. Copolymerization of *(5)* with trioxane (eq. (b)) then takes place.

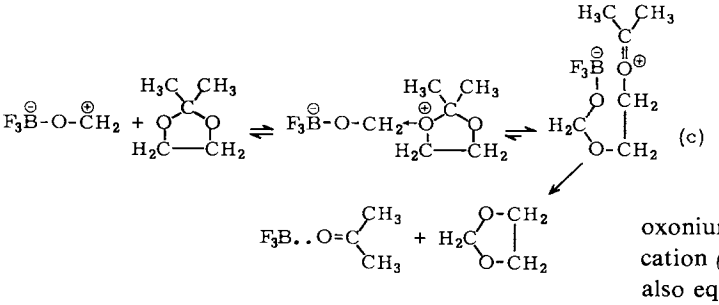
$$F_3B + O{=}CH_2 \longrightarrow F_3\overset{\ominus}{B}\text{-}O\text{-}\overset{\oplus}{C}H_2 \quad (1)$$



(b)

(2) *(3)* *(4)* *(5)* *(1)*

In the copolymerization of trioxane with 1,3-dioxolanes having one or two substituents in position 2, the carbonyl compound is displaced from the dioxolane derivative by formaldehyde with transacetalization and elimination to form the unsubstituted 1,3-dioxolane; it is only when this reaction is complete that monomeric formaldehyde can accumulate in the reaction mixture up to the ceiling concentration, so ultimately enabling the polymerization to proceed (eq. (c)).



(c)

The part played by formaldehyde in the initiation reaction can also be illustrated by another example. The less reactive compound tetrahydrofuran undergoes $Al(C_2H_5)_3$/epichlorohydrin-initiated polymerization to form high molecular weight products [49]. One would expect that the much more reactive trioxane would also polymerize with the same initiator system; however, this is not so, since formaldehyde immediately reacts with $Al(C_2H_5)_3$ to form aluminum alkoxides, which do not initiate cationic polymerization.

Finally, a number of observations suggest that the formaldehyde formed during the induction period takes part in the initiation step, and probably acts as a co-catalyst. This is understandable, since formaldehyde is more strongly nucleophilic than oxacycloalkanes; consequently, reaction (d) appears possible as the initiation step.

$$F_3B + O{=}CH_2 \longrightarrow F_3\overset{\ominus}{B}\text{-}O\text{-}\overset{\oplus}{C}H_2 \xrightarrow{+\ \text{trioxane}} F_3\overset{\ominus}{B}\text{-}O\text{-}CH_2\text{-}O\text{-}CH_2\text{-}O\text{-}CH_2\text{-}O\text{-}\overset{\oplus}{C}H_2 \quad (d)$$

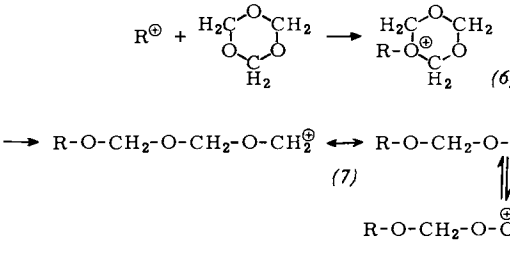
The co-catalysis is extremely difficult to detect, since polymerization is induced by initiator concentration as low as 4×10^{-5} mole/mole of trioxane, and the concentration of water in highly purified trioxane is also at least of this order of magnitude. The water could cause co-catalysis, by formation of a protonic acid from an ansolvo acid.

3.2. Initiation Reaction

It can be seen from the above discussion that the initiation reaction is subject to several influencing factors and therefore cannot be definitely formulated. The following possibilities have been proposed.

3.2.1. Classical Meerwein Mechanism

The initiation of the polymerization of trioxane by protonic acids, Lewis acids, or cation-forming components can be formulated in accordance with an oxonium ion/carbonium ion mechanism proposed by *Meerwein* [50] for the cationic polymerization of tetrahydrofuran (eq. (e)). Addition of an initiator cation to an oxygen atom of the trioxane first leads to an oxonium ion *(6)*, which gives a resonance-stabilized cation *(7)* by cleavage of one of the $^{\oplus}O-C$ bonds (see also eq. (a)).



(e)

(6) *(7)*

The possibility of resonance stablization undoubtedly contributes to the ease of cleavage of the trioxane ring. In spite of the resonance stabilization, however, the resulting cation *(7)* is sufficiently active for an electrophilic attack on the next trioxane ring, *i.e.* for the propagation of the reaction chain.

3.2.2. Initiation by Trioxane Cations

According to *Okamura et al.* [32], trioxane can be polymerized with peroxides, provided that an electron acceptor (*e.g.* maleic anhydride) is also present. The

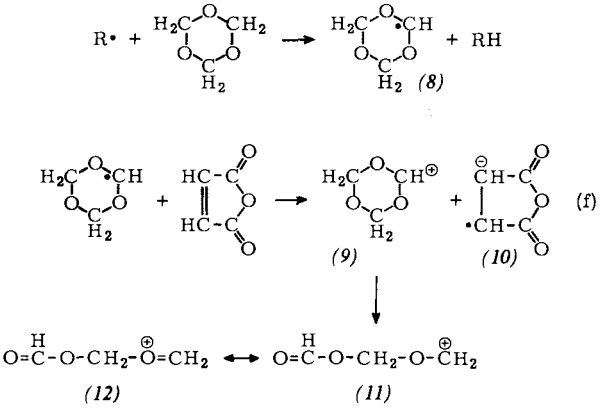
[48] *H. D. Hermann, K. H. Burg,* and *K. Weissermel,* Makromolekulare Chem., in press.

[*] As well as dioxolane, larger cyclic compounds and linear prepolymers are formed from formaldehyde and ethylene oxide in a similar way.

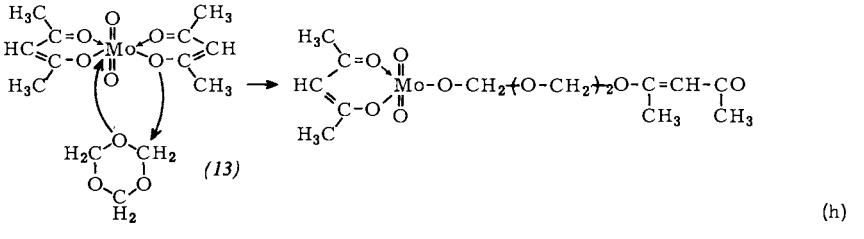
[49] *K. Weissermel* and *E. Nölken,* Makromolekulare Chem. *68,* 140 (1963).

[50] *H. Meerwein, D. Delfs,* and *H. Morschel,* Angew. Chem. *72,* 927 (1960).

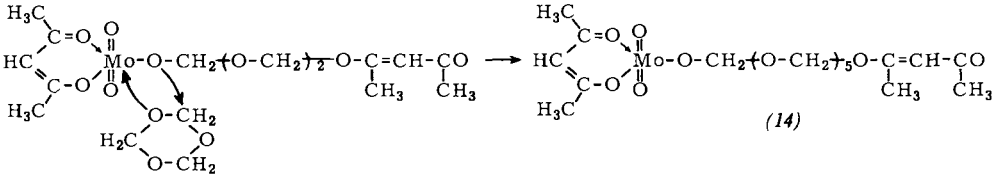
reaction may be assumed to adopt the following course. A free radical formed by the decomposition of the peroxide abstracts a hydrogen atom from a trioxane molecule as in an RH reaction, with the result that a trioxane radical *(8)* is formed. This radical then gives up an electron to maleic anhydride, with formation of a trioxane cation *(9)* and the maleic anhydride radical-anion *(10)*. The trioxane cation may initiate the polymerization of trioxane either directly or after ring cleavage to form the carbonium ion *(11)*, which is mesomeric with the oxonium ion *(12)* (eq. (f)).



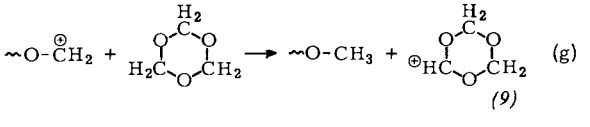
Initiation by trioxane cations *(9)* gives a polymer with ortho-ester end groups, while initiation by carbonium ions *(11)* gives formate end groups.



(h)



However, trioxane cations can also be formed from the monomer by hydride abstraction (see Section 3.4.3) without the formation of a free-radical intermediate: the hydride abstraction may be effected *e.g.* by the initiator or by a polyoxymethylene cation.



The polymerization again proceeds either *via* the cyclic cation *(9)* or *via* the carbonium ion *(11)* (cf. reaction (f)), and again yields polymers with ortho-ester or formate end groups.

The existence of trioxane cations is supported by mass-spectroscopic evidence. Cyclic acetals frequently give a peak corresponding to mass M – 1 [51]. It has also been suggested [52,53] that oxacycloalkane cations are formed during the polymerization of tetrahydrofuran.

3.2.3. Insertion Mechanism

A number of experimental observations suggest that trioxane also polymerizes by a mechanism similar to that of the polymerization of α-olefins. *Kennedy et al.* [54] postulated that the polymerization of trioxane in the presence of molybdenyl acetylacetonate proceeds by a non-cationic mechanism, in which coordination of the trioxane to the central atom of the chelate is followed by ring cleavage and ligand exchange to form oxymethylene units having acetylacetonate end groups (eq. (h)).

However, the possibility that the polymerization still ultimately proceeds *via* cations cannot be discounted.

The work of *Weichert* [55] on the MgI_2-initiated polymerization of cyclic formals also fits into a similar scheme. The initiation by MgI_2 is surprising, since no complex acids of this compound, *e.g.* of the form $H[MgI_3]$ or $H_2[MgI_2(OH)_2]$, are known. Concentrated aqueous solutions are neutral, and no hydrolytic formation of HI is observed. Consequently, the factor responsible for the initiation of polymerization is probably again the strong tendency of MgI_2 toward complex formation, in which the central atom can attain a maximum coordination number of 6 with compounds containing oxygen.

If the coordination sites are blocked by water or alcohol, polymerization does not take place.

3.3. Chain-Growth Reaction

The chain-growth reaction in the cationic polymerization of trioxane can be explained by the alternating oxonium ion/carbonium ion mechanism described by *Meerwein* [50] for the polymerization of tetrahydrofuran. The resonance-stabilized, but still sufficiently active ion *(7)*, which is formed by ring cleavage from the oxonium ion *(6)* formed in the primary step, adds

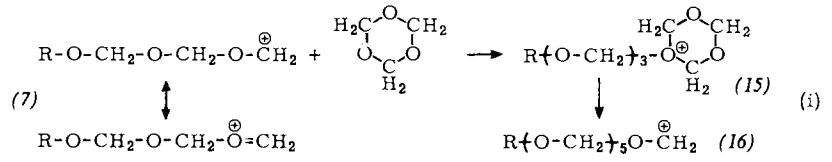
[51] *K. H. Burg, H. D. Hermann,* and *H. Rehling,* Makromolekulare Chem., in press.

[52] *I. Kuntz,* J. Polymer Sci. *B 4,* 430 (1966).

[53] *M. P. Dreyfuss, I. C. Westfahl,* and *P. Dreyfuss,* Meeting Amer. chem. Soc. Sept. 1966. Polymer Preprints *7,* 413.

[54] *C. D. Kennedy, W. R. Sorenson,* and *G. G. McClaffin,* Meeting Amer. chem. Soc., January 1966, Polymer Preprints *7,* 667 (1966).

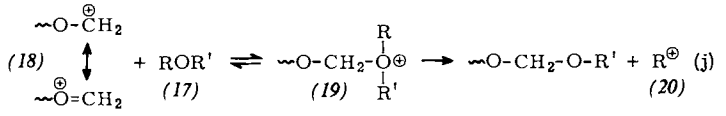
[55] *D. Weichert,* Plaste u. Kautschuk *10,* 12 (1963).



(i)

to a further molecule of trioxane. The resulting oxonium ion *(15)* is in turn converted into a resonance-stabilized cation *(16)*, which reacts once again with trioxane (eq. (i), see also eq. (e)).

The course of this chain reaction is undoubtedly strongly influenced by the cation and the solvent. The stability of the cation not only influences the chain length by retardation or acceleration of the chain termination, but evidently also suppresses side reactions of the end of the growing chain, *e.g.* transfer reactions, transacetalizations, and hydride shifts. The solvent must also be taken into account, since it can accelerate or retard the polymerization. Retardation is observed in the presence of dialkylethers. The cation *(18)* and the dialkyl ether *(17)* evidently exist in equilibrium with a very stable oxonium ion *(19)*. This ion *(19)* is cleaved to a small extent to form an alkyl cation *(20)* that has a very high energy and can carry on the reaction chain.



(j)

The cationic polymerization of formaldehyde, on the other hand, is not retarded by dialkyl ethers. In this case the growing carbonium ion *(18)* reacts much more rapidly with the nucleophilic formaldehyde than with the dialkyl ether, so that the normal chain reaction is not appreciably hindered.

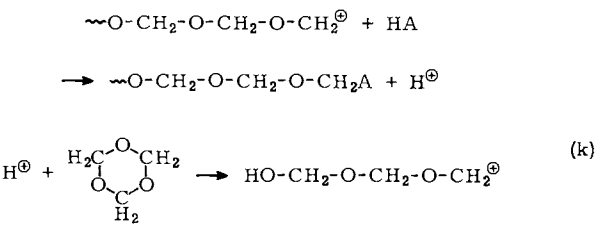
3.4. Side Reactions in the Polymerization of Trioxane

The growing polyoxymethylene cation can not only split off monomeric formaldehyde (cf. Section 3.1), but can also react with polar compounds, which may for example be present as impurities in the monomeric trioxane, with the result that the molecular weight of the resulting polymer is reduced (transfer reaction). However, polyoxymethylene cations can also react with oxygen atoms or methylene groups of the same or of adjacent polymer chains. Combination with oxygen atoms yields oxonium ions, which then decompose with chain cleavage (transacetalization); the reaction of polyoxymethylene cations with methylene groups, on the other hand, leads to the removal of hydride ions (hydride shift, cf. reaction (g)).

These side reactions are not merely of theoretical interest, since they have a decisive influence on the molecular weight, the molecular and chemical uniformity, and the stability of the resulting polyoxymethylenes.

3.4.1. Transfer Reaction

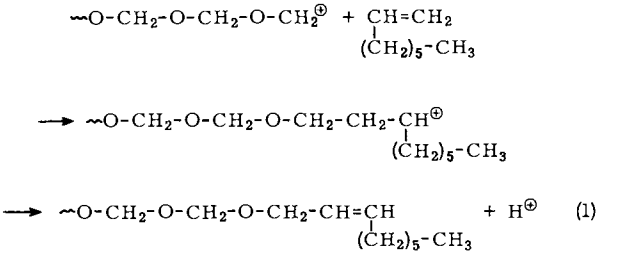
The transfer of the polymerization of trioxane by polar compounds containing mobile hydrogen atoms proceeds in accordance with eq. (k).



(k)

A = Anion

The anion A may for example be a hydroxide, alkoxide, or carboxylate ion. An extremely active compound HA is water [56,57], though alcohols and carboxylic acids are also very effective. Certain aromatic compounds, such as *m*-xylene, mesitylene, or anthracene, also react readily as transfer agents [18]. As in the transfer of the cationic polymerization of styrene [58], the aromatic compound first becomes attached to the polymer cation; this is followed by removal of a proton, which carries on the polymerization. The chain transfer by olefins probably also proceeds in a similar manner [59].



(l)

In addition to compounds with mobile hydrogen atoms, many other transfer agents are known, *e.g.* esters, orthoesters, anhydrides of carboxylic acids, and halogenohydrocarbons [60]; however, the activity of these compounds is relatively low. Very active transfer agents belonging to this group are esters of boric acid, peroxides [18], and in particular linear acetals, which react in accordance with eq. (m).

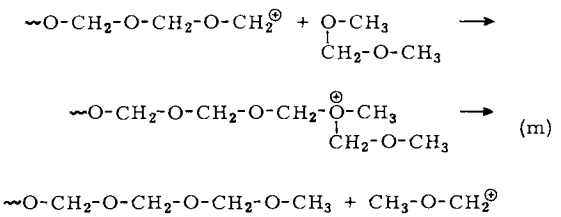
[56] *M. Kučera* and *E. Spousta*, Makromolekulare Chem. *82*, 60 (1965).

[57] *H. Baader, V. Jaacks*, and *W. Kern*, Makromolekulare Chem. *82*, 213 (1965).

[58] *A. R. Mathieson* in *P. H. Plesch*: The Chemistry of Cationic Polymerization. Pergamon Press, London 1963.

[59] *H. D. Hermann*, Makromolekulare Chem. *99*, 35 (1966).

[60] *V. Jaacks, H. Baader*, and *W. Kern*, Makromolekulare Chem. *83*, 56 (1965).



(m)

Finally, mention should also be made of polymeric compounds containing chain transferring groups, *e.g.* polyvinyl acetate and polyvinyl butyral [10,61], which permit the preparation of block and graft copolymers of trioxane by transfer copolymerization.

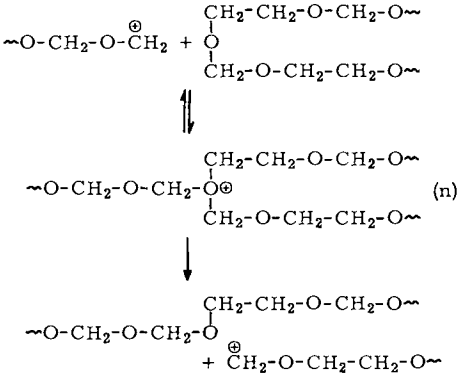
The importance of chain transfer agents in the polymerization of trioxane is not confined to the reduction of the molecular weight of the polymer and the preparation of block copolymers. They also have a particularly interesting effect on the stability of the polymer. Proton-donating transfer agents always strongly favor the formation of hemiacetal end groups, which decompose on heating, particularly in the presence of alkali. This decomposition leads to the complete breakdown of the macromolecule [1]. A particularly interesting group of transfer agents consists of those that give polymers with two stable end groups. Thus by transfer of the polymerization of trioxane by means of dimethyl formal, *Jaacks*, *Baader*, and *Kern* [60] obtained polymers having predominantly methoxy end groups, and which therefore contain a fraction having a high thermal stability. However, complete etherification of the end groups by chain transfer is not possible, since the much more active proton-donating transfer agent water cannot be completely excluded from the polymerization, and since the exclusive formation of stable end groups is prevented by hydride shift (cf. Section 3.4.3).

3.4.2. Transacetalization

In chain transfer with low molecular weight acetals, the polyoxymethylene cation attacks an acetal oxygen atom with formation of an oxonium ion, which then decomposes; a similar reaction should, in principle, also be possible between a polyoxymethylene cation and an oxygen atom in a polyoxymethylene chain. This special type of transfer reaction has been detected in the copolymerization of trioxane with ethylene oxide, and is described as transacetalization [10]. The transacetalization may be either intermolecular or intramolecular, and it has consequences that will be discussed below.

Intermolecular transacetalization involves the continuous cleavage and reconstitution of polyoxymethylene chains, and is formulated as indicated in eq. (n) for trioxane/ethylene oxide copolymers.

This side reaction competes with the chain growth reaction, and owing to constant cleavage and reconstitution, the polymers obtained are chemically and molecularly very uniform. The chemical uniformity is particularly clear *e.g.* in the copolymerization of trioxane with ethylene oxide. During the induction period, which is appreciably longer than in the homopolymerization of trioxane, a copolymer that is soluble in trioxane is formed; though this copolymer already contains all the comonomer in the form of mono-, di-, and triethylene oxide units [10], the product obtained on complete conversion does not consist of a mixture of high ethylene oxide copolymer and homopolymer or of a block copolymer, but of a



(n)

random copolymer, in which the ethylene oxide units are roughly uniformly distributed over the polyoxymethylene chains [*]. Thus the prepolymer formed during the induction period is later cleaved and incorporated in a rather random manner into the growing polyoxymethylene chain; it is therefore equivalent to a comonomer that takes part in the polymerization throughout the entire reaction time. Consequently, the copolymerization equation proposed by *Mayo* and *Lewis* cannot be applied to the copolymerization of trioxane, *i.e.* the calculation and discussion of copolymerization parameters is meaningful only if the transacetalization can be completely suppressed.

Additional possibilities for the modification of polyoxymethylenes are offered by the fact that linear prepolymers can also be used as "comonomers" for copolymerization with trioxane [10].

Intermolecular transacetalization also affects the molecular uniformity of homopolymers or copolymers of trioxane. Since the growing chains are continuously reacting with completed polymer molecules, cationically polymerized polyoxymethylenes have a relatively narrow molecular weight distribution corresponding to the Schulz-Flory normal distribution [62] with a ratio $Pw/Pn = 2$, such as also occurs *e.g.* in polycondensations. Thus this is a special case, in which the molecular weight distribution of a step reaction (transacetalization) is superimposed on the molecular weight distribution of a chain reaction (polymerization). In fact, polytrioxanes prepared under conditions in which transacetalization is suppressed have a much broader molecular weight distribution [**].

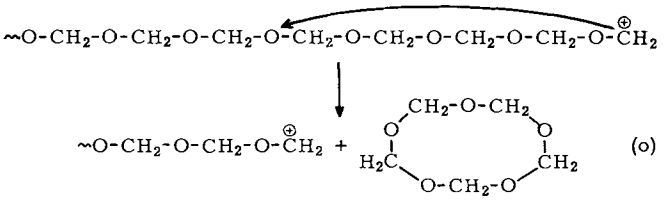
[61] *V. Jaacks* and *W. Kern*, Makromolekulare Chem. *83*, 71 (1965).

[*] A particularly suitable method for the determination of the sequence-length distribution is pyrolytic gas chromatography. See *K. H. Burg*, *E. Fischer*, and *K. Weissermel*, Makromolekulare Chem., in press.

[62] *H. L. Wagner* and *K. F. Wissbrun*, Makromolekulare Chem. *81*, 14 (1965).

[**] Unpublished results.

Intramolecular transacetalization in accordance with (o) leads to cyclic oligo- and/or polyoxymethylenes by reaction of the growing cation with an oxygen atom of the same macromolecule.



(o)

In addition to the lower members of the homologous series of cyclic oligomers of formaldehyde, such as tetroxane (1,3,5,7-tetraoxacyclooctane), pentoxane (1,3,5,7,9-pentaoxacyclodecane) and hexoxane (1,3,5,7,9,11-hexaoxacyclododecane), rings containing 15 CH_2O units have also recently been isolated and characterized [51]. Similarly, intramolecular transacetalization during the copolymerization of trioxane yields new cyclic formals of various ring sizes.

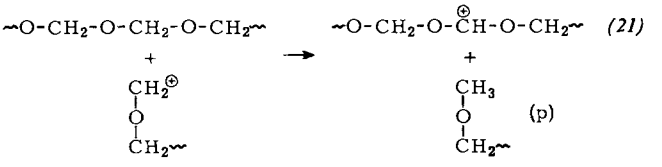
The transacetalization can be controlled within certain limits by variation of the reaction conditions. Since it proceeds *via* oxonium ions, it is temperature-dependent and so takes place particularly readily at high temperatures, both in the melt and in the solid state; it has not so far been detected at very low temperatures. Under comparable conditions, it is slower in solution polymerization than in bulk polymerization. Finally, the rate of transacetalization increases with increasing initiator concentration.

3.4.3. Hydride Shift

Transfer and rearrangement reactions involving the migration of a hydride ion have been observed in the cationic polymerization *e.g.* of styrene [63], 3-methyl-1-butene [64], and tetrahydrofuran [52,53]. The first indication of an initially inexplicable transfer reaction in the polymerization of trioxane was the observation that in most cases the number of initiator molecules does not correspond to the number of polymer molecules formed. One initiator molecule often leads to the formation of more than 20 polymer molecules [3], even when impurities that could cause transfer are carefully excluded [18].

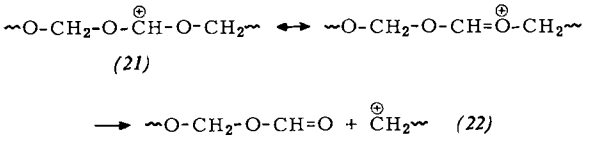
Further evidence was found during the quantitative investigation of the thermally stable polymer fraction, which amounts to up to 25 wt-% in the melt polymerization of trioxane. This discovery can be explained only by the presence of stable end groups in the polymer. Analytical studies finally showed that polytrioxane prepared in the absence of impurities contains approximately the same number of formate and methoxy end groups. The transacetalization that accompanies the polymerization ensures that these end groups are randomly distributed over the polymer molecules. It is therefore to be expected that polymer chains having two stable methoxy end groups will also be formed [18]. Polymers of this nature are stable even above 230 °C in the absence of oxygen, whereas polymers having formate end groups have only limited stability at high temperatures [60] and are readily degraded by alkali.

The results of these and other experiments strongly suggest the occurrence of a hydride shift during the polymerization of trioxane [18]. Thus an electrophilic attack by the polyoxymethylene cation leads to the removal of a hydride ion from a methylene bridge of its own or of an adjacent macromolecule (eq. (p)).



(21) (p)

The new cation *(21)* is resonance-stabilized and can be cleaved.



The hydride ion may be removed from any methylene bridge, *e.g.* from the middle of an adjacent polymer molecule, from the end of the same molecule, or even from trioxane. The predominant formation of the cation *(22)* may be regarded as verified by the observed decrease in the molecular weight and by the occurrence of formate end groups. However, it is also conceivable that the polymerization is directly initiated by the cation *(21)*; in this case, branched molecules containing ortho-ester groups should be formed.

Investigations on the stability of polyoxymethylenes under various conditions indicate that such ortho-ester groups could exist [65]; however, this grouping has not so far been detected, and its presence would be difficult to demonstrate.

3.5. Termination Reactions

According to the results obtained so far, no termination takes place in bulk polymerization of trioxane in the absence of reactive impurities, *i.e.* the polymer contains "living" polyoxymethylene cations. The evidence for this includes the fact that the hydride shift can be observed in the finished polymer even several hours after completion of the reaction.

We are grateful to Dr. K. H. Burg, Dr. K. H. Häfner, Dr. K. Küllmar, and Dr. C. Schott for years of helpful collaboration.

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Translated by Express Translation Service, London

[63] *P. H. Plesch*, J. chem. Soc. (London) *1953*, 1662.
[64] *J. P. Kennedy* and *R. M. Thomas*, Makromolekulare Chem. *53*, 28 (1962).
[65] *H. D. Hermann*, unpublished results.

Eliminations in Cyclic *cis-trans*-Isomers

BY W. HÜCKEL and M. HANACK [*]

Dedicated to my friend Georg Wittig on the occasion of his 70th birthday – (W. H.)

Solvolytic E1 eliminations from cis-alkylated p-toluenesulfonates of cycloalkanols (particularly menthols and decalols) lead almost exclusively to "Saytzeff hydrocarbons"; this fact is accounted for by the increase in the rate of solvolysis that results from the participation of the tertiary trans-hydrogen. The corresponding trans-alkylated compounds give mixtures. The solvolysis of these compounds is compared with the deamination of stereoisomeric primary amines and with the proton-catalysed dehydration of tertiary alcohols. E2 reaction of vicinally alkylated cycloalkane derivatives involves attack on the secondary hydrogen, and in the case of the trans isomers leads to pure "Hofmann hydrocarbon"; with the cis-isomers, competition occurs between the E1 and E2 reactions. The fact that the tertiary hydrogen is not attacked is explained by its anionic character. Reference is made to the competition of E1 and E2 reactions in exhaustive methylation.

Introduction

The first article dealing with the solvolysis of *p*-toluenesulfonates and chlorides of the menthol and decalol series [1] contained important information (from the preparative point of view) on the relationship between substitution and elimination processes, and it was recognized that E1 reactions and E2 reactions lead to fundamentally different results. Observations on this topic are scattered throughout the literature, with the result that many have been overlooked by various authors and their general significance has not been appreciated. The present review is an attempt to correct this situation.

All systematic investigations on E1 and E2 reactions have been based on comparison of the two contradictory elimination rules propounded by *Saytzeff* [2] and by *Hofmann* [3]. According to these rules, the course of elimination depends on the number of hydrogen atoms on the neighboring atoms.

The Saytzeff rule states that hydrogen is eliminated from the neighboring atom carrying the smallest number of hydrogen atoms, while according to the Hofmann rule elimination takes place from the neighboring atom with the largest number of hydrogen atoms [2, 3, 3a].

Other workers have tried to find a theoretical interpretation of this. We, on the other hand, have started by merely noting which of the two rules is obeyed. In certain cases it has been possible to gain an insight into the underlying principles on the basis of the reaction mechanism.

We have restricted our investigations to experiments with alicyclic compounds of known configuration and, in most cases, known conformation. The preferred carbon skeleton is the saturated cyclohexane ring, particularly in the menthane and decalin series. The standard substituents are an esterified hydroxyl group in the solvolysis experiments and an amino group in the deamination and exhaustive methylation experiments. The substituent is always situated on a secondary carbon atom, and may be eliminated either with a hydrogen atom from one of two CH_2 groups that are structurally not quite equivalent or with a hydrogen from either a CH_2 group or a CH group.

In previous investigations in the aliphatic series, a substituent on a secondary or tertiary carbon was usually given a choice of elimination with H from a CH_3 or from a CH_2 group. We decided to use cyclic compounds with five-, six-, or seven-membered rings; this has the advantage that the problem of simultaneous formation of *cis*- and *trans*-olefins does not arise. Moreover, in the comparison of stereoisomers, differences in electromeric and inductive effects, which might affect the rate and direction of elimination, are avoided.

[*] Prof. Dr. W. Hückel
Pharmazeutisch-Chemisches Institut der Universität
Wilhelmstr. 27
74 Tübingen (Germany)

Priv.-Doz. Dr. M. Hanack
Chemisches Institut der Universität
Wilhelmstr. 31
74 Tübingen (Germany)

[1] *W. Hückel, W. Tappe,* and *G. Legutke,* Liebigs Ann. Chem. *543,* 191 (1940).

[2] *A. M. Saytzeff,* Liebigs Ann. Chem. *179,* 296 (1875).

[3] *A. W. Hofmann,* Ann. Chem. Pharm. *78,* 253 (1851); *79,* 11 (1851).

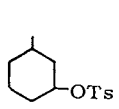
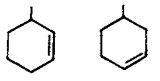
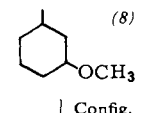
[3a] *W. Hückel:* Theoretische Grundlagen der organischen Chemie. 9th Edit. Akadem. Verlagsgesellschaft, Leipzig 1961, Vol. I, p. 759; *C. K. Ingold:* Structure and Mechanism in Organic Chemistry. G. Bell and Sons, London 1953, Chap. VIII, p. 427.

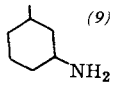
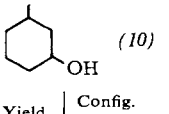
I. E1 Reactions and Substitutions in the Absence of a Neighboring Substituent

The difference between the rates of elimination in two alternative directions is smallest when the substituent is immediately flanked by two CH_2 groups, so that any dissymmetry is due only to more distant atoms. The relatively small importance of dissymmetry of this type when the configurations differ can be seen in the methanolysis of the *p*-toluenesulfonates *(1a)* to *(1d)* of the four stereoisomeric β-decalols. Substitution, which leads mainly to the methyl ether *(4)* having the opposite configuration [4], is accompanied by elimination to form a mixture of the Δ^1- and Δ^2-octalins *(2)* and *(3)* in a yield of 42 to 76.5%.

The total extent of elimination is greatest for the axial isomer *(1b)* of the *trans*-decalin series, though this is closely followed by the equatorial "extreme" *cis* form *(1c)* of the *cis*-decalin series. The hydrocarbon mixture contains more of the Δ^2-octalin in the *trans* series, as well as in the case of the *cis* isomer *(1d)* (though the preference for the Δ^2-octalin is less pronounced in this instance); *(1c)* gives more Δ^1-octalin. No relationship can be observed between the ratio Δ^1-octalin: Δ^2-octalin and the position (axial or equatorial) of the hydroxyl group.

Table 2. E1 reaction and substitution on methanolysis of 3-methylcyclohexyl *p*-toluenesulfonates [6] and on deamination of 3-methylcyclohexylamines by nitrous acid [7].

 (5)	 (6) : (7) (%)	(6) + (7) Total yield (%)	 (8) Yield (%)	Config. inversion (%)
cis-(5)	38 : 62	36	64	92
trans-(5)	29 : 71	58	42	96

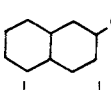
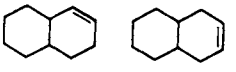
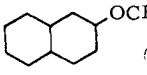
 (9)	(6) : (7) (%)	(6) + (7) Total yield (%)	 (10) Yield (%)	Config. inversion (%)
cis-(9)	33 : 67	34	96.6 [**]	10
trans-(9)	30 : 70	50 [*]	50 [***]	30

[*] Plus a trace of 1-methylcyclohexene.

[**] Plus 2% of di-(3-methylcyclohexyl) ether.

[***] Plus 2% of 1-methylcyclohexanol *(11)*; traces of bis-(3-methylcyclohexyl) ethers and 2- and 4-methylcyclohexanols.

Table 1. E1 reaction and substitution on methanolysis of the *p*-toluenesulfonates of the β-decalols [5].

	 (1)	M.p. (°C)	Configuration	 (2) : (3) (%)	(2) + (3) Total Yield (%)	 (4)	Total Yield (%)	Config. inversion (%)
trans	*(1a)*	75	$2^e9^c10^t$ (e) [*]	29 : 71	42	*(4a)*	58	> 99
	(1b)	53	$2^t9^c10^t$ (a)	33 : 67	76.5	*(4b)*	23.5	98
cis	*(1c)*	105	$2^e9^c10^c$ (e)	65 : 35	73	*(4c)*	27	98
	(1d)	18/31	$2^t9^c10^c$ (e)	44 : 56	63	*(4d)*	37	98

[*] e = hydroxyl group equatorial; a = hydroxyl group axial.

In 3-methylcyclohexyl *p*-toluenesulfonate *(5)*, the esterified hydroxyl group is again flanked by two CH_2 groups. On methanolysis, more cycloolefin is obtained from the *trans* isomer, which has an axial *p*-toluenesulfonate group, than from the *cis* isomer in which the *p*-toluenesulfonate group is equatorial. In both cases the methyl group directs the double bond into the Δ^3 position, but the effects differ in strength. The methyl ether *(8)* is again formed in an S_N2 reaction with the solvent [4], mainly with Walden inversion (Table 2).

This may be compared with the E1 deamination of the structurally analogous 3-methylcyclohexylamines by nitrous acid [7]. *trans*-3-Methylcyclohexylamine, in which the amino group is axial again gives more (and in this case much more) cycloolefin than the *cis* isomer, which has an equatorial amino group. However, the ratio of 3-methylcyclohexene *(6)* to 4-methylcyclohexene *(7)* is approximately the same (≈ 1:2); this suggests that the methylcyclohexenes are formed *via* the same planar ion.

The results of side reactions, which occur only to a small extent, are shown in Table 2. "Anomalous" substitution takes place only in the case of *trans*-3-methylcyclohexylamine, and leads mainly to the tertiary 1-methylcyclohexanol *(11)*. In normal substitution to form 3-methylcyclohexanol *(10)*, *trans*-3-methylcyclohexylamine gives 70% retention of configuration, and the *cis* isomer gives 90% retention.

In the deamination of β-decalylamines, elimination to form the octalin (except for one isomer $2^t9^c10^t$, axial, m.p. −1 °C)) is a minor side reaction, and has not yet been studied in any detail [7a].

II. E1 Reactions and Substitutions by Solvolysis in the Presence of an Adjacent Alkyl Group

Apparently anomalous substitutions and double bond shifts occur so regularly in vicinally alkylated *p*-toluenesulfonates *(12)* that it is necessary to extend

[4] *W. Hückel*, Nova Acta Leopoldina N. F., Vol. 30, No. 174 (1966).

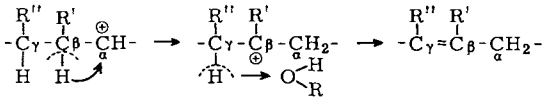
[5] *W. Hückel* and *D. Rücker*, Liebigs Ann. Chem. *666*, 30 (1963); *W. Hückel*, *R. Bross*, and *D. Rücker*, Liebigs Ann. Chem. *685*, 118 (1965); *W. Hückel* and *H. Waiblinger*, Liebigs Ann. Chem. *666*, 17 (1963).

[6] *W. Hückel* and *J. Kurz*, Liebigs Ann. Chem. *645*, 115 (1961).

[7] *W. Hückel* and *K.-D. Thomas*, Liebigs Ann. Chem. *645*, 177 (1961).

[7a] *W. Hückel*, Liebigs Ann. Chem. *533*, 15 (1937).

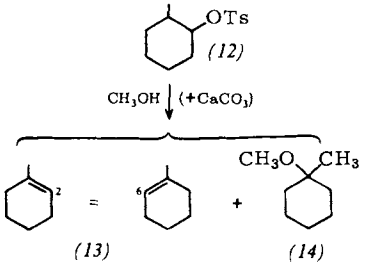
the scheme proposed by *Hughes*[8] for (E1 + S_N1) reactions in order to take into account, not only the neighbor C_β of the substituted C atom, but also the next atom but one, C_γ.



Extended Hughes scheme of E1 elimination and anomalous substitution on C_β.

With the aid of the extended Hughes scheme, it is possible to predict, not only normal substitution on C_α and the normal positioning of the double bond between C_α and C_β, but also the anionic migration of a β-hydrogen atom, with a consequent shift of the double bond into the position between C_β and C_γ.

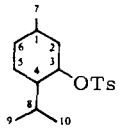
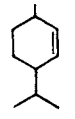
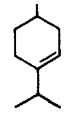
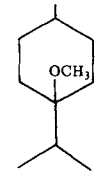
A hydride shift in accordance with the extended Hughes scheme is normally observed only with a tertiary β-hydrogen, and is recognized by the formation of a tertiary substitution product (substituent on C_β). Thus methanolysis of the *p*-toluenesulfonate of *cis*-2-methylcyclohexanol *(12)* gives a 27% yield of methyl ether, 85% of which is *(14)*. The principal methanolysis product (72%) is 1-methylcyclohexene *(13)*, and only 1% of 3-methylcyclohexene *(6)* is formed[9].



It is not known how much of the $\Delta^{1(2)}$-methylcyclohexene *(13)* is formed in the normal manner and how much is $\Delta^{1(6)}$-methylcyclohexene formed *via* the tertiary ion by migration of the double bond.

The course of the hydride shift can be determined in the menthane series. The tertiary 4-menthyl cation, like the 1-menthyl cation, is optically inactive. It can be formed from the 3-menthyl cation by hydride shift. A proton may be removed from C-3 or C-5 to give racemic Δ^3-menthene *(17)*, or from C-8 to give $\Delta^{4(8)}$-menthene *(18)*. (The corresponding $\Delta^{1(7)}$-methylenecyclohexane is not obtained from the *p*-toluenesulfonate of 2-methylcyclohexanol.) However, on solvolysis of all four menthyl *p*-toluenesulfonates *(15a)* to *(15d)*, the amount of *(18)* formed is always small. The quantity of tertiary ether *(19)* is greater, but only slightly so (maximum 13%, as the only S_N1 product from neomenthol). Thus evidence of the hydride shift is provided by the formation of *(18)* and *(19)* as well as of racemic *(17)* (Table 3).

Table 3. Methanolysis of the *p*-toluenesulfonates of the four stereoisomeric menthols [10].

	 *(15)* Tosylate of:	Configuration	Menthene : Methyl ether ratio	 *(16)* *cis* and *trans*	:	 *(17)* (Degree of racemization)	:	 *(18)* (%)	 *(19)* (%) [c]
(15a)	(−)-Menthol	1c3c4t	62:38	45	:	53 (18)	:	2	7
(15b)	(+)-Isomenthol	1c3t4c	85:15	49	:	49 (18)	:	2	29
(15c)	(+)-Neomenthol	1c3t4t	87:13	—	:	97 (22)	:	3	100 [a]
(15d)	(+)-Neoisomenthol [10b]	1c3c4c	85:15	—	:	88 (>50)	:	12	96 [b]

a] No secondary ether. [b] 4% of secondary ether. [c] Based on the total quantity of ether.

The connection between anomalous substitution and racemization in the menthane series was first recognized in the deamination of neomenthylamine, and was interpreted as resulting from a hydride shift[1]. The course of the reaction is admittedly more complicated[11] than was originally assumed.

The importance of the steric structure with regard to the direction of the E1 elimination from cyclic compounds can already be seen from the examples in the menthane series. From the behavior of many aliphatic halides and onium compounds *Ingold*[12] concluded that the Saytzeff rule is generally valid[14]. He explained this as resulting from a predominance of the electromeric over the inductive effect. *Ingold* further specified the "driving force" for the E1 elimination in accordance with the Saytzeff rule by formulation of hyperconjugation in the transition state[13]. Both the rule and the explanation have been accepted as generally valid[14].

It may, however, be objected that the Saytzeff rule was deduced empirically from observations on a structur-

[8] *E. D. Hughes*, J. Amer. chem. Soc. *57*, 708 (1935).

[9] *W. Hückel* and *A. Hubele*, Liebigs Ann. Chem. *645*, 115 (1961); *624*, 142 (1959).

[10a] *W. Hückel* and *C.-M. Jennewein*, Liebigs Ann. Chem. *683*, 100 (1965).

[10b] *W. Hückel* and *S. Gupté*, Chimia *20*, 276 (1966).

[11] *H. Feltkamp*, unpublished.

[12a] *C. K. Ingold*: Structure and Mechanism in Organic Chemistry. G. Bell and Sons, London 1953, p. 440 and 442.

[12b] *M. L. Dhar*, *E. D. Hughes*, and *C. K. Ingold*, J. chem. Soc. (London) *1948*, 2065, 2093.

[13] See [12a], p. 435; *E. D. Hughes* and *C. K. Ingold*, Trans. Faraday Soc. *37*, 675 (1941).

[14] *J. F. Bunnett*, Angew. Chem. *74*, 731 (1962); Angew. Chem. internat. Edit. *1*, 225 (1962).

ally unbalanced selection of compounds. The direction of elimination from halides was established only for tertiary halides in which there was a choice between adjacent CH_3 and CH groups; nearly all the secondary halides studied gave yields of less than 10% of an olefin, which was not examined further. The halides selected by *Ingold et al.* do not include the structural type $X-CHR-CH_2R$ corresponding to the secondary cycloalkanols with vicinal alkyl groups studied by us (Tables 4 to 8). Since many esters of secondary cycloalkanols do not obey the Saytzeff-Ingold rule, neither this rule nor its electronic interpretation can be universally valid, since *cis-trans* isomers would otherwise behave in the same manner, to a first approximation. Their fundamentally different solvolytic behavior, in elimination and in some substitution reactions, can be seen from a quick glance at Tables 4 to 8.

Table 4. Methanolysis of vicinally *cis*-alkylated cycloalkyl *p*-toluenesulfonates [15]. Quantity of Δ^1-"Saytzeff hydrocarbon".

Vicinal substituent	Δ^1-: Δ^3-Hydrocarbon ratios	Ratios of Hydrocarbons : Ethers
a) Cyclohexanols		
CH_3	99:1	73:27
C_2H_5	99:1	68:32
i-C_3H_7	100:0	88:12
t-C_4H_9 [16]	?	52:48
cyclo-C_6H_{11}	100:0	99:1
b) Menthols		
CH_3 (Neo-isocarvo; *cis*)	100:0	52:48
i-C_3H_7 (Neo-; *trans*)	97Δ^3 + 3$\Delta^{4,8}$:0	87:13
i-C_3H_7 (Neo-iso-; *cis*)	88Δ^3 + 12$\Delta^{4,8}$:0	85:15
c) α-Decalols		
$1^{c}9^{c}10^{c}$	87$\Delta^{1,9}$ + 13$\Delta^{9,10}$:0	86:14
$1^{t}9^{c}10^{t}$	75$\Delta^{1,9}$ + 24$\Delta^{9,10}$:1	76:24
d) Other cycloalkanols [5]		
CH_3 (7-Membered ring)	92:8	31:69
CH_3 (5-Membered ring)	92:8	40:60
i-C_3H_7(5-Membered ring)	99 (64$\Delta^{1,2}$+35$\Delta^{1,6}$):1	64:36

Table 5. Methanolysis of vicinally *cis*-alkylated cycloalkyl *p*-toluenesulfonates. Quantity of tertiary ether, in relation to the total quantity of ether formed.

Vicinal substituent	Ether	
	Total yield (%)	Molar ratio tertiary:others
a) Cyclohexanols		
CH_3	27	85:15
C_2H_5	32	100:0
b) Menthols		
CH_3 (Neo-isocarvo-)	48	70:30
i-C_3H_7 (Neo-)	13	100:0
c) α-Decalols		
$1^{c}9^{c}10^{c}$	10	100:0
$1^{c}9^{c}10^{t}$	24	92:8
d) Other cycloalkanols		
CH_3 (7-Membered ring)	69	40:60
CH_3 (5-Membered ring)	60	14:86
i-C_3H_7 (5-Membered ring)	36	57:43

[15] Tables 4 to 8 were compiled from: *W. Hückel et al.*, Liebigs Ann. Chem. *624* (1959) 142; *645*, 115 (1961); *672*, 62 (1963); *678*, 10 (1963); *685*, 105 (1965); *687*, 82 (1965); *687*, 102 (1965).

Table 6. Methanolysis of vicinally *trans*-alkylated cycloalkyl *p*-toluenesulfonates. Quantity of Δ^2-"Hofmann hydrocarbon" formed.

Vicinal substituent	Ratio of Δ^2-Hydrocarbon :Other hydrocarbons	Ratio of Hydrocarbons: Ethers
a) Cyclohexanols		
CH_3	72:28	47:53
C_2H_5	63:37	40:60
i-C_3H_7	53:47	64:36
t-C_4H_9 [16]	49:51	?
cyclo-C_6H_{11}	49:51	88:12
b) Menthols		
CH_3 (Isocarvo; *cis*)	66[*]:34	36:64
i-C_3H_7 (Menthol; *trans*)	46:54	62:38
i-C_3H_7 (Iso-; *cis*)	50:50	85:15
t-C_4H_9 (Isocarvo-; *trans*)	46:54	83:17
t-C_4H_9 (Neo-isocarvo; *cis*)	38:62 (32 *cis*-Δ^2 + 6 *trans*-Δ^2)	74:26
c) α-Decalols		
$1^{t}9^{c}10^{c}$	6$\Delta^{1,2}$:94	90:10
$1^{t}9^{c}10^{t}$	61$\Delta^{1,2}$:39	19:81
d) Other cycloalkanols		
CH_3 (7-Membered ring)	39:61	28:72
CH_3 (5-Membered ring)	0:100	25:75
i-C_3H_7 (5-Membered ring)	17:83	47:53

[*] Plus two unidentified hydrocarbons.

Table 7. Methanolysis of vicinally *trans*-alkylated cycloalkyl *p*-toluenesulfonates. Quantity of tertiary ether in relation to the total quantity of ether formed.

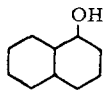
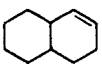
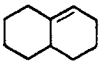
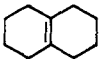
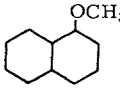
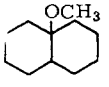
Tosylate of:	Ether	
	Total Yield (%)	Molar ratio tertiary : others
2-Methylcyclohexanol	53	6:94
2-Ethylcyclohexanol	60	30:70
Menthol	38	14:86
Isomenthol	15	30:70
α-Decalol ($1^{t}9^{c}10^{c}$)	10	66:34
α-Decalol ($1^{t}9^{c}10^{t}$)	81	< 1: > 99
2-Methylcycloheptanol	72	9:91
2-Methylcyclopentanol	75	70:30
2-Isopropylcyclopentanol	53	22:78

1. Vicinally *cis*-Alkylated Cycloalkyl *p*-Toluenesulfonates

All *cis*-alkylated cycloalkyl *p*-toluenesulfonates give more cycloolefin on solvolysis than the *trans* isomers, the cycloolefin being almost entirely that predicted by the Saytzeff rule. The mixture of cycloolefins obtained from *trans* *p*-toluenesulfonates contains two isomers, frequently in roughly equal quantities. This gives a *cis*-configuration rule for the solvolysis of vicinally alkylated cycloalkyl *p*-toluenesulfonates with adjacent alkyl groups. The hydride shift with simultaneous substitution is much more marked for *cis* than for *trans* isomers, as can be seen from the amount of tertiary ether formed (cf. Tables 5 and 7).

The α-decalols show that this *cis* rule depends on the configuration, and not on the conformation in the ground state. The equatorial *p*-toluenesulfonate of the "*cis*" alcohol *(20a)* from the *cis*-decalin series, like the axial *p*-toluenesulfonate of the "*cis*" alcohol *(20c)* from the *trans*-decalin series, gives almost exclusively

Table 8. Methanolysis products of the *p*-toluenesulfonates of the α-decalols. Quantity and percentage composition of the octalins and ethers.

 *(20)*	*(20a)*	*(20b)*	*(20c)*	*(20d)*
Mp. (°C)	93	55	49	62
Configuration	$1^{c}9^{c}10^{c}$ (e)	$1^{t}9^{c}10^{c}$ (e)	$1^{c}9^{c}10^{t}$ (a)	$1^{t}9^{c}10^{t}$ (e)
Total amount of hydrocarbon (%)	86	90	76	19
 *(21)*	< 1	6	1	61
 *(22)*	87	11	75	29
 *(23)*	13	82 (+ ? < 1)	24	10
Total amount of ether (%)	14	10	24	81
 *(24)*	Trace	34 (*cis*:*trans* ≈ 1:1) [*]	8 (1^{t}) [**]	96 (1^{c}) [**]:4 (1^{t})
 *(25)*	100 *cis* only	66 more *trans* than *cis*	92 *trans* only	Trace

[*] "*cis*" and "*trans*" refer to positions 9 and 10 of the skeleton.
[**] Inversion of the configuration.

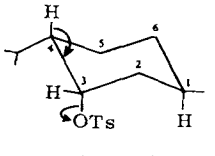
the Saytzeff hydrocarbon $\Delta^{1(9)}$-octalin *(22)*, which, together with the $\Delta^{9(10)}$-octalin *(23)* formed by hydride shift, amounts to > 99% of the total cycloolefin.

The *p*-toluenesulfonate of the normally equatorial "*trans*" alcohol *(20b)* of the *cis*-decalin series gives a 90% yield of cycloolefin, with unusually pronounced hydride-shift. This is an exception among the vicinally *trans*-alkylated cycloalkyl *p*-toluenesulfonates, for which there is no general rule. This is probably due to the flexibility, and the resulting variable conformation, of the *cis*-decalin skeleton, since the rigidly equatorial "*trans*" alcohol *(20d)* of the *trans*-decalin series behaves normally on solvolysis of its *p*-toluenesulfonate. It gives a mixture of $\Delta^{1(2)}$- and $\Delta^{1(9)}$-octalins, *(21)* and *(22)*, in a ratio of about 2:1; the principal reaction is a normal S_N2 reaction with inversion to form the secondary ether *(24)*, and S_N1 reaction with hydride shift to form the tertiary ether *(25)* takes place only to a very small extent. With the other isomers, the ether fraction consists mainly (66 to 100%) of the tertiary ether, of which two stereoisomers can be formed.

The vicinally *cis*-alkylated cycloalkyl *p*-toluenesulfonates are characterized, not only by the result of solvolysis, *i.e.* the formation of a large quantity of cycloolefin (of which 92 to 100% is Saytzeff hydrocarbon) accompanied by a largely anomalous S_N1 reaction, but also by the high rate of solvolysis, which is 20 to 100 times that of the isomeric *trans* *p*-toluenesulfonate[15]. This suggests that the solvolysis mechanisms are different.

It must be borne in mind that the formation of the Saytzeff hydrocarbon corresponds to *trans* elimination from *cis* *p*-toluenesulfonates and *cis* elimination from *trans* *p*-toluenesulfonates. In the case of the *cis* *p*-toluenesulfonates, it is independent of whether the tertiary hydrogen is axial or equatorial in the ground state, as has been known for some time for the *cis* alcohols of the *cis*- and *trans*-decalin series. The "extreme" *cis* form *(20a)* has an equatorial hydroxyl group, so that the vicinal tertiary hydrogen atom is *trans* and equatorial (*meso-trans* according to *Bredt*[17]); in the "*cis*" alcohol of the *trans* series, on the other hand, the two groups to be eliminated are axial. Both *(20a)* and *(20c)* solvolyse rapidly. Further examples were discovered later[18].

According to *Winstein*[19], the high solvolysis rate of vicinally *cis*-alkylated cycloalkyl *p*-toluenesulfonates



(26)

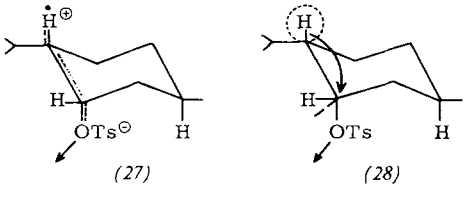
[16] *H. L. Goering* and *R. L. Reeves*, J. Amer. chem. Soc. *78*, 4931 (1956).
[17] *J. Bredt*, Liebigs Ann. Chem. *325*, 29 (1913).
[18] *W. Hückel* and *P. Heinzelmann*, Liebigs Ann. Chem. *687*, 82 (1965).
[19] *S. Winstein et al.*, J. Amer. chem. Soc. *74*, 1113 (1952).

is due to "participation" [*] of the adjacent hydrogen atom, though no details of the reaction products are given. This is illustrated for *trans*-elimination from neomenthyltosylate (formula *(26)*).

Nevertheless, *Winstein*'s view can also be interpreted on the basis of the reaction products. In the case of neomenthyltosylate, however, the formation of partially racemized Δ^3-menthene must be explained. Thus it is necessary to distinguish between the routes that lead to optically active menthene on the one hand and to the racemate on the other [20].

Winstein's model can be used directly for the route to optically active menthene. One need only assume that the electron pair that binds the tertiary hydrogen to C-4, and which assists in the removal of the acid residue from C-3, is fixed in the double bond between C-3 and C-4 (see formula *(27)*).

In the route leading to the racemate, the hydrogen atom is released together with its bonding electrons, and immediately attacks C-3 from the side opposite to the *p*-toluenesulfonate group, so assisting the release of the latter, while it is itself bound by S_N2 substitution. This yields the optically inactive 4-menthyl ion, which is stabilized either by loss of a proton from C-3 or C-5 to form racemic Δ^3-menthene, or by the solvent, which loses a proton, to form a derivative of 4-menthanol (cf. formula *(28)*).



(27) *(28)*

In *Winstein*'s model of neomenthyl *p*-toluenesulfonate, the arrangement of the leaving groups is *trans*-diaxial. This coplanar arrangement of the atoms taking part in the reaction, which satisfies the requirements for a four-center reaction [21], is not absolutely essential to intramolecular assistance of the elimination, *i.e.* to the formation of the optically active and the racemic Δ^3-menthene. The only requirement is that anionic hydrogen or a pair of electrons can attack C-3 from the rear. This is also possible in a *meso-trans* arrangement, but not in a *cis* or *meso-cis* arrangement such as exists in the *trans p*-toluenesulfonates.

The Saytzeff rule is almost always obeyed by the reactions of vicinally *cis*-alkylated *p*-toluenesulfonates of the cyclohexane series, since the solvolysis is intramolecularly assisted, and hence very fast. In the case of five-membered and seven-membered rings, the rates of hydrolysis of the vicinally *cis*-alkylated esters are only about seven times as fast and twice as fast, respectively, as those of the *trans* esters. The formation of the Saytzeff (Δ^1) hydrocarbon is again strongly favored, though less so than in the six-membered ring compounds [15].

2. Vicinally-*trans*-Alkylated Cycloalkyl *p*-Toluenesulfonates

Vicinally *trans*-alkylated cycloalkyl *p*-toluenesulfonates show no special preference for either of the two possible elimination routes (Table 6). The extent of anomalous substitution to give tertiary ethers with migration of a hydride ion always remains within reasonable limits (Table 7). The special position of the α-decalol *(20b)* has already been mentioned (Section II.1); this affects only the products, and not the kinetics. Except in the case of the *p*-toluenesulfonate of *(20b)*, the ratio of elimination to substitution products is always lower than with the *cis p*-toluenesulfonates. In many cases the frequencies of elimination of the hydrogen atom from the tertiary and from the secondary β-C atoms are approximately the same. Though the ratio of Δ^1- to Δ^2-hydrocarbon is occasionally as high as 72:28, one cannot say that the reaction follows the Hofmann rule, since the corresponding ratio of the reaction rates lies between 2:1 and 3:1 [*].

The formation of the Saytzeff hydrocarbon from *trans p*-toluenesulfonates must result from *cis*-elimination (cf. Section II.1) [**]. The *p*-toluenesulfonyl group is generally equatorial, while the *meso-cis* hydrogen is axial, and is therefore removed from the axial position. When secondary hydrogen is eliminated with roughly the same frequency as tertiary, it seems reasonable to assume (though there is no proof of this) that the secondary hydrogen is also removed from the axial position. In any case, statistical preference for the hydrogen of the CH_2 group rather than that of the CH group, which would favor elimination in accordance with the Hofmann rule, is of no importance.

In the solvolysis of the *trans p*-toluenesulfonates, the hydride shift involves the migration of the neighboring *cis*-hydrogen, together with its bonding electrons, from the tertiary carbon of the carbonium ion onto the adjacent carbon atom; this process is comparable with the anionic migration of a *cis*-methyl group in the Nametkin rearrangement [21a]. Hydrogen attached to a secondary carbon atom is not sufficiently anionic for

[*] *Winstein*'s term "participation" is generally used as synonymous with "assistance"; no exact definition is given for either of the two terms.

[20] *W. Hückel* and *C.-M. Jennewein*, Liebigs Ann. Chem. *683*, 100 (1965).

[21] For a detailed discussion of the applicability of the four-center principle, see *W. Hückel et al.*, Liebigs Ann. Chem. *624*, 142 (1959).

[*] For a long time, the only known solvolysis of a *trans*- *p*-toluenesulfonate was the ethanolysis of menthyl *p*-toluenesulfonate [1], which gave about 70% of Δ^3-menthene. This was described by *Winstein* as "a typical Saytzeff result" ([19], p. 1132), and *Ingold* also regarded this as characteristic of a solvolytic E1 elimination. However, even methanolysis gives only 54% of Δ^3-menthene.

[**] *Ingold* gives a plausible model, with a substantially planar carbonium ion, for a *cis*-elimination from the *meso-cis* position ("*syn*" position according to *Ingold*) on the cyclohexane ring.

[21a] *S. Nametkin*, Liebigs Ann. Chem. *432*, 207 (1923); *S. Nametkin* and *L. Brüssoff*, *ibid. 459*, 144 (1927); *J. Houben* and *E. Pfankuch*, *ibid. 489*, (1931); *J. Bredt*, J. prakt. Chem. [2] *131*, 145 (1931); *S. Nametkin*, Chem. J. Ser. A general. Chem. (Russ.) *4*, (66), 847 (1934); *J. J. Ritter* and *G. Vlases jr.*, J. Amer. chem. Soc. *64*, 583 (1942).

migration; thus there is no transition from the menthol to the carvomenthol series or *vice versa.*

The anomalies that are sometimes observed in eliminations from *trans* *p*-toluenesulfonates, which do not fit into the extended Hughes scheme (see Section I) [18], cannot be discussed in any detail at present, since too little is known about them.

Only a few solvolyses of *cis-trans* isomeric, vicinally alkylated cycloalkyl *p*-toluenesulfonates containing five-membered and seven-membered rings have been studied so far, and the results are shown in the tables. Mention should be made of the special case of *trans*-2-methylcyclopentyl *p*-toluenesulfonate, which differs from the other *trans* *p*-toluenesulfonates in that it gives only the Δ^1-cycloolefin together with appreciable quantities of tertiary ether.

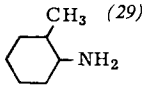
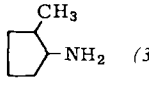
III. E1 Reactions in Deaminations

It was hoped that the deamination (by nitrous acid in dilute acetic acid) of cyclic primary amines having a neighboring substituent might yield more information than solvolysis about the direction of E1 eliminations from secondary ions because in this case the solvent is not directly involved in the ionization.

This hope was not fulfilled, since hydride shifts and similar anionic carbon shifts generally occur in the secondary ion before it is stabilized by loss of a proton to the solvent [22]. The only cases in which rearrangements do not take place, or occur only to a small extent, are those of the 2-methylcyclohexylamines *(29)* and the 2-methylcyclopentylamines *(30)*.

In addition to the Δ^1-hydrocarbon formed in accordance with the Saytzeff rule, the *cis* amines give not only the Δ^2-hydrocarbon, but also small quantities of isomers that have only been partly elucidated. *trans*-2-Methylcyclohexylamine *(29b)* yields 7% of ethylidenecyclopentane and a trace of vinylcyclopentane together with 72% of Δ^2-methylcyclohexene (cf. also Table 9). A comparison of the deamination of vicinally alkylated cycloalkylamines with the methanolysis of the *p*-toluenesulfonates of the alcohols having the same configuration shows that the hydride shift in the carbonium ion and the stabilization of the latter by loss of a proton to form the cycloolefin merely exhibit certain common features, but are in fact quite different. This is not surprising, since the solvation and energy conditions during the reaction are different. The small extent to which hydride shift takes place in the reactions of *trans*-2-methylcyclohexylamine *(29b)* and *trans*-2-methylcyclohexyl *p*-toluenesulfonate is surprising; the structure of the initially formed *trans*-2-methylcyclohexyl cation must be unfavorable for a hydride shift, since a considerable quantity of tertiary alcohol is obtained from all the other amines.

Table 9. Deamination of vicinally methyl-substituted cyclic primary amines with nitrous acid in acetic acid [23].

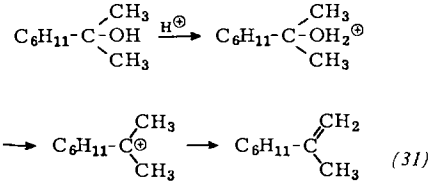
		Hydrocarbons		1-Methylalkanols
		Total yield (%)	containing Δ^1 (%)	total yield (%)
 *(29)*	*cis (29a)*	31	79	46
	trans (29b)	15	21	1
 *(30)*	*cis (30a)*	29	78	77
	trans (30b)	35	31	46

[22] See, *e.g.*, *W. Hückel* and *G. Ude*, Chem. Ber. *94*, 1036 (1961).

[23] *W. Hückel* and *K.-D. Thomas*, Liebigs Ann. Chem. *645*, 177 (1961); Chem. Ber. *96*, 2514 (1963).

IV. Proton-Catalysed E1 Reactions of Tertiary Alcohols

Tertiary alcohols are dehydrated by traces of concentrated sulfuric acid (about 0.001 wt-%) [24]. This reaction has been systematically studied only for dimethylcycloalkylcarbinols with three- to six-membered rings. The main product (90 to 97%) in every case is the isopropenyl compound. Thus in the stabilization of the intermediate carbonium ion by deprotonation, the proton is removed almost exclusively from a methyl group, *i.e.* in accordance with the Hofmann rule; practically no attack takes place on the tertiary hydrogen atom, and hydride shift occurs to only a small extent. Thus 1-cyclohexyl-1-methylethanol gives a 90% yield of 2-cyclohexylpropene *(31)* in accordance with the following E1 mechanism (3% of the products are isopropylidenecyclohexane, and 7% are endocyclic 1-isopropylcyclohexene formed by hydride shift).



(31)

There are one tertiary and six primary hydrogen atoms available for elimination from the carbonium ion; the corresponding statistical ratio of the reaction rates, *i.e.* 6:1, would correspond to 86% of the Hofmann hydrocarbon.

However, this calculation does not take into account the anionic migration of the tertiary hydrogen to $C^{\oplus}$. This makes the direct removal of the tertiary hydrogen as a proton even more difficult, and explains why the elimination is substantially in accordance with the Hofmann rule.

V. E2 Eliminations from Cycloalkyl *p*-Toluenesulfonates

In the study of E2 eliminations [25] leading to unsaturated hydrocarbons, we concentrated mainly on the elimination of a strong acid from its esters by strong bases, particularly by alkoxides. The results were compared with those of E1 eliminations during alcoholysis, and in some cases with exhaustive methylation and other eliminations, such as pyrolyses, which are not E2 reactions.

The bimolecular reaction begins with an attack by the base on a hydrogen atom. The removal of this hydro-

[24] *R. van Volkenburgh, K. W. Greenlee, J. M. Derfer*, and *C. E. Boord*, J. Amer. chem. Soc. *71*, 172 (1949); *G. Chiurdoglu* and *S. van Walle*, Bull. Soc. chim. belges *66*, 612 (1957).

[25] See [12a], p. 420, 421; *C. K. Ingold*, Proc. chem. Soc. (London) *1962*, 265; *J. Caspilla*, Chimia *18*, 37 (1964); [14].

gen atom as a proton is coupled with the release of the acid residue as an anion. This bimolecular process may occur in competition with other first and second order reactions. In eliminations with alkoxide in alcoholic solution, the competing reactions are solvolytic E1 elimination and S_N2 substitution. The accuracy of kinetic measurements is often not sufficient to distinguish simultaneously between bimolecular and monomolecular processes. Except in preliminary experiments, therefore, we made no attempt to detect competing reactions by determination of the reaction order.

We were able to compare and distinguish E2 and E1 reactions in the following cases. In the elimination of *p*-toluenesulfonic acid from vicinally alkylated cyclohexyl *p*-toluenesulfonates, the ratio of the isomeric hydrocarbons formed depends on the reaction conditions, which determine whether E2 or E1 elimination takes place or whether both reactions proceed simultaneously (see Table 10).

Table 10. Competition between E1 and E2 elimination in vicinally alkylated cycloalkyl *p*-toluenesulfonates. The amount of "Hofmann hydrocarbon" (3-alkylcycloolefin or Δ^1-octalin) is given as a percentage of the total amount of hydrocarbon.

Reaction type		E1	E1 + E2		
Reagent		CH_3OH	CH_3ONa	$i\text{-}C_3H_7ONa$	
2-Methylcyclohexanol	*cis*	1	7 (2.3)[*]	35	(10)
	trans	72	92 (2.3)	100	(7)
2-Methylcycloheptanol	*cis*	8		63	(7)
	trans	38		91	(7)
Menthol	$1^c3^c4^t$	46	100[**] 13		
Isomenthol	$1^c3^t4^c$	49	95.6 (10)	100[**] 13	
Neomenthol	$1^c3^t4^t$	0		45	10
α-Decalol (m.p. 49 °C)	$1^c9^c10^t$	1		67	(0.9)
α-Decalol (m.p. 62 °C)	$1^t9^c10^t$	61		77	(0.9

[*] The values in brackets signify wt.-%Na metal in methanol or isopropanol.

[**] With C_2H_5ONa (13 wt.-% Na in methanol).

The higher the alkoxide concentration, the higher is the ratio of Hofmann hydrocarbon to Saytzeff hydrocarbon; the proportion of Hofmann hydrocarbon can be as high as 100% in the case of the slowly solvolysing vicinally *trans*-alkylated cycloalkyl *p*-toluenesulfonates. It is therefore very probable that the E2 elimination, involving the adjacent CH_2 group, leads exclusively to the Hofmann hydrocarbon. The competing E1 elimination by alcoholysis and the S_N2 ether formation (cf. Section I [4]) become less important with decreasing ionizing power and dielectric constant of the alcohol ROH (replacement of CH_3OH by ROH). In order that the E2 reaction may be favored as strongly as possible in relation to the E1 reaction, the alkoxide concentration must be high and the alkyl group of the alkoxide must be as large and as highly branched as possible. Thus for E2 reactions, the order of preference is methanol < ethanol < isoamyl alcohol [26] ≈ isopropyl alcohol < t-butanol < 2-n-butylcyclohexanol [27]. By suppression of the E1 reaction, it is sometimes possible to avoid isomerization of intermediate carbonium ions.

The E2 reaction of slowly solvolysing esters of sulfonic acids at high alkoxide concentrations may be accompanied by cleavage of the O–S bond, with regeneration of the cycloalkanol:

$$\text{>C-O-SO}_2\text{R} \xrightarrow{\text{NaOR'}} \text{>C-OH} \xrightarrow{\text{HOR'}} \text{NaOH}$$

Even at high alkoxide concentrations, rapidly-solvolysed esters give the Saytzeff hydrocarbon as well as the Hofmann hydrocarbon. However, the quantity of the Hofmann hydrocarbon formed is so large as to indicate practically uniform E2 elimination, while the formation of the Saytzeff hydrocarbon is due to the solvolytic E1 elimination, which is not quite suppressed. The *p*-toluenesulfonate of the α-decalol having the configuration $1^c9^c10^t$ shows a surprising change in the direction of elimination by alkoxide. Even with only 0.9% of isopropoxide in isopropyl alcohol, the proportion of the Hofmann hydrocarbon ($\Delta^{1(2)}$-octalin) formed on solvolysis jumps from 1% to 67% [28], though the structure of the $1^c9^c10^t$-α-decalol is ideal for a diaxial *trans*-elimination of the tertiary hydrogen from C-9. The same alkoxide concentration is not sufficient to change the direction of elimination from the *p*-toluenesulfonate of $1^c9^c10^c$-α-decalol (m.p. 93 °C), which is solvolysed twice as rapidly as the $1^c9^c10^t$ isomer [28]. It is possible that in this case the E2 elimination affects the exposed equatorial tertiary hydrogen; however, the equatorial position of the ester group may be so unfavorable for the E2 elimination of secondary hydrogen that the fast E1 solvolysis still predominates (see below). E2 eliminations from other equatorial "*cis*" alcohols have not been studied as yet.

The *p*-toluenesulfonate of neomenthol, which has an axial *p*-toluenesulfonate group, gives 45% of *trans*-Δ^2-menthene with 8% of isopropoxide, while neomenthyl chloride with ethoxide gives only 25%. The partial racemization of the principal product, Δ^3-menthene, indicates that it is formed by an E1 reaction. The E2 mechanism is generally assumed to involve *trans*-elimination; however, this cannot be deduced from the formation of the Hofmann hydrocarbon. *Hückel* [1] explained the *trans*-elimination as being due to electrostatic repulsion of the alkoxide ion by the electronegative substituent, which hinders the approach of the ion on the *cis* side. Where *trans*-elimination is impossible, as in the case of β-hexachlorocyclohexane, a much higher activation energy is required for the *cis*-elimination [29].

[26] Practically camphor-free bornylene from bornyl chloride: *H. Meerwein* and *J. Joussen*, Ber. Dtsch. chem. Ges. *55*, 2531 (1922).

[27] *M. Hanack* and *R. Hähnle*, Chem. Ber. *95*, 191 (1962).

[28] *W. Hückel* and *D. Maucher*, Liebigs Ann. Chem. *645*, 115 (1961). The following correction is required on p. 115, Table 15, under "Ethanolysis": *cis*- (m.p. 93 °C) $\Delta^{1,2}$ 0, $\Delta^{1,9}$ 87, $\Delta^{9,10}$ 13%. *trans*-α (m.p. 49 °C) not investigated.

[29] *S. Cristol*, J. Amer. chem. Soc. *69*, 338 (1947); *S. Cristol*, *N. L. House* and *J. S. Meck*, J. Amer. chem. Soc. *73*, 674 (1951); *R. A. Pasternak*, Acta crystallogr. *4*, 315 (1951).

Ingold[30] used the four-center principle to explain the *trans* E2-elimination. In the case of cyclohexane derivatives, this means that the leaving group must be coplanar with the *trans* β-hydrogen atom, which is attacked by the proton acceptor.

The tertiary β-hydrogen is *trans* in neomenthol and *cis* in menthol; it is therefore eliminated from neomenthol to give the Saytzeff hydrocarbon, but not from menthol. Thus in menthol, the attack is directed exclusively toward the secondary *trans* hydrogen, which can assume a position that satisfies the requirements of the four-center principle[12b], though only in the energetically very unfavorable a,a,a conformation. As can be seen from molecular models, however, the axial position of the ester group and the β-hydrogen atom in molecules that can undergo E2 elimination can be so unfavorable energetically that this type of elimination cannot occur; examples are the α-decalols having the configurations $1^c9^c10^c$ (m.p. 93 °C) and $1^t9^c10^t$ (m.p. 62 °C). Thus the four-center principle cannot be regarded as a universal condition for an E2 reaction.

In any case, *trans*-elimination is facilitated by coplanarity of the appropriate groups, since in cases where the model shows that coplanarity is very unlikely, the molecule tries to evade the E2 reaction. In $1^c9^c10^c$-α-decalol, in which the axial hydroxyl group is hemmed in and sterically hindered by hydrogen atoms on more remote C atoms, the fast E1 elimination is not accompanied by E2 elimination, as it is in the reaction of $1^c9^c10^t$-α-decalol, in which the groups to be eliminated occupy the normal diaxial position. The hydroxyl group in the rigid $1^t9^c10^t$-α-decalol is equatorial; it can become axial only if at least one ring has the energetically unfavorable boat form, in which the hydroxyl group is also hindered by more distant hydrogen atoms[30a]. Since the *p*-toluenesulfonate is very stable to solvolysis, competition by the E1 reaction is less important in this case. However, the compound evades E2 elimination in 0.9% isopropoxide solution by undergoing cleavage of the O–S bond, with regeneration of the α-decalol (42% yield). Hydrocarbons are formed in a yield of only 58%, in which the proportion of the Hofmann hydrocarbon (Δ^1-octalin) has risen only to 77%, as against 61% in methanolysis (E1 reaction).

The same side reactions are observed with the *p*-toluenesulfonate of all-*cis*-3,5-di(t-butyl)cyclohexanol, in which the *p*-toluenesulfonate group is equatorial and is flanked by two CH_2 groups. In this case the two *cis*-t-butyl groups make a coplanar arrangement of the ester group and the *trans*-hydrogen impossible[31].

Ingold did not restrict his considerations to an E2 elimination from diaxial positions. The scheme given can be readily modified in such a way that it can also apply to elimination from the *meso-trans* position. Moreover, *Ingold* also gives another scheme for *cis*-E2-elimination, which is explicitly considered to be possible[32, 32a].

Our own observations indicate that E2 elimination always involves the secondary hydrogen; there is no reliable evidence of any attack on tertiary hydrogen. If there are two neighboring CH_2 groups available, more remote atoms have very little directing influence on the elimination, as in solvolysis. Accordingly, the addition of alkoxides in the β-decalol series has a very small, but definite effect on the ratio of Δ^1- to Δ^2-octalin during solvolysis; however, the E1 and E2-eliminations cannot be distinguished in this case (see Table 11). The result of the pyrolysis of the acetates, *i.e.* an intramolecular *cis*-elimination, which is not specific in a structural sense, is also shown for comparison.

Table 11. Elimination reactions of the *p*-toluene sulfonates and acetates of β-decalols. The proportions Δ^1-: Δ^2-octalin are listed [33].

	Configuration	Tosylate		Acetate Pyrolysis (550 °C)
		E1 with CH_3OH	E2 + (E1 ?) with i-C_3H_7ONa (10%)	
(1a)	$2^c9^c10^t$ (e)	29:71	25:75	57:43
(1b)	$2^t9^c10^t$ (a)	25:75	33:67	43:57
(1c)	$2^c9^c10^c$ (e)	65:35	72:28	56:44
(1d)	$2^t9^c10^c$ (e)	44:56	23:77	56:44

Though 10% isopropoxide solution leads almost exclusively to an E2 mechanism, this has a noticeable effect only in the *cis*-decalin series, where the Δ^1-: Δ^2-octalin ratio given by the *trans p*-toluenesulfonate is practically the reciprocal of the ratio obtained from the "extreme" *cis* isomer. On the other hand, no difference is found between these two isomers in the pyrolysis of the acetates, whereas a similar inversion of the ratio is found for the two isomeric *trans*-octalins. In the α-decalol series, the acetate of the "extreme" *cis* isomer (m.p. 93 °C), which has no *cis*-hydrogen in position 9, gives Δ^1-octalin in 100% yield. On the other hand, the acetate of *trans*-α-decalol (m.p. 62 °C), which has a *cis*-hydrogen on each side, gives a mixture of Δ^1- and $\Delta^{1(9)}$-octalin in the ratio 41:59; thus the tertiary hydrogen on C-9 is only slightly favored in relation to the secondary hydrogen on C-2.

Thus where there is no neighboring group to determine the direction of an elimination, this direction cannot be predicted since the effects of more distant atoms are largely unknown, though a steric effect can still be recognized.

VI. Exhaustive Methylation

Exhaustive methylation was long regarded as a typical E2 reaction, involving an attack by the hydroxide ion of the tertiary base on the *trans*-hydrogen of a β-C atom. It was discovered only a few years ago, by deter-

[30] *M. L. Dhar, E. D. Hughes, Ch. K. Ingold, S. Masterman, G. A. Maw,* and *L. I. Woolf,* J. chem. Soc. (London) *1948*, 2117.

[30a] Cf. *M. Hanack:* Conformation Theory. Academic Press, New York 1965, p. 180.

[31] *M. Hanack* and *K. W. Heinz,* unpublished.

[32] See [12a], p. 468, Fig. 35.-1 and 35.-2.

[32a] Cf. *C. H. De Puy, R. D. Thurn,* and *G. F. Morris,* J. Amer. chem. Soc. *84*, 1314 (1962).

[33] Earlier results, which appear to indicate that E2 eliminations in general proceed in a single direction ([1], survey on pp. 209–210), are superseded by these data [5].

mination of the order of the reaction [34], that a competitive E1 reaction may also take place, in which the trimethylamine is first split off. A proton is then removed from the remaining cation in a second step. This possibility had actually been considered previously [35]. Another competing reaction is α,β-elimination [36], but since this is a rare event, it will not be discussed here. The thermal decomposition of quaternary ammonium salts is very similar to that of sulfonium salts [37].

The E2 mechanism of exhaustive methylation causes vicinally *trans*-alkylated amines of the cyclohexane series to react mainly in accordance with the Hofmann rule, in analogy to E2 eliminations from esters by alkoxides. On the other hand, vicinally *cis*-alkylated cyclohexylamines react mainly by an E1 mechanism, and give the Saytzeff hydrocarbon. The E1 and E2 reactions again compete with each other.

Table 12. Results of the exhaustive methylation of vicinally alkylated amines of the cyclohexane series.

trans-Amine	Hofmann hydrocarbon (%)	
trans-2-Methylcyclohexylamine [37]	3-Methylcyclohexene	94
Menthylamine [39]	*trans*-Δ^2-Menthene	96
Isomenthylamine [39]	*cis*-Δ^2-Menthene	99
α-Decalylamine ($1^t9^c10^t$) [40]	*trans*-Δ^1-Octalin	100
cis-Amine	Saytzeff hydrocarbon (%)	
cis-2-Methylcyclohexylamine [38]	1-Methylcyclohexene	94–97
Neomenthylamine [39]	Δ^3-Menthene	89
Neoisomenthylamine [39]	Δ^3-Menthene, considerable excess	

More detailed investigations have been carried out only on menthylamine and neomenthylamine [34]. If the solution is sufficiently alkaline, the quaternary ammonium base formed from menthylamine gives 30% of *trans*-Δ^2-menthene by a bimolecular reaction, while 70% of the base escapes by cleavage into *N,N*-dimethylmenthylamine and methanol. The thermal decomposition of the quaternary iodide in water is first order and yields menthenes (Δ^2-: Δ^3-menthene = 32:68), following the Saytzeff rule.

The quaternary ammonium base from neomenthylamine undergoes a first-order decomposition to give a Δ^3-menthene that is 10% racemized, and which contains only 2% of Δ^2-menthene. Addition of hydroxide or alkoxide leads to an increase in the yield of Δ^2-menthene, but without an abrupt transition to the E2 mechanism. The rate constant of the E2 reaction can be extrapolated from the formation of menthene (which is not strictly second order), and the fraction of the neomenthylamine that reacts by an E2 mechanism can be calculated; this gives a Δ^3-menthene content of 88% of the total menthene when $OH^{\ominus}$ is added (1.36 M), and 65% when $OC_2H_5^{\ominus}$ is added (0.1 M). Thus the normal Hofmann hydrocarbon (Δ^2-menthene) content of 11% is the result of a competing E2 reaction, which unlike the cleavage of esters by alkoxide, does not proceed uniformly (if the calculation based on the extrapolated values is reliable).

The similarity of the direction of elimination from quaternary ammonium bases and *p*-toluenesulfonates having the C^3–C^4-*trans* configuration (cf. *(15)*) is the more remarkable in that the *p*-toluenesulfonates cannot have the same conformation as the ammonium bases, the $(CH_3)_3N^{\oplus}$ group of which is practically equivalent to a t-butyl group in its bulk and its low polarizability, and must therefore be equatorial. Consequently, coplanarity of the *trans* positions, which would favor the elimination, is impossible. This explains why the escape reaction accounts for 70% of the total conversion.

The bulk of the $(CH_3)_3N^{\oplus}$ group has not yet been taken into account in any of the discussions of exhaustive methylation. It necessitates modification of the explanation given by *Hughes* and *Wilby* [34] for the E1 elimination from the quaternary ammonium base of neomenthylamine, though the basic idea need not be entirely abandoned. This takes into account the intramolecular pressure exerted by the $^{\oplus}N(CH_3)_3$, which is assumed to be axial, on the adjacent axial hydrogen atoms. However, this pressure must also act in the equatorial position, for which the axial isopropyl group, which is *meso-cis* in neomenthyl derivatives, tends to eject trimethylamine. Though the isopropyl group in the quaternary base of menthylamine is also close to the $(CH_3)_3N^{\oplus}$ group, the *meso-trans* groups can move aside from one another as a result of intramolecular movements such as occur when the cyclohexane ring "flips", whereas *meso-cis* groups come closer together.

The reaction may be further facilitated by the electron pair bonding the tertiary hydrogen, which, as in the solvolysis of neomenthyl *p*-toluenesulfonate, is responsible for the Δ^3-double bond, provided that this leads to optically active Δ^3-menthene. This would be compatible with the small degree of racemization of the menthene, which, nevertheless, indicates moderate hydride shift.

In any case, *Hughes* appears to be correct in his basic idea that neomenthyltrimethylammonium hydroxide reacts in stages, the trimethylammonium group leaving first as a neutral molecule, and the tertiary hydrogen then being removed from the resulting cation by a proton acceptor. Nevertheless, it will be necessary to investigate the exhaustive methylation of vicinally *cis*-alkylated cyclohexylamines other than neomenthylamine in order to elucidate the competing reactions, particularly in connection with the calculation of the proportion of Saytzeff hydrocarbon on separation of the E1 and E2 reactions. Thus the attack of the proton acceptor on the tertiary hydrogen would be a process that has no parallel in

[34] *E. D. Hughes* and *J. Wilby*, J. chem. Soc. (London) *1960*, 4094.

[35] *W. Hückel*: Theoretische Grundlagen der organischen Chemie. 3rd Edit., Akad. Verlagsgesellschaft, Leipzig 1940, Chap. 7; 9th Edit., 1961, p. 534.

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[40] *W. Hückel*, *H. Naab*, and *A. Gercke*, Liebigs Ann. Chem. *502*, 136 (1933).

E2 eliminations from esters. Moreover, *cis-trans* isomeric amines with rigid five-membered rings and with flexible seven-membered rings, the exhaustive methylation of which has not been studied as yet, should also be used for comparison purposes.

VII. The Saytzeff and Hofmann Rules

Examination of the E1 and E2 eliminations described above in order to determine whether they obey one of the two rules shows that the relationships that have until now been regarded as generally valid [41] do not hold. E1 eliminations do not all follow the Saytzeff rule, nor do E2 eliminations from halides and esters of sulfonic acids, and the Hofmann rule in the E2 mechanism is not predominantly restricted to onium compounds. However, the behavior of the cycloalkane derivatives clearly shows that the steric structure of a molecule in the ground state can have a decisive effect on the mode of reaction.

The Saytzeff rule follows from those E1 eliminations that proceed rapidly with participation of tertiary hydrogen. When the steric conditions for the participation of tertiary hydrogen are not satisfied, the Saytzeff rule may still be more or less strictly obeyed if a hydride shift in the initially formed ion leads to a tertiary carbonium ion. The stabilization of this ion by loss of a proton to give a trisubstituted or tetrasubstituted "ethylene" then competes to a greater or lesser degree with stabilization of the initially formed primary or secondary carbonium ion by deprotonation, which leads to an olefin having a less highly alkylated double bond. For thermodynamic reasons, eliminations leading to equilibria obey the Saytzeff rule.

[41] See [14], p. 733, top of the left-hand column.

The Hofmann rule is obeyed with statistical probability when all the hydrogen atoms available for elimination are equally suitable; in the least favorable case, *i.e.* when there is a choice between a CH_3 and a CH_2 group, 2/3 of the product is Hofmann hydrocarbon. The relative yield of the Hofmann hydrocarbon can be higher if the reactivity increases with the number of protons on a group. This is so *e.g.* in the case of tertiary hydrogen, which has an anionic character owing to the inductive effect; this hydrogen remains intact in E2 eliminations, which are induced by a proton acceptor, and even in E1 reactions it may be taken up by the solvent to a smaller extent than "primary" or "secondary" hydrogen. Thus vicinally *trans*-alkylated and vicinally *cis*-alkylated cycloalkyl *p*-toluenesulfonates undergo *trans* E2-elimination involving the secondary hydrogen, even when the tertiary *trans*-hydrogen occupies the sterically favorable coplanar positions (see Section V).

If there is a choice between secondary and primary hydrogen, no generalizations can be made in view of the small statistical superiority of the primary hydrogen. The attack on a given hydrogen atom may be facilitated or hindered by steric factors; the elimination will be accelerated or retarded, depending on whether the hydrogen and the leaving group are more or less coplanar. The importance of electronic effects as compared with steric effects is unknown, since the steric factors can only be roughly estimated in general. The importance of bulk in E2 reactions in the aliphatic series has been discussed by *H. C. Brown* [42].

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The Chemistry of Bunte Salts

BY H. DISTLER [*]

Bunte salts can be obtained, not only from alkyl halides and sodium thiosulfate, but also from compounds containing activated multiple bonds, and sodium thiosulfate. The Bunte salts prepared by the new method, contrary to earlier observations, are cleaved by alkalis into the unsaturated starting compounds and sodium thiosulfate. This reaction, which is used for the fixation of unsaturated compounds (e.g. to cellulose), and other reactions of the Bunte salts are discussed. The industrial applications and biological properties of the Bunte salts are also mentioned.

1. Introduction

Alkali metal *S*-alkylthiosulfates and *S*-arylthiosulfates are known as "Bunte salts". Since sodium *S*-ethylthiosulfate [1] was first prepared by *Bunte* (1874), many articles dealing with the chemistry of this class of substances have been published [2].

When *Bunte* synthesized sodium *S*-ethylthiosulfate, which he obtained by heating an aqueous solution of sodium thiosulfate with ethyl bromide, his main

[*] Dr. H. Distler
Badische Anilin- & Soda-Fabrik AG., Oxyd-Abteilung
67 Ludwigshafen (Germany)

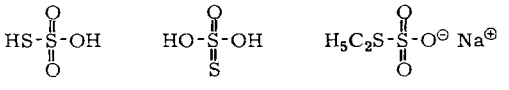
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object was to find conclusive proof of the constitution of thiosulfuric acid, which was still very uncertain at

$$C_2H_5Br + Na_2S_2O_3 \longrightarrow C_2H_5S_2O_3Na + NaBr \qquad (a)$$

that time. Of the possible isomeric forms *(1)* and *(2)*, the synthesis and chemical behavior of sodium *S*-ethylthiosulfate are compatible only with a derivative



(1) *(2)* *(3)*

of the structure *(1)*. This is shown in particular by *Bunte*'s observation that sodium *S*-ethylthiosulfate gives ethylthiol on acid hydrolysis.

$$\underset{(3)}{H_5C_2S_2O_3Na} + H_2O \xrightarrow{H^{\oplus}} NaHSO_4 + H_5C_2SH$$

The structure *(3)* was confirmed by a series of syntheses and secondary reactions, and also agrees with the results of UV [3], Raman, and IR measurements [4, 108].

The thiosulfate anion should contain different nucleophilic centers, and the nucleophilic strength should be greatest on the sulfur atom. It seemed desirable to check this experimentally, since it is well known that many nucleophiles, *e.g.* thiolate, add smoothly to compounds containing activated double bonds. The addition of thiolate ion to vinylsulfonic acid derivatives may be cited as an example [eq. (b)] [5].

$$R'-O-SO_2-CH=CH_2 + RS^{\ominus} \longrightarrow [R'-O-SO_2-\overset{\ominus}{C}H-CH_2-S-R] \xrightarrow{+H^{\oplus}} R'-O-SO_2-CH_2-CH_2-S-R \qquad (b)$$

We found that, in general, the addition of thiosulfate ions to vinylsulfonic acid derivatives proceeds smoothly and almost quantitatively in accordance with equation (c), to give Bunte salts *(4)* that crystallize well from water. The same reaction conditions were then used in an attempt to add thiosulfate ion to other

$$R'-O-SO_2-CH=CH_2 + S_2O_3^{2\ominus} \longrightarrow [R'OSO_2-\overset{\ominus}{C}H-CH_2-\overset{\ominus}{S_2O_3}] \xrightarrow{H^{\oplus}} \underset{(4)}{R'OSO_2-CH_2-CH_2-S_2O_3^{\ominus}} \qquad (c)$$

compounds containing activated double bonds, such as acrylic and methacrylic acids and their derivatives, as well as methyl vinyl ketone. *Kerber* and *Starnick* [6] carried out an independent study of the direct addition of sodium thiosulfate to compounds containing activated double bonds and obtained identical results.

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These authors ultimately extended the method to compounds containing activated triple bonds, which give Bunte salts *(5)* containing a C–C double bond.

$$R-CO-C\equiv CH + S_2O_3^{2\ominus} \longrightarrow [R-CO-\overset{\ominus}{C}=CH-\overset{\ominus}{S_2O_3}] \underset{OH^{\ominus}}{\overset{H^{\oplus}}{\rightleftharpoons}} \underset{(5)}{R-CO-CH=CH-S_2O_3^{\ominus}} \qquad (d)$$

In the study of the reactions of Bunte salts obtained by the direct addition of thiosulfate to activated multiple bonds, a surprising result was obtained on cleavage with aqueous alkali. Acid hydrolysis of Bunte salts yields thiols [1], alkaline degradation was reported to yield sodium sulfite [7, 8], alkylsulfenic acids, alkylsulfinic acids, disulfides, thiocarboxylic acids [9, 10], *etc.* However, we have found that Bunte salts obtained by direct addition of thiosulfate to activated multiple bonds are converted back into the

$$R-CH_2-CH_2-S_2O_3^{\ominus} \xrightarrow{OH^{\ominus}} [R-\overset{\ominus}{C}H-CH_2-\overset{\ominus}{S_2O_3}] + H_2O \longrightarrow R-CH=CH_2 + S_2O_3^{2\ominus} \qquad (e)$$

unsaturated starting compounds on treatment with aqueous alkalis. This behavior is particularly interesting and significant for the fixation of unsaturated compounds on fibers, *e.g.* cellulose.

2. Methods for the Preparation of Bunte Salts

a) Bunte Salts from Alkyl Halides and Alkali Metal Thiosulfate

The original method [1] for the synthesis of sodium *S*-alkylthiosulfates consists in the reaction of alkyl halides with sodium thiosulfate in aqueous solution at high temperature [see equation (f)].

$$RX + Na_2S_2O_3 \longrightarrow R-S_2O_3^{\ominus}Na^{\oplus} + NaX \qquad (f)$$

This method, which was frequently used (see [1, 2, and 11–18]), was extended to the preparation of Bunte salts

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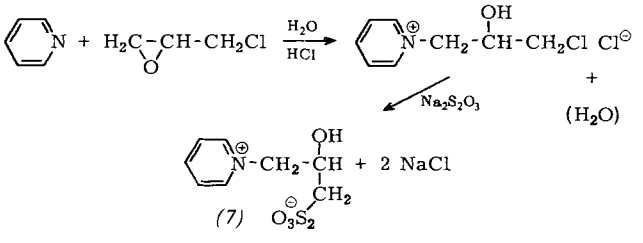
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from secondary alkyl halides [19,13,20–22]. Tertiary alkyl halides apparently do not react with sodium thiosulfate. *Lecher* and *Hardy* [23] found it advantageous to use thallium(I) thiosulfate instead of sodium thiosulfate, since the isolation of the readily soluble Bunte salt is facilitated by the low solubility of the thallium chloride formed.

Even alkyl halides RX with a very wide variety of substituents in the residues R react with sodium thiosulfate – generally without side reactions. For example, alkyl halides that also contain primary [23–27], secondary [22,28], or tertiary amino groups [16,27,20,22,23] can be converted into Bunte salts. These can sometimes be isolated as inner salts *(6)* [160].

$$Cl{-}CH_2{-}CH_2{-}NH_3Cl + Tl_2S_2O_3 \longrightarrow \underset{(7)}{H_3\overset{\oplus}{N}{-}CH_2{-}CH_2{-}S_2O_3^{\ominus}} + 2TlCl$$
(6)

Betaine-like compounds can also be obtained from pyridine, chloroepoxypropane, and sodium thiosulfate [29].



Halogenated fatty acid derivatives of amines [30,31,15] also undergo this reaction. This class of substances was extensively studied in connection with the synthesis of thioctic acid (lipoic acid) [32–35] and its intermediates [36–39]. Dyes containing thiosulfate groups, which may carry various substituents, are being produced on the industrial scale [40–60]. It is reported [61] that sodium thiosulfate reacts only with terminal halogen atoms in polychlorinated hydrocarbons. Chlorinated ethers [62–65] and thioethers [66,67] as well as various substituted benzyl halides [68,69] also react under the classical conditions of the synthesis of Bunte salts.

The alkyl halide is made to react with aqueous sodium thiosulfate solution, usually in the presence of a solubilizing agent such as methanol or ethanol. The reaction is usually complete after one or more hours under reflux. Dioxane may also be advantageously used as the solvent in some cases [70]; aqueous acetic acid has been recommended in particular for aminoalkyl halides [20]. Prolonged heating should be avoided. The reaction mixture generally becomes homogeneous when the reaction is complete. The course of the reaction can be readily followed by determination of the thiosulfate. Isolation of the product is occasionally hindered by the sodium chloride formed in the reaction. The Bunte salts can be purified conveniently by hot extraction with alcohol, in which most of them are readily soluble.

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b) Bunte Salts from Disulfides and Alkali Metal Bisulfite

The reaction of a disulfide with sulfite is reversible, as indicated in equation (g) [71–73].

$$R{-}S{-}S{-}R + SO_3^{2\ominus} \rightleftharpoons RS^{\ominus} + R{-}S_2O_3^{\ominus} \qquad (g)$$

The equilibrium can be displaced in favor of the formation of Bunte salts by the addition of oxidizing agents.

$$R{-}S{-}S{-}R + 2\,SO_3^{2\ominus} \xrightarrow{-2e^{\ominus}} 2\,R{-}S_2O_3^{\ominus}$$

This reaction is utilized in the determination of cysteine and cystine with "Folin's reagent", a phosphorus-tungsten heteropolyacid [74].

Bunte salts have also been prepared from aromatic disulfides and in particular from amino-substituted disulfides and sodium or potassium bisulfite [75, 76]. Nitro-substituted aromatic disulfides are reported to react similarly and to give excellent yields; depending on the oxidation potential of the intermediate thiol, sodium bisulfite itself can act as the oxidizing agent, promoting almost complete Bunte-salt formation. The course of the reaction can be explained to some extent by the scheme proposed by *Lecher* and *Hardy* [23],

$$4\,R{-}S{-}S{-}R + 4\,KHSO_3 \quad 4\,RSH + 4\,R{-}S_2O_3K \qquad (h)$$

$$4\,RSH + 2\,KHSO_3 \rightarrow 2\,R{-}S{-}S{-}R + K_2S_2O_3 + 3\,H_2O \qquad (i)$$

$$2\,R{-}S{-}S{-}R + 6\,KHSO_3 \rightarrow 4\,R{-}S_2O_3K + K_2S_2O_3 + 3\,H_2O$$

in which the bisulfite, as the oxidizing agent, is brought into the correct relationship with the thiol in equation (i). This would readily explain the very good yields of Bunte salts in the reaction of aromatic disulfides with bisulfites, even in the absence of air [23].

c) Bunte Salts from Thiols and Alkali Metal Sulfites in the Presence of an Oxidizing Agent

The reaction of thiols with sulfurous acid in the presence of an oxidizing agent, *e.g.* elementary iodine, gives the desired Bunte salts only in poor yields [77].

$$RSH + SO_3^{2\ominus} \xrightarrow{-2e^{\ominus}} R{-}S_2O_3^{\ominus} + H^{\oplus}$$

In reactions with aromatic thiols, *Bernthsen* [78] used air as the oxidizing agent. "Oxidative sulfitolysis", *i.e.* the reaction of sulfurous acid with thiols or disulfides [71, 72], has been studied in protein chemistry with particular reference to the quantitative colorimetric determination of cysteine and cystine with Folin's reagent [74].

d) Bunte Salts from Thiols and Chlorosulfonic Acid, Sulfur Trioxide, or SO_3-Pyridine Complexes

Aliphatic thiols, preferably with long (C_8–C_{18}) branched or unbranched chains, react at low temperatures with chlorosulfonic acid in the presence of an inert diluent such as ether in accordance with reaction (j). Subsequent neutralization with alkali metal hydroxide or ammonium hydroxide yields Bunte salts having surface-active properties [79].

$$RSH \xrightarrow[-HCl]{+\,ClSO_3H} R{-}S_2O_3H \xrightarrow{MOH} R{-}S_2O_3M + H_2O \qquad (j)$$

When sulfur trioxide is used instead of chlorosulfonic acid as the sulfating agent, compounds of the same type are obtained at −78 °C in difluorodichloromethane [80]:

$$RSH + SO_3 \longrightarrow R{-}S_2O_3H$$

At higher temperatures the thiol is oxidized [81] to the disulfide, *e.g. (8)*.

$$2\,C_6H_5SH + SO_3 \longrightarrow (C_6H_5S)_2 + SO_2 + H_2O \qquad (8)$$

SO_3-pyridine complexes [82] give quantitative yields of pyridinium *S*-arylthiosulfates such as *(9)* [83, 114].

$$C_6H_5SH + SO_3{\cdot}C_5H_5N \longrightarrow C_6H_5{-}S_2O_3^{\ominus}C_5H_6N^{\oplus} \qquad (9)$$

e) Bunte Salts from Sulfenyl Chlorides or Amides and Sulfurous Acid

Amides of aromatic sulfenic acids react with sulfurous acid to form *N*-substituted ammonium *S*-arylthiosulfates *(10)* [84].

$$Ar{-}S{-}NRR' + H_2SO_3 \longrightarrow Ar{-}S_2O_3^{\ominus}\,{}^{\oplus}NH_2RR' \qquad (10)$$

In most cases it is sufficient merely to digest the amide in concentrated aqueous sulfurous acid with gentle warming. The Bunte salts are readily obtainable by treatment of the ammonium salts *(10)* with alkali metal hydroxides.

Aromatic sulfenyl chlorides [85] react with alkali metal sulfite in aqueous media to form Bunte salts *(11)*.

$$C_6H_5S{-}Cl + Na_2SO_3 \longrightarrow C_6H_5S_2O_3Na + NaCl \qquad (11)$$

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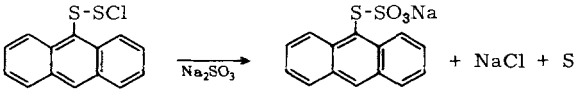
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[85] *Geigy*, Dissertation, Universität München, 1923.

The method is not generally applicable, and is restricted to relatively stable sulfenyl chlorides.

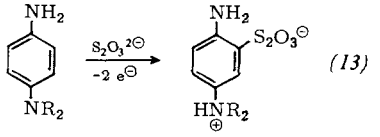
9-Anthryl dithiochloride, which is similar in structure, and which is readily obtainable from anthracene and sulfur monochloride, is converted by aqueous sodium sulfite solution into the sodium salt of *S*-(9-anthryl)-thiosulfuric acid *(12)*, with separation of elementary sulfur [86].



(12)

f) Bunte Salts from Aromatic 1,4-diamines and Thiosulfuric Acid in the Presence of an Oxidizing Agent

Bernthsen [78] observed that in the presence of aluminum thiosulfate and dichromate in acid solution, *p*-dimethylaminoaniline reacts to form *S*-(2-amino-5-dimethylammoniophenyl)thiosulfate *(13)*.



(13)

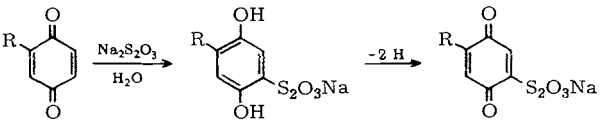
R = CH_3

The same inner salt is obtained by the reaction of 4-nitroso-*N*,*N*-dimethylaniline with aqeous thiosulfuric acid. In this case the nitroso group evidently brings about the substitution of the aromatic amine by thiosulfate [87,88].

The Bernthsen method has been studied for a number of 1,4-phenylenediamines, and has also been extended to related amines [89–92]. Di- and tetrathiosulfates of 1,4-phenylenediamine can be prepared by addition of the oxidizing agent and thiosulfate [93] in a suitable excess.

g) Addition of Thiosulfate to Quinones

p-Quinones add sodium thiosulfate in the presence of aqueous acetic acid [88,94,95] to give the sodium salts of substituted *S*-(2,5-dihydroxyphenyl)thiosulfuric acids *(14)*.



(14)

The reaction is applicable to quinones in general [96], including 1,4-naphthoquinones [88]. The Bunte salts *(14)* can be dehydrogenated under mild conditions to quinonethiosulfates [88].

h) Addition of Thiosulfate to Divinyl Sulfone

Sodium thiosulfate adds to divinyl sulfone in aqueous bicarbonate solution [97,98].

$$O_2S(CH{=}CH_2)_2 \xrightarrow[H_2O]{Na_2S_2O_3} O_2S(CH_2{-}CH_2{-}S_2O_3Na)_2$$

(15)

Because of the sensitivity of the Bunte salt *(15)* toward alkali, the reaction is best carried out in the presence of carbon dioxide. Dyes with vinyl sulfone residues have recently been converted into Bunte salts under similar conditions [99]. Under conditions analogous to those suggested by *Stahmann et al.* for the formation of Bunte salts from divinyl sulfone [97], aromatic vinyl sulfones can be converted into arylsulfonylethylthiosulfuric acids or their alkali metal salts [100]. They are much more stable toward alkalis than the sulfates of similar structure.

i) Reaction of Epoxyalkanes with Sodium Thiosulfate

Whereas 1,2-epoxyalkanes generally react with sodium bisulfite or thiosulfate with ring cleavage to form derivatives of 2-hydoxyethanesulfonic acid (isethionic acid) [101,102], cases have also been reported in which epoxyalkanes react with thiosulfate in the neutral or weakly alkaline range to give *S*-(2-hydroxyalkyl)thiosulfates [103,104]. An example of such a reaction is shown in equation (k).

$$H_2C\text{-}CH\text{-}CH_2Cl \xrightarrow[H_2O]{Na_2S_2O_3} ClCH_2\text{-}\underset{OH}{CH}\text{-}CH_2\text{-}S_2O_3Na \qquad (k)$$

[86] *P. Friedländer* and *A. Simon*, Chem. Ber. *55*, 3969 (1922).

[87] *M. T. Bogert* and *J. A. Updike*, J. Amer. chem. Soc. *49*, 1373 (1927).

[88] *G. Heller*, J. prakt. Chem. *108*, 257 (1924).

[89] *A. Bernthsen*, Chem. Ber. *25*, 3128 (1892).

[90] *A. Weinberg*, Chem. Ber. *25*, 1610 (1892).

[91] *M. T. Bogert* and *M. G. Sevag*, J. Amer. chem. Soc. *53*, 660 (1931).

[92] *J. J. Levkoev, N. N. Sveshnikov, J. N. Gorbacheva, N. S. Barvyn*, and *T. V. Krasnova*, Ž. obšč. Chim. *24*, 280 (1954); Chem. Abstr. *49*, 4627 (1955).

[93] *A. G. Green* and *A. G. Perkin*, J. Chem. Soc. (London) *83*, 1201 (1903).

[94] *W. Alcalay*, Helv. chim. Acta *30*, 578 (1947).

[95] BASF, German Pat. 175070 (1905).

[96] *M. T. Bogert* and *H. P. Howells*, J. Amer. Chem. Soc. *52*, 837 (1930).

[97] *M. A. Stahmann, C. Golumbic, W. H. Stein*, and *J. S. Fruton*, J. org. Chemistry *11*, 719 (1946).

[98] *G. C. Tesoro* and *D. Ferry*, US.-Pat. 3153077 (Oct. 13, 1964), (Stevens and Co.).

[99] Farbwerke Hoechst AG., Belg. Pat. 650713 (July 17, 1964).

[100] *F. Meininger* and *E. Hoyer*, German Publ. Pat. Appl. 1204666, Farbwerke Hoechst AG. (Oct. 12, 1963).

[101] *C. C. J. Culvenor, W. Davies*, and *N. S. Heath*, J. chem. Soc. (London) *1949*, 278.

[102] *F. Webel*, German Pat. 569148 (1931), I.G.-Farben; *W. M. Lauer* and *A. Hill*, J. Amer. chem. Soc. *58*, 1873 (1936).

[103] *Van R. Gaertner*, US.-Pat. 2921083 (Jan. 12, 1960); Chem. Abstr. *54*, 9331 (1960).

[104] *P. Schlack*, German Pat. 865597 (Feb. 2, 1953); Chem. Abstr. *48*, 10049 (1954).

j) Addition of Thiosulfate to Activated Multiple Bonds

With few exceptions, *e.g.* the preparation of *S*-2,2,2 - trifluoro - 2 - (trifluoromethyl)ethylthiosulfate $[(F_3C)_2CH-S_2O_3Na]$ [105], which was obtained from hexafluorothioacetone and sodium bisulfite, the methods described in Sections 2a–2i for the synthesis of Bunte salts have been in use for some time.

We have discovered a new, simple method for the preparation of Bunte salts *i.e.* the addition of thiosulfate in aqueous solution to compounds containing activated double bonds, in accordance with reaction (l).

$$R-CH=CH_2 + S_2O_3^{2\ominus} \underset{aq.}{\rightleftharpoons} [R-\overset{\ominus}{C}H-CH_2-S_2O_3^{\ominus}] \underset{OH^{\ominus}}{\overset{H^{\oplus}}{\rightleftharpoons}} R-CH_2-CH_2-S_2O_3^{\ominus} \quad (l)$$

The discovery of this method resulted from consideration of the reactivity of the thiosulfate ion. It had been recognised even by *Bunte* [1] that thiosulfate must contain centers of differing reactivity, since only *S*-alkyl thiosulfates are obtained with alkyl halides [*]. A simple model shows that the four nucleophilic centers of the thiosulfate ion differ in their hydration sheath in aqueous solution (Fig. 1).

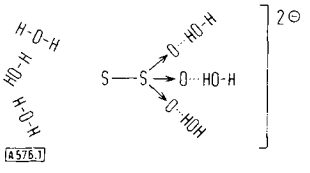
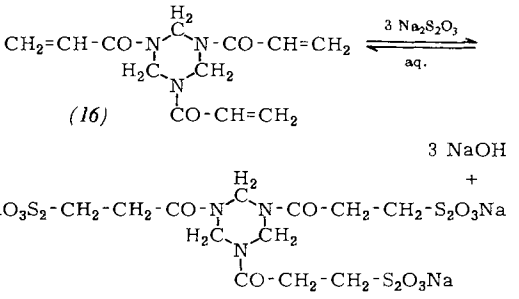


Fig. 1. Model representation of the solvation of the thiosulfate ion.

Whereas the oxygen atoms of the anion form hydrogen bonds with the water molecules, so that a structured and relatively stable solvation sheath is built up in the neighborhood of the three oxygen atoms, only a labile hydration sheath is found in the vicinity of the sulfur, owing to the low tendency of the latter to form hydrogen bonds. Thus reactions will take place preferentially on the S atom, where the hydration sheath is most easily stripped off.

Consequently, in nucleophilic substitutions such as equation (a) or in the nucleophilic addition of the thiosulfate ion to activated multiple bonds [*e.g.* equations (c) and (d)], the sulfur atom of the solvated anion reacts preferentially.

Examples of compounds containing activated double bonds that give Bunte salts on reaction with thiosulfate are derivatives of acrylic and α-methacrylic acids, vinylsulfonic acid, and methyl vinyl ketone. The applicability of the method has already been confirmed with a large number of monomers [107]. Polyunsaturated compounds such as the hexahydrotriazine derivative *(16)* [147] or the resorcinol ester of bisvinylsulfonic acid [5] also add on one or more thiosulfate ions. The solubility of *(16)* ("triacrylformal") in water is greatly improved by the introduction of one, two, or three thiosulfate groups.

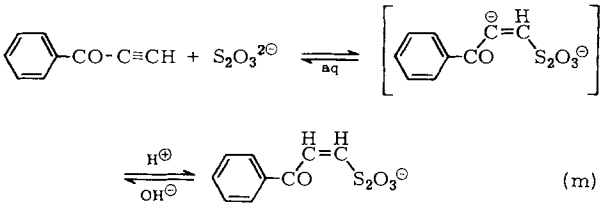


(16)

The reaction is generally carried out at pH = 3–9, and preferably in neutral solution at 60–100 °C. Since one mole of alkali is liberated for every mole of thiosulfate used, preparations are carried out at pH = 6–8, this pH value being maintained by the addition of an acid.

At lower pH values and at temperatures between 60 and 80 °C, the thiosulfate begins to decompose. If the addition of the thiosulfate is not controlled by introduction of an acid, the reaction immediately stops. It has been found very advantageous to use a weak acid such as acetic or propionic acid, since it is then possible to work in acetate buffer, in which both thiosulfate and the Bunte salt are stable. Solvents such as methanol or ethanol can be advantageously used for the reaction of compounds that are sparingly soluble in water. The reaction can also be carried out in fused hydrated sodium thiosulfate, in the absence of water or other solvents. Iodometric titration may be used to follow the course of the reaction (time 1–2 hours).

According to *Kerber* and *Starnick* [109], the addition of thiosulfate to compounds containing activated triple bonds can be carried out under similar conditions. The reaction of 1-phenyl-2-propyn-1-one *(17)* may be assumed to proceed in accordance with equation (m).



(m)

The resulting Bunte salts occur mainly as *cis* compounds, and are remarkable in that they contain the first known example of a thiosulfate group directly attached to an olefinic C-atom (cf. [2], page 74). *Kerber* and *Starnick* observed no further reaction of the unsaturated Bunte salts with thiosulfate.

3. Reactions of Bunte Salts

The principal reactions of Bunte salts have been described in detail by *Milligan* and *Swan* [2]; the present discussion will therefore be confined to more recent work. Bunte salts resulting from the nucleophilic addition of thiosulfate to activated multiple bonds exhibit a particularly interesting behavior in alkaline media. These rections have been studied in detail; they offer new possibilities, primarily in connection with the fixation of unsaturated organic compounds *e.g.* to cellulose, leather, and polypeptides.

[105] *W. J. Middelton, E. G. Howard,* and *W. H. Sharkey,* J. Amer. chem. Soc. *83,* 2589 (1961).

[106] *M. Schmidt, A. Bauer,* and *H. Rampf,* Angew. Chem. *70,* 399 (1958).

[*] *O*-Substituted esters of thiosulfuric acid cannot be obtained in this way. *O*-Alkyl thiosulfates are extremely unstable substances, which can be obtained, *e.g.* by the reaction of free thiosulfuric acid with diazomethane in ether at *ca.* −50 °C [106].

[107] *H. Distler,* unpublished.

[108] *A. Simon* and *D. Kunath,* Chem. Ber. *94,* 1980 (1961).

[109] *R. Kerber* and *J. Starnick,* unpublished.

a) Behavior of Bunte Salts toward Acids

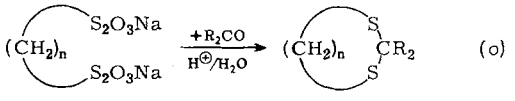
The hydrolysis of sodium *S*-ethylthiosulfate by aqueous acid was correctly recognized by *Bunte*[1] [eq. (n)].

$$C_2H_5{-}S_2O_3Na + H_2O = NaHSO_4 + C_2H_5SH \qquad (n)$$

The salt must generally be heated for several hours with dilute acid for complete hydrolysis. Except in special cases (the reaction of sodium benzoylmethylthiosulfate with acid gives 2,5-diphenyl-1,4-dithiin), the method is suitable for the preparation of thiols[15,17,23,110,111].

A particularly interesting use of Bunte salts is for the preparation of thioacetals and thioketals[14,112], which are obtained from carbonyl compounds and thiols. The Bunte salts are hydrolysed with acid in the presence of aldehydes or ketones.

Cyclic thioacetals and thioketals can be obtained in this way by the use of the α,ω-alkylenebis(thiosulfates) and formaldehyde or acetone respectively[12,113] [eq. (o)].



(o)

n = 2,3; R = H, CH_3

b) Behavior of Bunte Salts toward Alkalis

According to the literature, the alkaline degradation of Bunte salts is very complex[86]. On the basis of the degradation products (sulfenic acids[7,8,114,115], disulfides, carboxylic acids, thiocarboxylic acids, sulfurous acid, thioethers, and sulfinic acids), several reaction mechanisms, in some cases strongly contradictory, have been proposed[9,10,116,117]. On the other hand, a clear and unambiguous reaction course was found for *S*-alkylthiosulfates, resulting from the addition of thiosulfate to compounds containing activated multiple bonds. In 1946 *Stahmann et al.*[97] observed that the Bunte salt *(15)* of divinyl sulfone partially decomposes into a substance that readily takes up iodine. In 1961, *Tesoro et al.*[118,98] assumed that the divinyl sulfone is reformed in accordance with equation (p) during the reaction of the divinyl sulfone

$$(NaO_3S_2{-}CH_2{-}CH_2)_2SO_2 + 2\ NaOH \longrightarrow \underset{(15)}{} SO_2(CH{=}CH_2)_2 + 2\ Na_2S_2O_3 + 2\ H_2O \qquad (p)$$

Bunte salt with cellulose in alkaline media. Bunte salts of vinyl sulfones are reported to behave in a similar manner[119].

So far as we know, no definite proof of the course of the reaction is as yet available, presumably because divinyl sulfone is immediately hydrated in accordance with equation (q) in the presence of aqueous alkali[118]. The resulting bis(β-hydroxyethyl) sulfone *(17)* reacts with divinyl sulfone under the catalytic influence of hydroxide ions to form a water-insoluble adduct having a high molecular weight.

$$(CH{=}CH_2)_2SO_2 + 2\ H_2O \xrightarrow{(OH^{\ominus})} \underset{(17)}{SO_2(CH_2{-}CH_2OH)_2} \qquad (q)$$

The Bunte salts of aryl vinylsulfonates such as *(18)*, which crystallize very readily, can be quantitatively, converted back into the unsaturated starting compounds by treatment with aqueous alkali [equation (r)].

$$p\text{-}O_2N{-}C_6H_4{-}OSO_2{-}CH_2{-}CH_2{-}S_2O_3Na \xrightarrow{NaOH} \underset{(18)}{} p\text{-}O_2N{-}C_6H_4{-}OSO_2{-}CH{=}CH_2 + Na_2S_2O_3 + H_2O \qquad (r)$$

No hydration of the resulting vinylsulfonate under the influence of the hydroxide ions could be observed. Thus the degradation of these Bunte salts *(18)* in alkaline media is the reverse of their formation [see eq. (1)]. This cleavage evidently takes place with all Bunte salts formed by the addition of thiosulfates to activated CC multiple bonds. Deviations from this rule are to be expected only as a result of secondary reactions, such as hydration of the double bond under the influence of strong alkali[118].

c) The Alkaline "Fixation" of Bunte Salts on Cellulose and Other Fibers

In the fixation of dyes and unsaturated compounds on fabrics, the functional groups of the fiber react as nucleophiles, *e.g.* OH groups of cellulose, amino and thiol groups of wool, or amide groups in synthetic polyamides.

Whereas reactive dyes undergo a reaction with cellulose that may be regarded as nucleophilic substitution or as nucleophilic addition[159,120], "Bunte salt dyes"[121] do not react with the fiber. Suitable pretreatment with condensing agents such as sodium sulfide solution is followed by a polycondensation to give a water-fast bond *via* disulfide bridges [cf. eq. (s)].

$$2\ R{-}S_2O_3Na + Na_2S \longrightarrow R{-}S{-}S{-}S{-}R + 2\ Na_2SO_3 \qquad (s)$$

$$R{-}S{-}S{-}S{-}R + Na_2SO_3 \xrightarrow{(Na_2S)} R{-}S{-}S{-}R + Na_2S_2O_3$$

[110] *A. Schöberl* and *M. Kawohl*, Mh. Chem. *88*, 478 (1957).

[111] *T. S. Price* and *D. F. Twiss*, J. chem. Soc. (London) *95*, 1725 (1909).

[112] *G. G. Stoner* and *G. Dougherty*, J. Amer. chem. Soc. *63*, 987 (1941).

[113] *Y.G. Mazover*, Ž. obšč. Chim. *19*, 843 (1949); Chem. Abstr. *44*, 3436 (1950).

[114] *A. Dornow*, Chem. Ber. *72*, 568 (1939).

[115] *K. Fries*, Chem. Ber. *45*, 2965 (1912).

[116] *E. Fromm* and *F. Erfurt*, Chem. Ber. *42*, 3816 (1909).

[117] *T. S. Price* and *D. F. Twiss*, J. chem. Soc. (London) *97*, 1175 (1910).

[118] *G. Tesoro*, *P. Linden*, and *St. B. Sello*, Textile Res. J. *31*, 283 (1961).

[119] *G. Tesoro* and *A. Oroszlan*, Textile Res. J. *33*, 93 (1963).

[120] *O. A. Stam*, J. Soc. Dyers Colorists *80*, 416 (1964).

[121] *K. Schimmelschmidt*, *H. Hoffmann*, and *E. Baier*, Angew. Chem. *74*, 975 (1962); Angew. Chem. internat. Edit. *2*, 30 (1963).

Since "Bunte salt dyes" in general must contain two or more *S*-alkylthiosulfate groups per molecule, it is understandable that condensation with sodium sulfide on the cellulose will lead to a highly cross-linked polydisulfide. Similar highly cross-linked polysulfides were obtained by *Tabushi et al.*[122] with Bunte salts that were prepared *via* chloromethylated polystyrene and sodium thiosulfate and then condensed with sodium sulfide.

Unlike cellulose, wool should react directly with the "Bunte salt dyes" by means of its free SH groups to give disulfides[120,123].

Bunte salts formed by nucleophilic addition to activated multiple bonds should be particularly suitable for "fixation" in alkaline media. This must be assumed to involve 1,2-elimination of thiosulfate ions in the aqueous alkali [eq. (t)].

$$R\text{-}CH_2\text{-}CH_2\text{-}S_2O_3^{\ominus} \xrightarrow{OH^{\ominus}} [R\text{-}\overset{\ominus}{C}H\text{-}CH_2\text{-}S_2O_3^{\ominus}] + H_2O$$
$$\xrightarrow{\text{stabilization}} R\text{-}CH{=}CH_2 + S_2O_3^{2\ominus} \qquad (t)$$

R = *e.g.* COOR′, COOH, $CO\text{-}NH_2$, $SO_2\text{-}OR'$, CO-R′, SO_2NH_2, $SO_2\text{-}NR'_2$

The vinyl derivative can again undergo nucleophilic additions. Nucleophilic reagents in general, such as thiols and alcohols, amines, *etc.*, are suitable for this reaction. The compound is then fixed on cellulose in the usual manner. R′SH, $R'NH_2$ and R'_2NH add on in the same way.

$$R\text{-}\overset{\delta\ominus}{C}{=}\overset{\delta\oplus}{C}\text{-} \underset{-R'O^{\ominus}}{\overset{+R'O^{\ominus}}{\rightleftharpoons}} R\text{-}\overset{\ominus}{C}\text{-}C\text{-}OR' \underset{-H^{\oplus}}{\overset{+H^{\oplus}}{\rightleftharpoons}} R\text{-}\underset{H}{C}\text{-}C\text{-}O\text{-}R'$$

R = $COOR''$, COOH, $CONH_2$, SO_2OR'', $CO\text{-}R''$, $SO_2\text{-}NH_2$, $SO_2\text{-}NR''_2$

It is possible in principle to fix many unsaturated monomers that have recently become readily available, and which are often sparingly soluble in water, by masking as Bunte salts as described above. When the Bunte salts derived *e.g.* from 1,3,5-tris(vinylcarbonyl)-hexahydro-*s*-triazine *(16)* (triacrylformal)[124] or resorcinol bis(vinylsulfonate)[5] are used, cross-linking effects occur.

d) Behavior toward Oxidizing Agents

The oxidation of *S*-alkylthiosulfates yields disulfides, sulfonic acids, or their derivatives, depending on the oxidizing agent and the reaction conditions. On oxidation of *S*-ethylthiosulfate with nitric acid, *Bunte*[1] obtained ethanesulfonic acid and sulfuric acid. Hydrogen peroxide leads mainly to disulfides[68,103,125–127], as does iodine in hot aqueous ethanol[68,103,127–129,125]. Oxidation with bromine water yields both disulfides[18,19,30] and sulfonic acids[130].

e) Behavior toward Halogens in the Presence of Water

In 1936 *Johnson et al.* found[131,132] that sulfur compounds in general can be converted into sulfonyl halides *(19)* by halogenation in water.

$$R\text{-}S\text{-}R' \xrightarrow[2\ H_2O]{3\ Cl_2} R\text{-}SO_2Cl + 4\ HCl + R'Cl$$
(19)

Bunte salts can be converted similarly into the corresponding sulfonyl halides[133–136]. For analytical purposes[137], bromine water is used instead of chlorine water, so that not only *S*-alkylthiosulfates, but also thiols, disulfides, thiocyanates, and similar sulfur compounds can be converted into sulfonyl bromides. These react with a cyanide to liberate cyanogen bromide, which can then be determined colorimetrically.

f) Reduction of Bunte Salts

The reduction of *S*-alkylthiosulfates with conventional agents, such as sodium amalgam[77], zinc and acid[78,89,93,94,138], or alkaline sodium arsenite solution[7,8] leads to thiols. However, this method is of little importance for the preparation of thiols, which can be obtained much more elegantly by cleavage of *S*-alkylthiosulfates with acid.

g) Reaction with Cyanides

S-Alkylthiosulfates are smoothly converted into thiocyanates in the presence of aqueous alkali metal cyanide solution, even at room temperature[76,139].

$$R\text{-}S_2O_3Na + NaCN \longrightarrow RSCN + Na_2SO_3$$

Dyes containing *S*-alkylthiosulfate residues can be readily converted into thiocyanates in this manner; these can sometimes undergo ring closure with ad-

[122] *J. Tabushi, S. Saito,* and *R. Oda,* J. chem. Soc. Japan, ind. Chem. Sect. (Kogyo Kakagu Zassi) *67*, 478 (1964).

[123] *A. Demian,* Rev. Chim. (Bukarest) *16*, 255 (1965).

[124] *R. Wegler et al.,* Chem. Ber. *81*, 527 (1948).

[125] *H. E. Westlake* and *G. Dougherty,* J. Amer. chem. Soc. *64*, 149 (1942).

[126] *T. F. Twiss,* J. chem. Soc. (London) *1914*, 36.

[127] *G. G. Stoner* and *G. Dougherty,* J. Amer. chem. Soc. *63*, 987 (1941).

[128] *T. S. Price* and *D. F. Twiss,* J. chem. Soc. (London) *95*, 1489 (1909).

[129] *M. Viscontini, K. Adank, N. Merkling, K. Ehrhardt,* and *P. Karrer,* Helv. chim. Acta *36*, 835 (1953).

[130] *H. J. Backer,* Recueil Trav.chim.Pays-Bas *49*, 1048 (1930).

[131] *J. B. Douglass* and *T. B. Johnson,* J. Amer. chem. Soc. *60*, 1486 (1938).

[132] *T. B. Johnson* and *J. M. Sprague,* J. Amer. chem. Soc. *58*, 1348 (1936).

[133] *C. Ziegler* and *J. M. Sprague,* J.org.Chemistry *16*, 621 (1951).

[134] *G. Geiseler* and *R. Kuschmiers,* Chem.Ber. *93*, 2041 (1960).

[135] *J. M. Sprague,* US.-Pat. 2531367; Chem. Abstr. *45*; 3418 (1951).

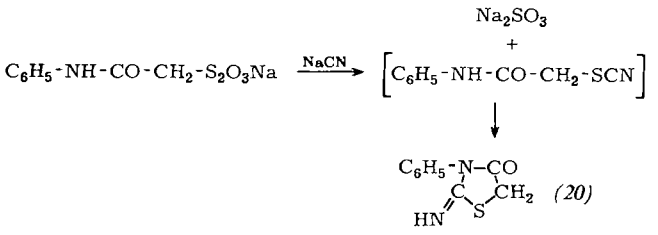
[136] *G. Dougherty* and *R. H. Barth,* US.-Pat. 2293971; Chem. Abstr. *37*, 889 (1943).

[137] *B. Saville,* Chem. and Ind. *1956*, 660.

[138] *A. P. Tiselskii,* Ukrain. Chim. Ž. *24*, 749 (1958); Chem. Abstr. *53*, 20039 (1959).

[139] *H. B. Footner* and *S. Smiles,* J. chem. Soc. (London) *1925*, 2887.

jacent groups [121]. For example, *S*-phenylcarbamoylmethylthiosulfate gives 2-imino-3-phenyl[1,3]thiazolidin-4-one *(20)*, ("3-phenylpseudothiohydantoin"), presumably *via* a linear thiocyanate [30].



(20)

h) Reaction with Iodides, Thiocyanates, and Thiourea

Bunte salts react with iodides, and with thiocyanates as pseudohalides, in the acidic range to form disulfides. Thiourea is reported to behave similarly [2].

i) Reaction with Thiols and Alkali Metal Sulfides

Thiols react with *S*-alkylthiosulfates in alkaline solution to form disulfides [139].

$$RS^{\ominus} + R'-S_2O_3^{\ominus} \rightleftharpoons R-S-S-R' + SO_3^{2\ominus}$$

When R and R′ are the same, the resulting disulfides are symmetrical. Systems in which R and R′ are dissimilar do not yield unsymmetrical disulfides, but give equimolar mixtures of the symmetrical disulfides. However, high yields of unsymmetrical disulfides are reported to be obtained when the reaction is carried out in weakly acidic solutions [140].

The reaction of sulfide ions with Bunte salts in aqueous solution is very complex. Hydrodisulfides together with sodium sulfite [141] as well as disulfides [78] or trisulfides [19] have been suggested as intermediates and/or reaction products. The behavior of dyes containing *S*-alkylthiosulfate residues toward aqueous sulfide solutions is of industrial importance. The reaction leads mainly to water-insoluble aliphatic disulfides, which, unlike aromatic disulfides, are stable toward sulfide ions [121] (cf. Section 3c); the following reactions probably occur:

$$2\ R-S_2O_3Na + Na_2S \longrightarrow R-S-S-S-R + 2\ Na_2SO_3$$

$$R-S-S-S-R + Na_2SO_3 \xrightarrow{Na_2S} R-S-S-R + Na_2S_2O_3$$

Bunte salts formed by nucleophilic addition of thiosulfate to activated double bonds react differently. The hydroxide ions probably split the Bunte salt into thiosulfate and a compound containing an activated CC double bond. The much more nucleophilic thiolate ion then competes with the thiosulfate ion to form the thioether *(21)* [5, 142] in accordance with equation (u).

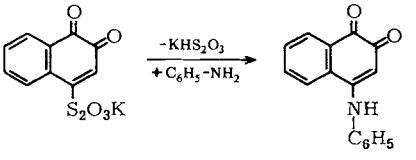
$$R-CH_2-CH_2-S_2O_3^{\ominus} \xrightarrow{OH^{\ominus}} [R-\overset{\ominus}{C}H-CH_2-S_2O_3^{\ominus}] + H_2O \longrightarrow R-CH=CH_2 + S_2O_3^{2\ominus} \quad (u)$$

$$R-CH=CH_2 + R'S^{\ominus} \longrightarrow [R-\overset{\ominus}{C}H-CH_2-S-R'] + H^{\oplus} \longrightarrow R-CH_2-CH_2-S-R' \quad (21)$$

R = *e.g.*, $COOR''$, $CONH_2$, SO_2OR'', COR'', SO_2NH_2, $COOH$

j) Reaction with Amines

S-Alkylthiosulfates generally react with amines to form disulfides [2]. An exception was found with Bunte salts of quinones, which undergo nucleophilic substitution with aromatic amines to give the arylaminoquinone, *e.g. (22)* [143].



(22)

A number of marked deviations from normal behavior are observed in the reaction of Bunte salts with amines. These have been extensively studied, particularly by *Swan* and *Milligan* [30, 144].

4. Properties and Use of Bunte Salts

a) General Characteristics

Owing to the presence of the NaS_2O_3 groups, the *S*-alkylthiosulfates are mostly very readily soluble in water, methanol, ethanol, and other polar solvents. The Bunte salts can be purified by recrystallization from alcohol or alcohol-water mixtures. The salts are occasionally obtained with one molecule of water of crystallization per molecule. Neutral aqueous solutions are frequently decomposed within a few minutes at 100 °C, as can be seen from the turbidity of the solution. Salts of alkali metals or, less commonly, of alkaline earth metals can be used for their isolation. Lead and silver salts are occasionally suitable for the characterization of a compound. It should be noted that *S*-alkylthiosulfates, which crystallize excellently from *e.g.* alcohol, do not have a true melting point, but rather a sort of sintering point, at which the salt agglomerates like a glass. Dry heating [1, 145] frequently leads to decomposition above 100 °C. According to *Bunte* [1], sodium *S*-ethylthiosulfate decomposes into diethyl disulfide, sulfur dioxide, and sodium sulfate.

$$2\ CH_3CH_2-S_2O_3Na \xrightarrow{>100\,^{\circ}C} SO_2 + (C_2H_5)_2S_2 + Na_2SO_4$$

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Further characterization is possible by the reaction of the *S*-alkyl-thiosulfates in aqueous alkali with Hg(II) chloride solution, which leads after brief warming to mercaptides such as *(23)* [11].

$$CH_3CH_2-S_2O_3^{\ominus}Na^{\oplus} + HgCl_2 + H_2O \longrightarrow C_2H_5SHgCl + HCl + NaHSO_4$$

(23)

b) Spectra of Bunte Salts

Kunath [146] and *Simon* [108] found a number of characteristic absorption bands for Bunte salts in the regions 640–660 cm^{-1}, 1040–1050 cm^{-1}, and 1190 to 1250 cm^{-1}. We have been able to confirm these data for a large number of Bunte salts [148]: the bands are generally situated at 648–650 cm^{-1}, 1040–1048 cm^{-1}, and 1210–1215 cm^{-1}.

c) Biological Action

Sodium *S*-ethylthiosulfate exhibits a striking synergic effect when used with the bacteriostat 2-mercaptobenzothiazole and its derivatives against *Staphylococcus aureus* [149]. A similar synergic effect was observed with sodium *S*-ethylthiosulfate and 2-mercaptobenzothiazole against the tubercle bacillus [150].

Sodium *S*-(3-nitrophenyl)thiosulfate is reported to have a particularly strong preventative and curative action against fowl coccidiosis [23]. According to our own observations, Bunte salts obtained *e.g.* by addition of thiosulfate to aryl vinylsulfonates have a considerable effect on *Aspergillus niger* [151]. Other adducts of thiosulfate with acrylic acid derivatives have a systemic-nematocidal action [151].

d) Industrial Use

Most patents dealing with the production and the use of Bunte salts are concerned with the textile industry. The "Bunte salt dyes" [121] have attracted particularly wide industrial interest in this field. Bunte salts derived from divinyl sulfone have recently found industrial use in the finishing of textiles, and particularly of cotton [161, 152, 153], in the Stevenset Super-Crease Process developed by *J.P.Stevens* (U.S.A.) [162].

The hydrophilic Bunte-salt group gives long-chain hydrophobic compounds a surface activity comparable with that of the sulfation products of fatty alcohols [154, 28, 155–158, 62–64].

I am grateful to Dr. Lützel for perusal of this article. I should like to thank Dr. Feichtmayr for stimulating discussions, particularly on the reactivity of the thiosulfate anion.

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COMMUNICATIONS

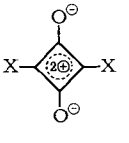
The Cyclobutenediylium Cation, a Novel Chromophore from Squaric Acid

By *H.-E. Sprenger* and *W. Ziegenbein* [*]

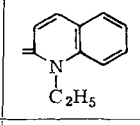
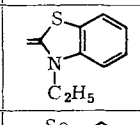
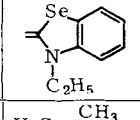
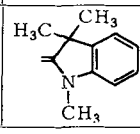
Dedicated to Professor F. Asinger on his 60th Birthday

Tertiary amines [1] and azulenes [2], like active pyrroles and phenols [3], condense smoothly with squaric acid (dihydroxycyclobutenedione), giving products that contain the structural element of cyclobutenonolate. Although these compounds are deeply colored it is problematical whether they are to be regarded as cyanine dyes [4]. In agreement with the conceptions of aromatic character and the results of other authors [5], structure *(1)* can be assigned to these dyes.

We have introduced, as nucleophilic components, the bases obtained by elimination of HI from 2-methyl-substituted quinolinium, benzothiazolium, and benzoselenazolium iodide. These also yield crystalline, intensely colored, betaine-like dyes *(2)*, which were hitherto unknown. The Fischer base reacts analogously with squaric acid giving the condensation

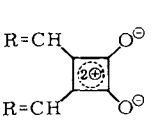


(1a), X = *N*, *N*-Dialkylaminophenyl
(1b), X = 1-Azulenyl
(2), X = CH=Z

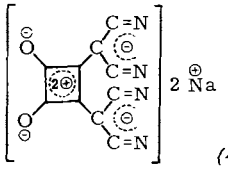
Compound	Z	λ_{max} (mμ)	M.p. (°C)	Yield (%)
(2a)		*730*, 670, 480, 443, 334, 273 ($CHCl_3$)	320 (decomp.)	30
(2b)		*670*, 490, 372, 347, 291 ($CHCl_3$)	300 (decomp.)	80
(2c)		*678*, 495, 435, 390, 354, 290 (Dimethylformamide)	286 (decomp.)	42
(2d)		*630*, 279.5 ($CHCl_3$)	301.5	92

product *(2d)* which was simultaneously synthesized by *Treibs* and *Jacob*[6] though by a different route. These cyclobutenediylium dyes *(2a)* to *(2d)* are very stable, high-melting compounds with a metallic sheen, give intensely colored solutions, and dissolve with difficulty in alcohols or ether but more readily in methylene dichloride, benzonitrile, or dimethylformamide.

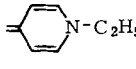
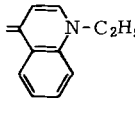
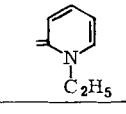
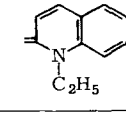
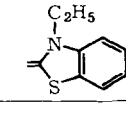
Deeply colored, crystalline cyclobutenediylium dyes of the general formula *(3)* are obtained from squaric diesters and 2- or 4-methyl-substituted pyridinium, quinolinium, or benzo-



(3)



(4)

Compound	R	λ_{max} (mμ) in dimethylformamide	M.p. (°C)	Yield (%)
(3a)		600 (ε = 126900), 555 (67000), 495 (15900), 458 (10300), 369 (17300), 338 (13500)	328 (decomp.)	35
(3b)		670 (ε = 87600), 615 (58400), 565 (18300), 490 (11100), 423 (10400), 368 (9500), 330 (6800), 291 (8200), 278 (9600)	257 (decomp.)	68
(3c)		540 (ε = 50000), 350 (18000), 290 (8000)	218 (decomp.)	16
(3d)		600 (ε = 53300), 558 (61000), 407 (13000), 372 (22300), 280 (16000)	320	55
(3e)		520 (ε = 122900), 338 (12600), 312 (9500), 276 (10400)	274 (decomp.)	28

thiazolium iodides. Under the same conditions malonodinitrile gives a 92% yield of the deep yellow salt *(4)* [λ_{max} (in water): 380 mμ (ε = 34000), 265 (12000), 226 (15400)].

The structures of compounds *(2)* to *(4)* were proved by elemental analysis and UV, IR, and NMR spectra[**]. Dyes of types *(2)* and *(4)* can be differentiated by thin-layer chromatography.

Preparation of (2b): *N*-Ethyl-2-methylbenzothiazolium iodide (305.3 g) and squaric acid (57 g) are boiled in a mixture of butanol (1500 ml), benzene (600 ml), and quinoline (129 g) for *ca.* 20 h with simultaneous removal (azeotropic distillation) of the water formed. After cooling, the crystals (with a green metallic sheen) are filtered off and, when washed with ether and dried, are analytically pure. Compounds *(2a)*, *(2c)*, and *(2d)* are obtained analogously, compound *(2d)*, however, without use of quinoline.

Preparation of (3a): *N*-Ethyl-4-picolinium iodide (24.9 g, 100 mmoles) and diethyl squarate (8.5 g, 50 mmoles) are dissolved in butanol (200 ml) and heated to the boiling point. Sodium butoxide solution (50 ml, containing 5.5 wt-% of sodium) is added dropwise and the whole is heated under reflux for a further 10 min. Subsequent cooling yields crystals which are filtered off, boiled with a methanol/water mixture (1:1 v/v; 100 ml), washed several times with methanol and ether, and recrystallized from dimethylformamide. Compounds *(3b)* to *(3e)* were obtained analogously.

Preparation of (4): Malonodinitrile (6.6 g, 100 mmoles) and dibutyl squarate (11.3 g, 50 mmoles) are dissolved in butanol (100 ml) and heated under reflux. A sodium butoxide solution (50 ml, containing 5.5 wt-% of sodium) is added dropwise and the whole is stirred for a further 2 h under reflux. The crystals formed are removed by filtration. After being washed with methanol and ether and dried for two days in a vacuum over phosphorus pentoxide at 50 °C the product is analytically pure.

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[*] Dr. H.-E. Sprenger and Dr. W. Ziegenbein
Forschungslaboratorien der Chemische Werke Hüls AG.
4370 Marl (Germany)

[**] We thank Dr. *Th. Böhm-Gössl*, Dr. *R.-J. Frenzel*, and *G. Peitscher* for measurement and interpretation of the spectra.

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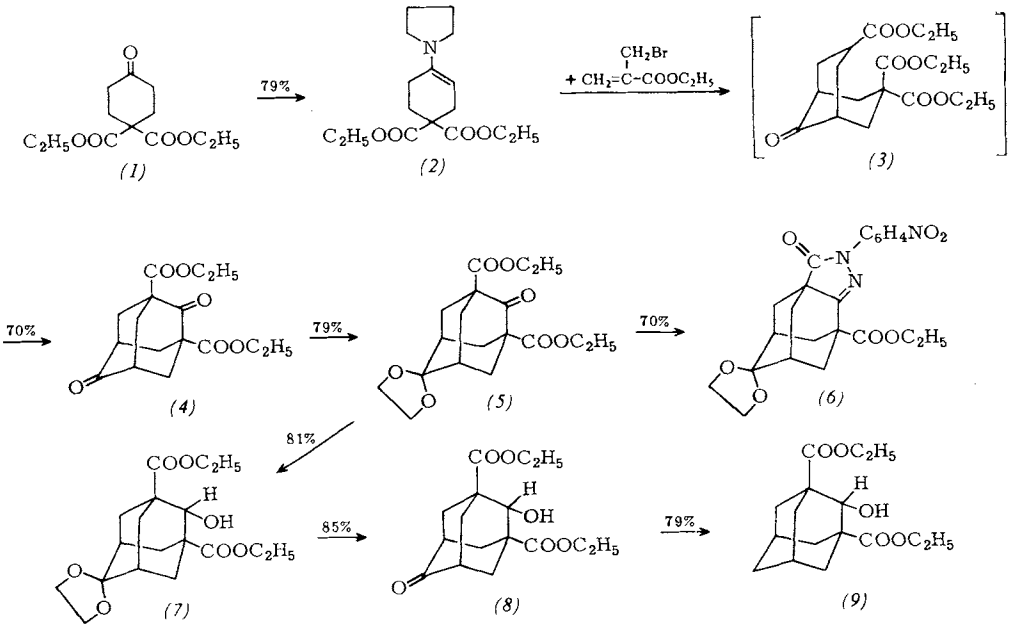
A New Synthesis of the Adamantane Ring System

By *H. Stetter* and *H. G. Thomas*[*]

Dedicated to Professor B. Helferich on his 80th Birthday

The synthesis of bicyclic ring systems by the action of dimethyl γ-bromomesaconate on enamines of cyclic ketones was recently reported[1]. Starting from this observation we have developed a new, prolific synthesis of the adamantane ring system whose value lies in the fact that it provides a route to adamantane derivatives that cannot be obtained by direct substitution.

The starting material is diethyl 4-oxocyclohexane-1,1-dicarboxylate *(1)*, which is accessible from malonic ester and 3-bromopropionic ester in one step and in high yield[2]. This is converted by pyrrolidine into the enamine *(2)*. Refluxing *(2)* with ethyl 2-(bromomethyl)acrylate[3] in ethanol/acetonitrile (1 : 1) for six hours and subsequent fractionation under



vacuum affords diethyl 2,6-dioxoadamantane-1,3-dicarboxylate *(4)*, b.p. 203–206 °C/3 mm, m.p. 113–114 °C, directly. Wolff-Kishner reduction of this product to the known adamantane-1,3-dicarboxylic acid[4] serves as a proof of structure. We assume that triethyl 9-oxobicyclo-[3.3.1]nonane-3,3,7-tricarboxylate *(3)* is formed as intermediate in the reaction *(2)* → *(4)* and then undergoes cyclizing ester condensation.

Ethylene glycol converts the ketone *(4)* into the monoketal *(5)*, m.p. 118 °C, whose structure is proved by formation of a pyrazolone *(6)*, m.p. 183–184 °C, with *p*-nitrophenylhydrazine. Catalytic hydrogenation of *(5)* afforded the hydroxy ketal *(7)*, m.p. 99 °C, from which diethyl 2-hydroxy-6-oxoadamantane-1,3-dicarboxylate *(8)*, m.p. 111–112 °C, is formed on hydrolysis. 2-Hydroxyadamantane-1,3-dicarboxylic acid *(9)*, m.p. 229–230 °C, was obtained by Wolff-Kishner reduction of *(8)*.

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[*] Prof. Dr. H. Stetter and Dr. H. G. Thomas
Institut für Organische Chemie der Technischen Hochschule
Prof.-Pirlet-Strasse 1
51 Aachen (Germany)

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Reaction of Benzyne with α-Methylstyrene

By *E. Wolthuis* and *W. Cady*[*]

Dedicated to Professor G. Wittig on the occasion of his 70th birthday

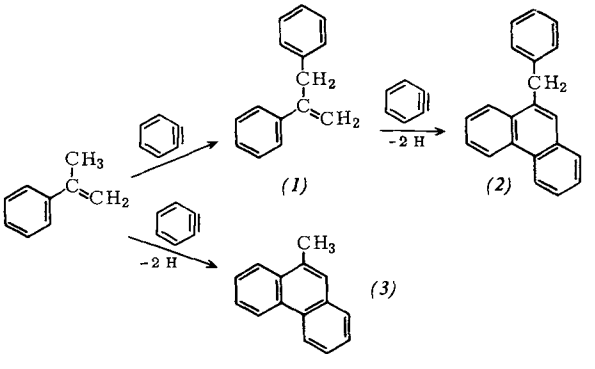
Benzyne reacts with isosafrole and isoeugenol by normal 1,4-addition to give substituted phenanthrenes[1]. We have found that benzyne reacts with α-methylstyrene by substitution as well as by addition.

Solutions of 0.1 mole of anthranilic acid in tetrahydrofuran (THF) and 0.19 mole of isoamyl nitrite in THF were added simultaneously to a solution of 0.1 mole of α-methylstyrene in THF at 55–60 °C. The solvent was subsequently removed under vacuum and the residue was dissolved in benzene. The benzene solution was extracted with dilute sodium hydroxide to remove dark, acidic material, including acridone, and finally evaporated to dryness. The residue was dissolved in hexane, filtered to remove any precipitated acridone, and chromatographed on a column of alumina. Elution with hexane, and finally with hexane containing up to 20% benzene, gave the following products, in the order in which they are listed.

2,3-Diphenylpropene *(1)*[2], 6.19 g (32%), b.p. 100–105 °C/1 mm, 293 °C/750 mm. Its identity was established by its NMR spectrum, by hydrogenation, and by bromination.

9-Benzylphenanthrene *(2)*[3], 4.70 g (17.5%), m.p. 155 to 156 °C; picrate, m.p. 120.5–121 °C. Its structure was confirmed by NMR and UV spectroscopy.

9-Methylphenanthrene *(3)*[4], 0.75 g (4%), m.p. 93.1 to 93.6 °C; picrate, m.p. 154.5–156 °C. The structure was confirmed by NMR and UV spectroscopy.



Compound *(3)* is the expected product from a normal Diels-Alder reaction followed by aromatization with loss of hydrogen. The intermediate dihydro compound was sought but not detected; presumably the hydrogen was captured by benzyne, but our efforts to detect the formation of benzene by gas chromatography failed.

Compound *(1)* is formed apparently by substitution of the reactive allylic hydrogen by a phenyl group. The yields of *(1)* and *(3)* indicate that this substitution competes well with the 1,4-addition reaction.

Compound *(2)* is formed from *(1)* by further 1,4-addition reaction with benzyne. Evidence for this is the fact that when

benzyne was generated in a solution of *(1)* in THF, the only product isolated was *(2)*.

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[*] Dr. E. Wolthuis and W. Cady
Chemistry Department, Calvin College
1331 Franklin Street, S.E.
Grand Rapids, Michigan 49506 (U.S.A.)

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The Thermal Decomposition of Some Diphenylphosphinothioic Amides. A New Route to Arylcyclophosphazatrienes

By *R. A. Shaw* and *E. H. M. Ibrahim* [*]

Dedicated in sincere admiration to Professor Georg Wittig on the occasion of his 70th birthday

We recently described some novel reactions [1] in the thermal decomposition of phenylphosphonothioic diamides. We now report an even more diverse behavior in the thermal decompositions of diphenylphosphinothioic amides *(1)*.

The parent compound *(1a)* decomposes at 280 °C with evolution of ammonia to give the linear dimer bis(diphenylphosphinothioic)amide *(2a)* (yield 68 %, m.p. 213 °C). Two

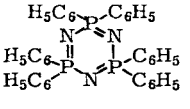
$(C_6H_5)_2P(S)NHR$ — $(C_6H_5)_2P(S)-NR-(S)P(C_6H_5)_2$

(1a), R=H — *(2a)*, R=H

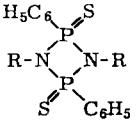
(1b), R=CH_3

(1c), R=C_6H_5 — *(2c)*, R=C_6H_5

side reactions also occur leading to 2,2,4,4,6,6-hexaphenylcyclotriphosphazatriene *(3)* (yield 7 %, m.p. 232 °C) and the cyclic dimer, 2,4-diphenylcyclodiphosphazane 2,4-bissulfide *(4a)* (yield 17.3 %, m.p. 242 °C) with the elimination of the elements of hydrogen sulfide and benzene respectively. We have proved structures of *(2a)*, *(3)*, and *(4a)* by elemental analyses, molecular-weight determinations, infrared spectroscopy, and for *(3)* by mixed melting point, and for *(2a)* and *(4a)* by hydrolytic degradation.



(3)



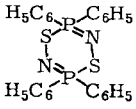
(4a), R = H

The thermal decomposition of *(1b)* (300–310 °C, *ca.* 1/2 h) yields *(3)* as the major product. A new compound bis(diphenyl-*N*-methylimidophosphinic) thioanhydride *(5b)* (yield 2.5 %, m.p. 169–170 °C) and the methyl ester of diphenyl phosphinodithioic acid *(6b)* (yield 12.6 %, m.p. 85 °C) are also obtained. The structure of *(5b)* was established by elemental analysis, molecular-weight determination, infrared and ^1H-NMR spectroscopy.

$(C_6H_5)_2P(NCH_3)-S-(CH_3N)P(C_6H_5)_2$ — $(C_6H_5)_2P(S)-SR$

(5b) — *(6b)*

The thermal decomposition (310–320 °C, *ca.* 1/2 h) of *(1c)* takes yet another course. The products are the linear dimer *(2c)* (yield 43 %, m.p. 220 °C) and a 3,3,6,6-tetraphenyl-1,4,2,5,3,6-diazadithiadiphosphorine *(7)* (yield 36 %, m.p. 265 °C), which is also obtained in the thermal decomposition of phenylphosphonothioic dianilide [2]. The structure of *(7)* was evidenced by elemental analysis, molecular-weight determination, and hydrolytic degradation to diphenylphosphinic acid [1].



(7)

All compounds have satisfactory elemental analyses.

Since the yield of *(3)* decreases rapidly in the series *(1b)* > *(1a)* > *(1c)*, *i.e.* R = CH_3 > R = H > R = C_6H_5, the electron supply to the nitrogen atom of the amide *(1)* seems to be an important factor in the formation of the cyclotriphosphazatriene *(3)*.

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[*] Prof. R. A. Shaw and E. H. M. Ibrahim
Department of Chemistry
Birkbeck College (University of London)
Malet Street
London W.C. 1 (England)

[1] *E. H. M. Ibrahim* and *R. A. Shaw,* Chem. Commun. *1967,* 244.

[2] *R. A. Shaw* and *F. B. G. Wells,* Chem. and Ind. *1960,* 1189; *K. G. Acock, R. A. Shaw,* and *F. B. G. Wells,* J. chem. Soc. (London) *1964,* 121.

Ring Inversion in Cycloheptane and in Cycloheptene Derivatives

By *R. Knorr, C. Ganter,* and *J. D. Roberts* [*]

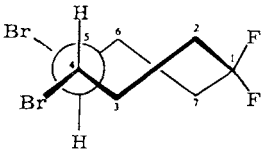
Dedicated to Professor G. Wittig on the occasion of his 70th birthday

Rapid pseudorotation [1] causes interconversion of substituent groups between "above" and "below" positions in cycloheptanes even at −150 ° [2] unless restrictions are imposed by bulky groups [2b, 3]. An especially interesting example of cycloheptane conformational preferences and rates of cycloheptane-ring inversion is provided by 4,5-*trans*-dibromo-1,1-difluorocycloheptane (m.p. = 52–54 °C). This substance was prepared from 4-cycloheptenone *via* several steps.

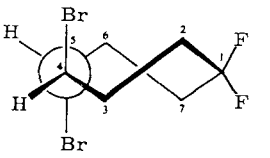
The ^{19}F-NMR spectrum of a 15 % solution of the substance in dimethyl ether was recorded (56.4 MHz; proton decoupling) at temperatures between *ca.* 25 ° and −126 °C. At temperatures below −118 °C two single lines (in the intensity ratio 74:26) were observed at 348 Hz and 550 Hz upfield from internal trifluoroacetic anhydride. These lines collapsed above −114 °C to a single line at the weighted center, 400 Hz.

The two resonances at 348 and 550 Hz are best ascribed to the separate conformations *(1a)* and *(1b)*, respectively. In each of these conformations of the twisted chair *(1)*, which has C2 symmetry, the fluorines are equivalent and will not show F–F coupling. Inspection of molecular models suggests that severe repulsive interactions occur in most of the other possible conformations and that *(1a)* is likely to be a little more flexible than *(1b)*.

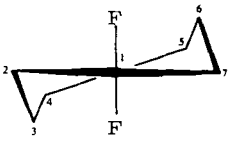
The equilibrium ratio *(1b)*/*(1a)* = 0.35 was found to be temperature independent (signal weighted center constant at 400 Hz) from +25 to 126 °C in the same way as has been reported for 1,2-*trans*-dibromocyclohexane [4]. Exchange life times of τ_a and τ_b ($\tau_a : \tau_b$ = 74 : 26) were obtained by comparison with computer-simulated line shapes; at −114 °C, the coalescence point, τ_a = 0.0077 sec. The Eyring activation parameters determined for *(1a)* → *(1b)* between −126 °C and −77 °C were $\Delta H^{\ddagger}$ = 9.8 ± 0.3 kcal mole^{-1} and $\Delta S^{\ddagger}$ = +15 ± 3 e.u. The relatively high positive entropy of



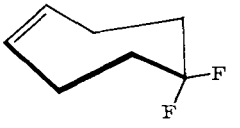
(1a), 74%



(1b), 26%



(1)



(2)

activation suggests that the transition state for the process by which the fluorines become equivalent may be for conversion to the flexible boat form rather than for pseudorotation, which would be expected to proceed by way of highly strained intermediate conformations.

5,5-Difluorocycloheptene was prepared from *trans*-4,5-dibromo-1,1-difluorocycloheptane by debromination with zinc dust. The ^{19}F–NMR spectrum of a 10 % solution in propene (with the protons decoupled) showed a single AB system from −147 °C to the coalescence point of −92 °C, above which a single line was obtained at 4080 Hz. The A and B chemical shifts below −115 °C were 3280 Hz and 4882 Hz (upfield from internal standard bromotrifluoromethane) and the coupling constant J_{FF} was 248 Hz. At −92 °C, the half life was 0.00023 s. The Eyring activation parameters calculated for all points between −147 °C and −44 °C, $\Delta H^{\ddagger} = 7.4 \pm 0.1$ kcal/mole, $\Delta S^{\ddagger} = -0.2 \pm 2$ e.u., were comparable to those reported for some related systems [5,6].

The results are in accord with the assumption that the molecule exists in the chair conformation *(2)* and that the fluorines become equivalent by a ring-inversion process analogous to that which occurs with 1,1-difluorocyclohexane [2b].

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[*] Dr. R. Knorr, Dr. C. Ganter, and Prof. J. D. Roberts
Gates and Crellin Chemistry Laboratories [**].
California Institute of Technology
Pasadena
California 91109 (U.S.A.)

[**] Contribution No. 3511.

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[2a] *J. D. Roberts* and *R. Knorr*, unpublished results on 1,1,3,3-tetrafluorocycloheptane.

[2b] Cf. *J. D. Roberts*, Chem. in Britain *2*, 529 (1966).

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The Wittig Rearrangement of a Tertiary Amine[1]

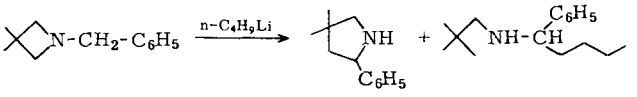
By *A. G. Anderson* and *M. T. Wills* [*]

Dedicated to Professor G. Wittig on the occasion of his 70th birthday

The rearrangement of ethers induced by the action of strong bases was discovered by *Wittig* and *Löhmann* [2] twenty-five years ago and has since been studied extensively [3].

We have now found that treatment of 1-benzyl-3,3-dimethylazetidine *(1)* with a three molar excess of butyl-lithium in ether solution (0.13 M) under reflux for 24 h gives a Wittig rearrangement product, 4,4-dimethyl-2-phenylpyrrolidine *(2)* (18.6 %, n_D^{25} 1.5200) and *N*-(2,2-dimethylpropyl)-1-phenylpentylamine *(3)* (16.7 %, n_D^{25} 1.4837). Most of the starting material (> 60 %) is recovered unchanged. The formation of both *(2)* and *(3)* from *(1)* can be interpreted in terms of each of the various mechanisms (ion-pair, S_Ni, radical) which have been proposed [5] for the Wittig ether rearrangement.

The products gave spectra (see data below) and elemental analyses in agreement with the assigned structures, and *(2)* was also synthesized, for comparison, from β,β-dimethyl-γ-nitrobutyrophenone, by hydrogenation to the corresponding amine, cyclization to 4,4-dimethyl-2-phenyl-1-pyrroline and finally, reduction with lithium aluminum hydride.



(1) *(2)* *(3)*

The metalation of several different tertiary benzylamines with butyl-lithium has been examined by *Hauser et al.* [4], and evidence was obtained that ortho metalation occurred directly and that this was the exclusive reaction in the case of benzyl-dimethylamine. In contrast, our results indicate the formation of a 2-lithio intermediate in an amount not less than that represented by the total yields of *(2)* and *(3)*.

Spectral data:

Compound *(2)*: IR bands at 3.3, 3.4 (s), 3.5, 6.2 (w), 6.7, 6.85 (doublet) (s), 7.3 (s), and 14.3 (s) μ.

^{1}H–NMR peaks (δ in ppm relative to tetramethylsilane in carbon tetrachloride) at 1.09 (4-methyls), 2.77 (pair of doublets for 5-methylene), 4.2 (pair of doublets for 2-methine), 7.2 (multiplet for 2-phenyl), and multiplet centered at 1.6 for 3-methylene and N–H.

Compound *(3)*: IR bands at 3.3, 3.4 (s), 3.5, 3.6, 6.2 (w), 6.7, 6.85 (doublet) (s), 7.2., 7.35 (s), 8.45, 8.95 (s), and 14.3 (s) μ. ^{1}H–NMR peaks (δ in ppm relative to tetramethylsilane in carbon tetrachloride) at 0.85 (methyl groups), 2.1 (methylene bonded to N), 3.4 (triplet for methine), and 7.1 (phenyl).

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[*] Prof. A. G. Anderson and Dr. M. T. Wills
Department of Chemistry, University of Washington
Seattle, Washington 98105 (U.S.A.)

[1] *M. T. Wills*, Ph. D. Thesis, University of Washington, 1965. Supported in part by State of Washington Initiative 171 Funds for Research in Biology and Medicine.

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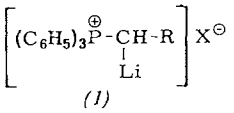
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(Cyclopropylmethylene)triphenylphosphorane[1]

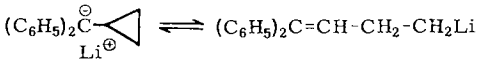
By *A. Maercker* [*]

Dedicated with respect and gratitude to Professor G. Wittig on his 70th Birthday

Wittig reagents that are prepared from phosphonium salts and phenyl-lithium differ significantly from ylides that are free from lithium salt [2] and are therefore often formulated as metalated phosphonium salts *(1)* [3].

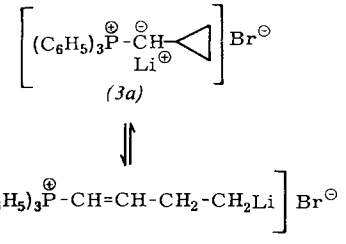


(1)



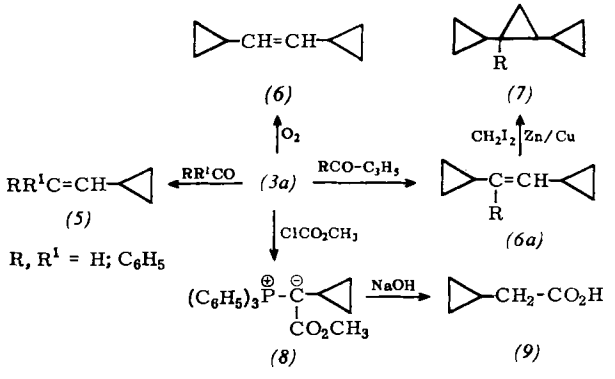
(2a) (2b)

To obtain information about the nature of the lithium-carbon bonding in these ylides we have prepared compound *(1)* with R = cyclopropyl. Our experiments with the system *(2a)* ⇌ *(2b)* [4] had shown that the open-chain form was present when the lithium-carbon bond was covalent (in ether) but that the cyclopropylmethanide *(2a)* was present when the bond was ionic (in tetrahydrofuran); thence it was expected that the ylide *(3a)* should be stable if the lithium-carbon bond is more strongly ionized than in *(2a)*, otherwise rearrangement to *(3b)* should take place.



(3a) (3b)

(Cyclopropylmethyl)triphenylphosphonium bromide *(4)*, which is obtained (77 % yield; m.p. 175–177 °C) by boiling triphenylphosphine and cyclopropylmethyl bromide for 10 days in benzene, reacts with ethereal phenyl-lithium to yield the yellowish-red ylide *(3a)*, which affords cyclopropylethylene derivatives *(5)* (see Table) by Wittig reactions [5] with carbonyl compounds even at room temperature.



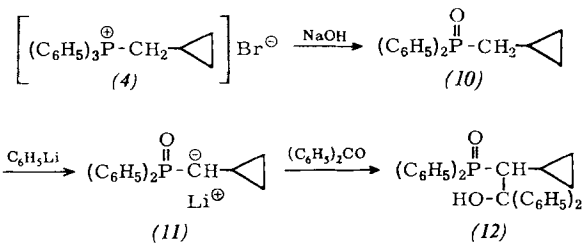
(6) (7) (5) (3a) (6a) (8) (9)

R, R¹ = H; C_6H_5

Cyclopropylethylene derivatives *(5)* prepared (12 h in ether at room temperature).

R	R¹	Yield (%)	B.p. (°C/mm)
C_6H_5	C_6H_5	67	95/0.01
C_6H_5	H	90	99/13
C_6H_5	Cyclopropyl	86	65/0.01

When *(3a)* is autoxidized [6] or is treated with cyclopropyl ketones in ether at room temperature, 1,2-dicyclopropylethylene derivatives *(6a)* are formed, which are converted into tercyclopropanes *(7)* by the Simmons-Smith reaction [7]. On reaction with methyl chloroformate in ether, *(3a)* undergoes transylidation [8], leading to the yellow (cyclopropylmethoxycarbonylmethylene)triphenylphosphorane *(8)* (yield 41 %; m.p. 133–137 °C), which on hydrolysis affords cyclopropylacetic acid *(9)* (84 %) and triphenylphosphine oxide (98 %). On no occasion was ring opening to give *(3b)* observed, so that the lithium-carbon bond in *(3a)* must be largely ionized [9].



(4) (10) (11) (12)

Boiling the phosphonium bromide *(4)* with 2 N NaOH yields the phosphine oxide *(10)* (yield 95 %; m.p. 134–136 °C). The methanide *(11)* that is obtained therefrom by treatment with phenyl-lithium in ether is also stable and does not rearrange even when converted into the magnesium salt. However, the system *(2a)* ⇌ *(2b)* with magnesium as cation is present in the open-chain form, *i.e.*, is covalent, even in hexamethylphosphoric triamide. Benzophenone and *(11)* afford the alcohol *(12)* (yield 80 %; m.p. 218–218.5 °C), which gives 2-cyclopropyl-1,1-diphenylethylene *(5)*, (R = R¹ = C_6H_5) (55 %) and diphenylphosphinic acid (50 %) when boiled with potassium t-butoxide in benzene [10]. The oxide *(10)* is also converted into the olefin *(5)* directly when boiled with potassium t-butoxide and benzophenone [10], but the yields are not so good.

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[*] Dr. A. Maercker
Institut für Organische Chemie der Universität
Henkestr. 42
852 Erlangen (Germany)

[1] I thank Prof. Dr. *G. Hesse* for his interest and the Deutsche Forschungsgemeinschaft for financial support of this work.

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Testosterone as Protective Agent of the Water Beetle Ilybius [1]

By *H. Schildknecht*, *H. Birringer*, and *U. Maschwitz* [*]

Dedicated to Professor G. Wittig on his 70th Birthday

From the edges of South German lakes and pools we have caught, among other Dytiscidae (water beetles), two species of the genus *Ilybius*, *I. fenestratus* and *I. fuliginosus*. By carrying out our preparations in insect Ringer solution we were able to isolate the pygidial bladders lying at the posterior

end of the body and the prothoracic protective bladders in the anterior portion (see Fig. 1). The substances produced in the glands act as protective agents for the beetles against microorganisms and cold-blooded vertebrates.

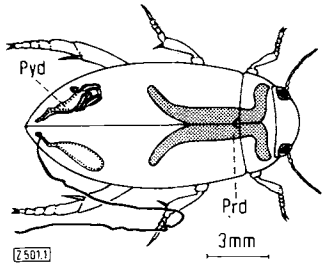


Fig. 1. *Ilybius* with prothoracic (Prd) and pygidial bladders (Pyd).

If the prothoracic bladders are compressed in methanol, a yellow solution is obtained which can be separated into components by thin-layer chromatography [silica gel GF_{254} (Merck); cyclohexane/ethyl acetate (1:1)]. On repeated chromatography we were able to isolate the main component as a viscous oil, which crystallized after several days. We began analysis of all the active constituents of *Ilybius* immediately after their isolation.

Main component: An enone chromophore was indicated by a UV absorption maximum at 241 mμ and was recognized also in the IR spectrum at 1660 ($\nu_{C=O}$) and 1610 cm^{-1} ($\nu_{C=C}$). An OH group indicated by its band at 3360 cm^{-1} was more accurately characterized by a ν-C–OH vibration at 1055 cm^{-1}, since this lies in the expected region for alicyclic secondary alcohols with five- or six-membered rings. A band at 3020 cm^{-1} indicated one or more hydrogen atoms on the C=C double bond. The molecular weight, determined by mass spectrometry, was 288. Experience gained in the analysis of the protective secretions of other water beetles[2,3] enabled us to identify the main component of this protective secretion as testosterone (17β-hydroxy-4-androsten-3-one). For further characterization we converted the natural product by reaction with acetic anhydride/pyridine into an acetate whose melting point (after thin-layer chromatography) was 134.5–136 °C (lit.: 135 to 138 °C). The IR spectra of this substance and of a comparison sample were identical.

The fact that *Ilybius*, like other Dytiscidae, ejects a milky secretion from the prothoracic glands when touched indicates that we are dealing here also with protective substances. To demonstrate this we fed *I. fenestratus* to toads (of the families *Bufonidae* and *Pelobatidae*) and grass frogs. The results were impressive. A hungry toad (*Bufo bufo*) that had eaten four beetles within 5 min was, after 20 min, obviously in pain and brought up two living beetles covered in a bloody slime. The spadefoot toads (*Pelobates fuscus*) and frogs also became severely ill after such meals and some of them brought up living water beetles. After one or two such meals of *Ilybius* these animals would eat no more beetles, even when hungry. Thus these dytiscidae seem to be excellently protected against the amphibia that live in the shore regions.

To test the effectiveness of testosterone as a component of the secretion we placed goldfish in an aqueous testosterone solution (10 mg/ml). Within a few minutes excitation and muscular weakness were observed. After 25 min the fish could no longer equilibrate and finally lay senseless on the bottom of the aquarium, but they recovered completely when placed in fresh water. It is thus shown that testosterone, like other steroids examined by us[2–4], is stupificient for fish. It is surprising that testosterone causes the same symptoms as cortexone although for vertebrates the former acts as male sex hormone and the latter as corticosteroid.

Ochs[5] has reported that water beetles, and in particular *Gyrinus*, are used in the Alps as an aphrodisiac for cattle and horses. According to our observations to date, *Gyrinus*, which belongs to another family of beetle, does not produce steroids. It seems probable that the local farmers confused *Gyrinus* with *Ilybius* since they have the same habitat and similar appearance.

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[*] Prof. Dr. H. Schildknecht, Dipl.-Chem. H. Birringer, and Dr. U. Maschwitz
Organisch-Chemisches Institut der Universität
Tiergartenstr.
69 Heidelberg (Germany)

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

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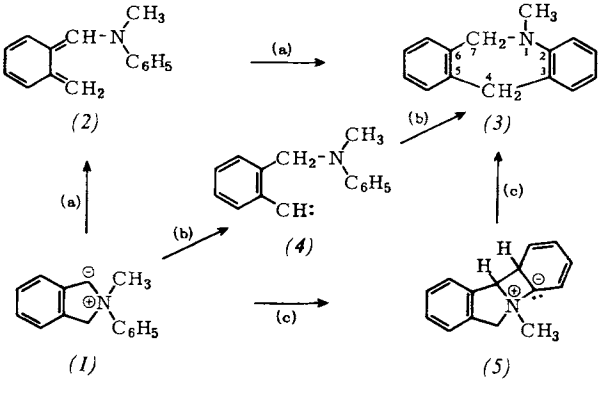
The Mechanism of the Wittig Rearrangement of *N*-Methyl-*N*-phenylisoindolinium Iodide

By *P. P. Gaspar* and *T. C. Carpenter*[*]

Dedicated to Prof. Georg Wittig on the occasion of his 70th birthday

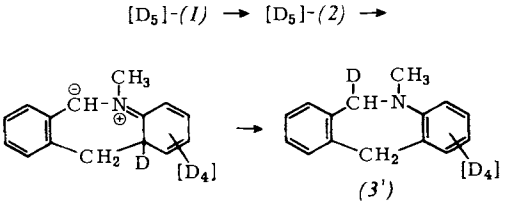
Wittig, *Closs*, and *Mindermann* interpreted the formation of *N*-methyl-1-aza-2,3;5,6-dibenzocycloheptadiene-(2,5)*(3)* from the reaction of *N*-methyl-*N*-phenylisoindolinium iodide with phenyl-lithium[1] as resulting from the ylide rearrangement (a).

Other possible mechanisms include α-elimination to a carbene (b) and a variant of a Sommelet rearrangement (c).



The conversion of a sample of *(1)* whose *N*-phenyl group is labeled with deuterium into *(3)* permits a distinction between mechanism (a) and mechanisms (b) and (c).

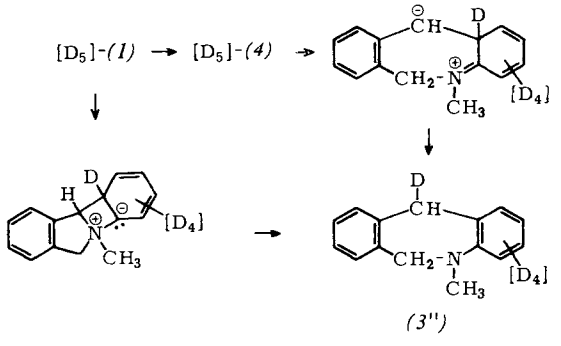
When *N*-methyl-*N*-phenylisoindolinium iodide containing 68.4 % deuterium was treated with phenyl-lithium in ether, (3′) was obtained containing 1.27 ± 0.03 protons in the



7-position and 2.01 ± 0.02 protons in the 4-position, as determined from the NMR spetrum, *i.e.* the deuterium content of the 7-position is 0.73 ± 0.05 atom and that of the 4-position is 0.00 ± 0.05 atom. Mechanism (a), as proposed by *Wittig et al.* is thus confirmed by the observation that product *(3)*, or *(3')*, is formed in yields greater than 73 %.

The methylene NMR resonances of *(3)* at −4.26 and −4.07 ppm with respect to tetramethylsilane (in CS_2) were assigned by comparison with the NMR spectrum of *(3)* containing deuterium in the 4-position only. [4−D]-*(3)* was prepared by metalation of *(3)* with phenyl-lithium (proved by *Wittig et al.*[1] to occur exclusively at the 4-position) followed by quenching with heavy water.

Had mechanisms (b) or (c) been operative, *N*-phenyl ring deuterium would have been incorporated into the 4-position, and loss of label due to metalation would have occured. This would have yielded product *(3'')* with significantly lower deuterium content than that of the labeled starting material. Intervention of a benzocyclobutene, formed by a Stevens rearrangement of *(1)* in mechanism (a) and subsequently opening to *(2)*, is considered unlikely because of the known stability of 1-aminobenzocyclobutene[2,3]. Further experiments to trap the intermediate *(2)* are underway.



(3'')

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[*] Prof. P. P. Gaspar and T. C. Carpenter
Department of Chemistry, Washington University
Saint Louis, Mo., 63130 (U.S.A.)

[1] *G. Wittig, G. Closs,* and *F. Mindermann,* Liebigs Ann. Chem. *594,* 89 (1955).

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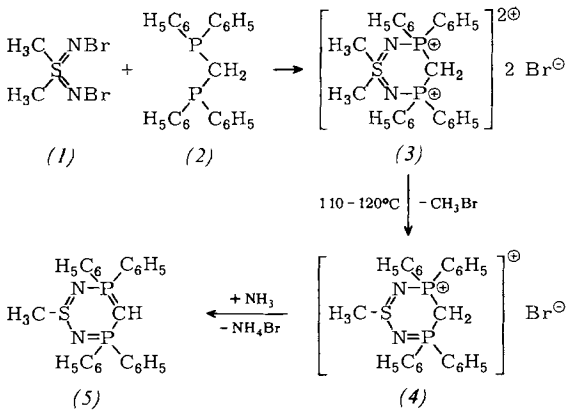
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1-Methyl-3,3,5,5-tetraphenyl-1-thia-3,5-diphospha^{V}-2,6-diazine[1]

By *R. Appel* and *D. Hänssgen*[*]

Dedicated to Professor Georg Wittig on his 70th Birthday

N,N'-Dihalogeno derivatives of dialkylsulfur diimides (sulfur diimines) *(1)* react with phosphines by nucleophilic substitution, the halogen leaving as anion and two new phosphorus-nitrogen bonds being formed[2]. Application of this reaction to ditertiary diphosphines has made possible the synthesis of new ring systems that contain the elements P, S, and N as well as methylene groups. Reaction of the diimide *(1)* with methylenebis((diphenylphosphine) *(2)* in benzene/acetonitrile (75:100 v/v) gives the dibromide *(3)* and heating this at 110–120 °C in a high vacuum leads to loss of one molar equivalent of methyl bromide with formation of the monobromide *(4)*. A proton can then be removed from the methylene group of *(4)* by means of liquid ammonia, leading to the uncharged 1-methyl-3,3,5,5-tetraphenyl-1-thia-3,5-diphospha^{V}-2,6-diazine *(5)*.



(1) *(2)* *(3)* *(4)* *(5)*

	M.p. (°C)	Ratio $H(C_6H_5)$: $H(CH_3)$: $H(CH_2)$ and (CH)
(3)		20 : 6 : 2
(4)	255–257 (decomp.)	20 : 3 : 2
(5)	140–142	20 : 3 : 1

The structures of compounds *(3)* to *(5)* are evidenced by elemental analyses, ionic equivalents of *(3)* and *(4)*, the molecular weight of *(5)*, and the behavior of the various types of proton (NMR spectra). Conductivity measurements and conversion of the cyclic bromides into nitrates and picrates by double decomposition prove the ionic structure of compounds *(3)* and *(4)*.

The salts *(3)* and *(4)* are soluble in polar organic solvents such as alcohols and dimethyl sulfoxide, but insoluble in ether and hydrocarbons. *(5)* dissolves readily in benzene and chloroform.

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[*] Prof. Dr. R. Appel and Dipl.-Chem. D. Hänssgen
Anorganisch-Chemisches Institut der Universität
Meckenheimer Allee 168
53 Bonn (Germany)

[1] Part XXI of Non-Metallic Derivatives of Imines. – Part XX: [2].

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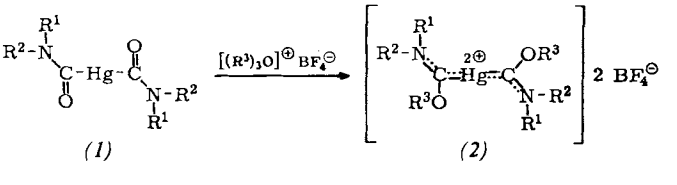
Complexes of Alkoxy(dialkylamino)carbenes and Hg^{2+} Obtained from Dicarbamoylmercury Compounds

By *U. Schöllkopf* and *F. Gerhart*[*]

Dedicated to Professor G. Wittig on his 70th Birthday

Fischer and *Maasböl*[1] obtained metal-carbene complexes from carbonyl-metal π-complexes. We have investigated the question whether carbonyl-metal σ-compounds can also be transformed into metal-carbene adducts.

After we had treated biscarbamoylmercury compounds *(1)*[2] in methylene chloride at room temperature with 2 mol. equiv. of trimethyl- or triethyl-oxonium fluoroborate and had concentrated the solutions, we obtained crystalline compounds[3] that we formulate as adducts of alkoxy(dialkylamino)carbenes with Hg^{2+} ions *(2)*.



(1) *(2)*

	R^1	R^2	R^3	M.p. (°C)	NMR (τ) [c] $\diagdown N-CH \diagup$	$-O-CH \diagup$
(2a)	C_2H_5	C_2H_5	CH_3	207 [a]	5.99 (q); 6.21 (q)	5.43 (s)
(2b)	C_2H_5	C_2H_5	C_2H_5	202 [a]	6.02 (q); 6.25 (q)	5.14 (q)
(2c)	CH_3	$CH_2C_6H_5$	C_2H_5	228 [b]	5.06 (s); 6.37 (s)	5.02 (q)

[a] Reprecipitated from methylene chloride or nitromethane by ether.

[b] One of the possible isomers (12 %), obtained crystalline by reprecipitating the crude product from nitromethane by ether.

[c] In CD_3NO_2 or CD_3OD.

The NMR spectra are in good agreement with this structure. The non-equivalence of the *N*-alkyl groups indicates hindered rotation about the C–N bond; it might also result from hindered rotation about the Hg–C bond, with free rotation about the N–C bond, but then the two groups R^3 would be non-equivalent. Further study is needed to decide how much weight attaches to the mesomeric limiting structure with a mercury-carbon double bond, *i.e.*, how far it is justified to describe the compounds as metal-carbene adducts.

That the complexes react with hydroxide ions was shown by treatment of *(2b)* with aqueous sodium hydroxide, which led to mercury, *N,N*-diethylurethane, diethylformamide, and ethanol. This reaction can be used for their quantitative determination. The reaction can be formulated as attack by the base on one of the two carbon atoms. Lithium perchlorate or perchloric acid precipitates the corresponding perchlorate [$ClO_4^{\ominus}$ in place of $BF_4^{\ominus}$ in *(2b)*] from an aqueous solution of *(2b)*.

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[*] Prof. Dr. U. Schöllkopf and Dipl.-Chem. F. Gerhart
Organisch-chemisches Institut der Universität
Windausweg 2
34 Göttingen (Germany)

[1] *E. O. Fischer* and *A. Maasböl*, Angew. Chem. *76*, 645 (1964); Angew. Chem. internat. Edit. *3*, 580 (1964). Cf. *O. S. Mills* and *A. Y. Redhouse*, Angew. Chem. *77*, 1142 (1965); Angew. Chem. internat Edit. *4*, 1082 (1965). For intermediate formation of a metal-carbene complex see *P. W. Jolly* and *R. W. Pettit*, J. Amer. chem. Soc. *88*, 5044 (1966).

[2] *U. Schöllkopf* and *F. Gerhart*, Angew. Chem. *78*, 675 (1966); Angew. Chem. internat. Edit. *5*, 664 (1966).

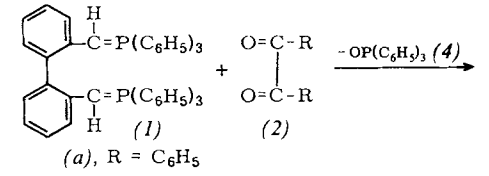
[3] Elemental analysis of all the compounds gave satisfactory results.

A New Route to Dibenzonorcaradiene Derivatives

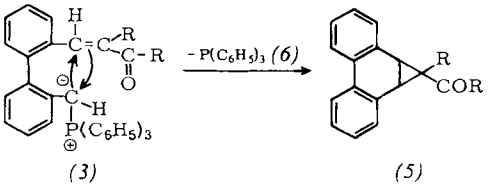
By *H. J. Bestmann* and *H. Morper* [*]

Dedicated to Professor G. Wittig on his 70th Birthday

Reaction of the bisylide *(1)*, readily obtained from 2,2'-bis-(bromomethyl)biphenyl [1,2], with 1,2-dicarbonyl compounds *(2)* in benzene or dioxane gives dibenzonorcaradiene derivatives *(5)*, triphenylphosphine oxide *(4)*, and triphenylphosphine *(6)*.



(a), R = C_6H_5
(b), R = CH_3



We assume that compound *(3)* is first formed by a Wittig reaction and is then converted into *(5)* by intramolecular nucleophilic attack by the ylide on the double bond [3] with formation of the cyclopropane ring and loss of triphenylphosphine. We can as yet make no statement about the steric arrangement of the substituents R and R–CO in compounds *(5)*.

(5a): Yield 60 %; m.p. 157 °C; mass spectrum, M^+ at *m/e* = 372. Proton resonance, singlet for the two protons of the cyclopropane ring at τ = 6.08, multiplets for the aromatic protons at τ = 3.34, 2.71, and 2.39; UV spectrum (in cyclohexane), λ_{max} 217 nm, 236 (shoulder), 245 (shoulder), 270, 278 (shoulder), 301, 313; IR spectrum, λ_{max} 6.1 μ.

(5b): Yield 25 %; m.p. 129 °C; mass spectrum, M^+ at *m/e* = 248. Proton resonance, one singlet for the protons of each methyl group at τ = 9.32 and 7.72, a singlet for the cyclopropane protons at τ = 6.77, and multiplets for the aromatic protons at τ = 2.72 and 2.09; UV spectrum, λ_{max} 223 nm, 241, 272, 280 (shoulder), 299, 312; IR spectrum, λ_{max} 5.96 μ. Elemental analysis gave the expected results for compounds *(5)*.

Preparation of (5)

Compound *(2)* is added to a solution of *(1)* [the bisphosphonium salt from which *(1)* is obtained must be dried carefully in a high vacuum over P_2O_5] in anhydrous benzene or dioxane and the whole is boiled until the red color of the ylide has disappeared. An excess of methyl iodide is then added and the reaction mixture boiled for an hour; the triphenylmethylphosphonium iodide that has separated is subsequently filtered off. The solvent is next distilled off and the residue taken up in hot ethanol. Compound *(5)* crystallizes on cooling.

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[*] Prof. Dr. H. J. Bestmann and Dipl.-Chem. H. Morper
Institut für Organische Chemie der Universität
Henkestr. 42
852 Erlangen (Germany)

[1] *D. M. Hall, M. S. Lesslie*, and *E. E. Turner*, J. chem. Soc. (London) *1950*, 711.

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Mössbauer Spectrum of the Iron in Glauconite

By *U. Hofmann, E. Fluck*, and *P. Kuhn* [*]

Dedicated to Professor G. Wittig on his 70th Birthday

Glauconite is closely related to the micaceous clay mineral illite and is almost identical with seladonite [1]. These three minerals are colored more or less green because of their iron content. Seladonite is used as a green pigment under the name Veronese Green. These minerals are layer silicates. Their ideal formula

$$K\,(Al_2,\ Fe^{III}_2,\ Fe^{II}_3,\ Mg_3)\ (OH)_2\ [Si_3AlO_{10}]$$

octahedral layer — tetrahedral layer

corresponds to the formula of mica, but the potassium content is often rather lower than that of the ideal formula.

The green color has been assumed to be due to Fe(II) ions, since so far as we know there is only one oxygen-containing compound that is colored green by Fe(III) ions, namely, an olive-green modification of $NaFeO_2$ [2]. All other Fe(III) compounds are colorless, yellow, brown, or red.

Since chemical analysis does not give reliable results for FeO, the Mössbauer spectrum of the ^{57}Fe in glauconite has been measured[3].

Several glauconites gave Mössbauer spectra that were insufficiently resolved, probably because they contained too little iron. However, from Rosenthaler Formsand Ia, supplied by Firma Bongsche Mahlwerke, Süchteln/Rheinland, we were able to slurry a material which contained only 2 % of quartz and 0.3 % of calcite in addition to glauconite. Its iron content was 15.5 % (calculated as Fe_2O_3), which was bound in the glauconite lattice, as well as 0.6 % of free Fe_2O_3. Chemical analysis gave 0.9 % of FeO and 15.4 % of Fe_2O_3.

For iron-containing silicates at −130 °C the isomeric shift in the spectrum, referred to $Na_2[Fe(CN)_5NO]\cdot 2\ H_2O$, is for Fe(III)ions at +0.5 to +0.75 mm/sec, and for Fe(II) ions at +1.3 to 1.6 mm/sec[4]. The center of the observed doublet (see Fig. 1) is at +0.72 mm/sec and thus shows Fe(III).

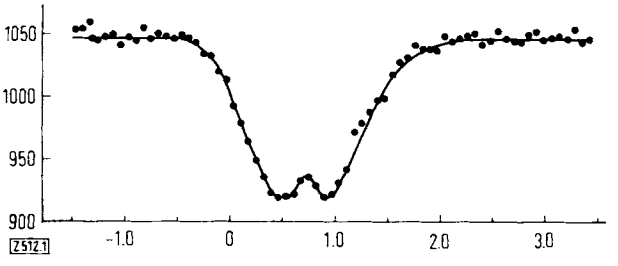


Fig. 1. Fe-Mössbauer spectrum of a glauconite.
Ordinate: Counts (arbitrary units).
Abscissae: Velocity (mm/sec).

The small content of Fe(II) found analytically does not appear in the Mössbauer spectrum.

For iron(III) silicates the quadrupole splitting of the doublet amounts to up to 1 mm/sec. For the glauconite examined it was 0.57 mm/sec. Our Mössbauer spectrum indicates approximately the same coordinative environment for all the iron ions. This means that almost all the Fe(III) ions lie in the octahedral layer of the lattice and not in the tetrahedral layer.

Since, according to the Mössbauer spectrum and the chemical analysis, only a very small amount of Fe(II) is present, the green color of the glauconite is apparently caused by Fe(III) ions in an octahedral environment. The same should be true for seladonite and, in general, for layer silicates that contain iron in the lattice.

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[*] Prof. Dr. U. Hofmann, Doz. Dr. E. Fluck, and
Dipl.-Phys. P. Kuhn
Anorganisch-Chemisches Institut der Universität
Tiergartenstr.
69 Heidelberg (Germany)

[1] *J. W. Gruner*, American Mineralog. *20*, 699 (1935); *E. Maegdefrau* and *U. Hofmann*, Z. Kristallogr. (A) *98*, 31 (1937).

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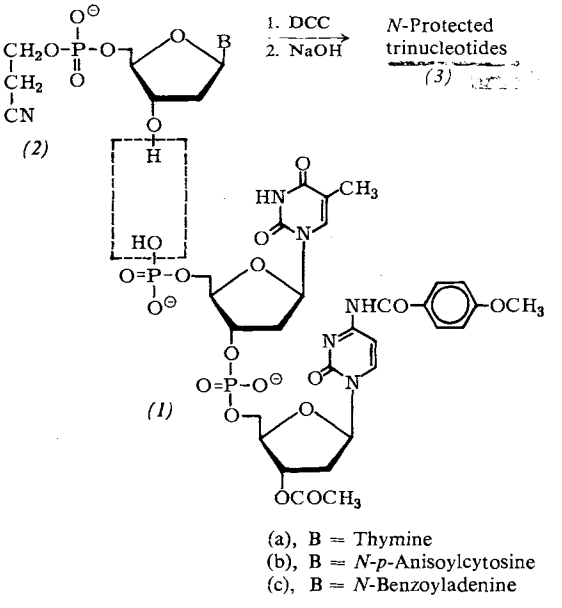
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Synthesis and Template Properties of Deoxyoligonucleotides with Repeating Triplet Sequences[1]

By *F. Cramer, W. Frölke*, and *H. Matzura*[*]

Dedicated to Professor G. Wittig on his 70th Birthday

For the synthesis of higher oligonucleotides the hitherto customary procedure of stepwise addition of one nucleotide at a time must be replaced by methods in which relatively short oligonucleotides are joined to larger units (block condensation). We have condensed trinucleotides of the type pXpTpC[2] to give oligonucleotides $(pXpTpC)_n$. The protected dinucleotide pTpC *(1)*[3] was treated with the 2-cyanoethylnucleotides *(2)*. In contrast to the procedures used hitherto, synthesis was effected in such a way that a free OH



(a), B = Thymine
(b), B = *N*-*p*-Anisoylcytosine
(c), B = *N*-Benzoyladenine

group on C-3′ of the mononucleotide reacted with a phosphate group on C-5′ of the dinucleotide.

For preparation of the dinucleotide components *(1)*, thymidine 5′-(2-cyanoethyl phosphate) was treated with *N*-*p*-anisoyl-3′-*O*-acetyldeoxycytidine 5′-phosphate in the molar ratio 1:1. After partial hydrolysis with 1 N NaOH the yield of pure 5′-*O*-phosphorylthymidylyl-(3′ → 5′)-*N*-*p*-anisoyldeoxycytidine was 38 to 40 %[3]. Then followed acetylation of the free 3′-hydroxyl group of the dinucleotide with acetic anhydride. Compound *(1)* was next treated with a 2-molar quantity of the mononucleotide *(2)*. For preparation of the 2-cyanoethyl esters of the mononucleotides and of the di- and tri-nucleotides, the corresponding pyridinium salts were treated with dicyclohexylcarbodiimide (DCC) in anhydrous pyridine; the reaction time for condensation of 2-cyanoethanol with the mononucleotides was 24 h at room temperature, but in the synthesis of the di- and tri-nucleotides a reaction time of 3 days gave the best results. After removal of the 2-cyanoethyl and acetyl protecting groups the reaction mixtures were separated on DEAE-cellulose columns (carbonate form), elution being in a triethylammonium hydrogen carbonate gradient at 3 °C. Yields of only *N*-protected trinucleotides amounted to 49.9 % *(3a)*, 44.5 % *(3b)*, and 45.2 % *(3c)*.

0.05 Mole of each trinucleotide *(3a)*–*(3c)* was condensed as pyridinium salt by a three-fold excess of 2,4,6-triisopropylbenzenesulfonyl chloride[4] in anhydrous pyridine for 12 h at room temperature, giving hexa-, nona-, dodeca-, and in part higher polynucleotides. The yields after removal of the protecting groups and paper-chromatographic purification in 1-propanol/conc. aq. NH_3/water (55:10:35) are shown in Table 1.

Table 1. Percentage product distribution after block condensation of the trinucleotides *(3)*.

Trinucleotide used	Distribution of the products [a]				
	Cyclic trinucleotide	$n = 1$	$n = 2$	$n = 3$	$n \geqslant 4$
(3a)	24.4	22.2	17.9	16.3	19.7
(3b)	23.2	24.6	22.2	12.4	17.5
(3c)	23.5	18.7	18.2	13.2	26.4

[a] n = Number of trinucleotide units per oligonucleotide chain.

The oligomers from dodecanucleotide upwards were used as single-strand templates for RNA-polymerase (E.C. 2.7.7.6)[5]. The introduction of nucleoside triphosphates (of which in each case one was labeled with ^{14}C in parallel experiments) into RNA was monitored for periods up to 2 h and corresponded to the ratio of bases in the DNA templates (Table 2).

Table 2. Introduction of nucleotides into RNA with synthetic templates.

Template	Introduction (nmoles) after 90 min		
	A	U	G
$(CTC)_{n\geqslant 4}$	4.65	—	9.50
$(ATC)_{n\geqslant 4}$	4.20	4.10	3.90
$(TTC)_{n\geqslant 4}$ [a]	24.30	—	12.20

[a] In this experiment a 2.5-fold amount of enzyme was used. Reactants: 0.25 ml at 20 °C. 0.03 M tris-acetate buffer (pH = 7.9), 0.13 M NH_4Cl, 0.03 M Mg acetate. — 10^{-3} M GTP and 0.5×10^{-3} M ATP, or ATP, GTP, and UTP (all three 10^{-3} M), or 10^{-3} M ATP and 0.5×10^{-3} GTP. — 0.01 M Phosphoenol pyruvate, 20 µg/ml pyruvate kinase, 1.0 O.D. unit of templates, 100 µg of protein (enzyme activity 200 units/mg protein).

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[*] Prof. Dr. F. Cramer, Dipl.-Ing. W. Frölke, and Dr. H. Matzura
Max-Planck-Institut für experimentelle Medizin, Abteilung Chemie
Hermann-Rein-Str. 3
34 Göttingen (Germany)

[1] Part 10 of Synthesis of Oligo- and Poly-nucleotides. — Part 9: *F. Eckstein*, Chem. Ber., in press.

[2] The following abbreviations are used:

p = Phosphate	ATP = Adenosine triphosphate
X = Any nucleoside	GTP = Guanosine triphosphate
T = Thymidine	UTP = Uridine triphosphate
C = Cytidine	DCC = Dicyclohexylcarbodiimide
A = Adenosine	RNA = Ribonucleic acid
U = Uridine	DNA = Deoxyribonucleic acid
G = Guanosine	

[3] Cf. *E. Ohtsuka, M. W. Moon*, and *H. G. Khorana*, J. Amer. chem. Soc. *87*, 2956 (1965).

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Synthesis of Tetrakis(trimethoxyphosphine)nickel(0) [1]

By *Th. Kruck* and *M. Höfler* [*]

In studies of the complex chemistry of trifluorophosphine we have repeatedly observed that polar solvents (water, alcohols, primary and secondary amines) cause a characteristic rapid solvolysis of the phosphorus-fluorine bonds while the metal-phosphorus bonds remain intact. We therefore tried to effect planned P—F fissions with formation of new P—X bonds in order to obtain new species of phosphine complexes of transition metals without alteration of the type of compound. We have now effected exchange reactions of the type:

$$M{-}PF_3 + n\ M'X \rightarrow M{-}PF_{3-n}X_n + n\ M'F$$

(M' = alkali metal; X = OR, R, NR_2, *etc.*; $n = 1$ to 3)

for several trifluorophosphine-metal complexes (M = Ni, Pt, Fe, and Cr).

Particular interest centers on reactions in which an excess of M'X is used and complete exchange of fluorine leads to homogeneous phosphine complexes. An example is the synthesis of tetrakis(trimethoxyphosphine)nickel(0), which had not been isolated previously[2]:

$$Ni(PF_3)_4 + 12\ NaOCH_3 \rightarrow Ni[P(OCH_3)_3]_4 + 12\ NaF$$

This compound is formed quantitatively. It is a colorless non-electrolyte that crystallizes well and is readily soluble in the usual solvents except cold petroleum ether. The ^{31}P—NMR spectrum[3] (Spectrospin-KIS-2, 30 MHz, saturated solution in petroleum ether, 26 °C, 80 % H_3PO_4 as external standard) contains a signal at −164.3 ppm broadened to *ca.* 28 Hz by P—H coupling.

Experimental:

A solution of sodium (4.0 g, 174.5 mg-atoms) in methanol (50 ml) is added dropwise, with stirring, to a solution of $Ni(PF_3)_4$ [4] (5.4 g, 13.2 mmoles) in methanol (10 ml). The mixture is then boiled for 3 h under reflux and, after cooling, the methanol is distilled off in a vacuum. The viscous residue is extracted with four portions, each of 30 to 50 ml, of petroleum ether. The united extracts are freed from petroleum ether. If the crude product still contains P—F bonds (IR spectrum) it is treated again with an excess of $NaOCH_3$. Recrystallization from petroleum ether gives odorless, colorless crystals that melt at 132 °C and decompose only slowly above 220 °C with formation of a brown color and separation of metal.

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[*] Prof. Dr. Th. Kruck and Dr. M. Höfler
Institut für Anorganische Chemie der Universität
Zülpicherstr. 47
5 Köln (Germany)

[1] Part 1 of Fluorine-Exchange Reactions of Trifluorophosphine Complexes.

[2] The existence of this compound was indicated only by Raman spectroscopy; see *M. Bigorgne* and *A. Zelwer*, Bull. Soc. chim. France *1960*, 1986.

[3] We thank *P. Junkes* for measurement of the ^{31}P—NMR spectrum.

[4] *Th. Kruck* and *K. Baur*, Chem. Ber. *98*, 3070 (1965).

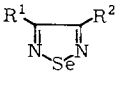
Synthesis of 1,2,5-Selenadiazole and some of its Derivatives

By *V. Bertini* [*]

Weinstock et al.[1] have recently synthesised 1,2,5-selenadiazole *(1)*[2] in 7 % yield. We have now succeeded in preparing this compound [b.p. 142 °C/770 torr, $n_D^{25} = 1.6179$, $\lambda_{max} = 282$ nm[3] (log ε = 3.85) in isooctane] in 43 % yield.

A solution of 0.045 moles of ethylenediamine in 30 ml of *N,N*-dimethylformamide was added slowly to 0.135 moles of SeO_2 in 110 ml of *N,N*-dimethylformamide and the reaction mixture maintained at 120 °C under reflux for 40 minutes. The product was separated by steam distillation.

Under similar conditions, 0.030 moles of propylenediamine and 0.090 moles of SeO_2 yield 3-methyl-1,2,5-selenadiazole *(2)*[2] [b.p. 162 °C/770 torr, $n_D^{25} = 1.5807$, $\lambda_{max} = 287$ nm (log ε = 3.83) in isooctane] in 35 % yield.



(1), $R^1 = R^2 = H$
(2), $R^1 = H$, $R^2 = CH_3$
(3), $R^1 = R^2 = CH_3$

We have also found that *vic* dioximes, like aliphatic *vic* diamines, react with SeO_2 to give 1,2,5-selenadiazole derivatives. Thus, 3,4-dimethyl-1,2,5-selenadiazole *(3)*[2] [m.p. 87 °C, $\lambda_{max} = 287$ nm[3] (log ε = 3.88) in isooctane] has been prepared in 45 % yield by refluxing 0.006 moles of dimethylglyoxime and 0.030 moles of SeO_2 in 30 ml of

N,N-dimethylformamide for 45 minutes. The solid product, obtained by steam distillation of the reaction mixture, was purified by crystallization from n-pentane.

Compounds *(1)*, *(2)* and *(3)* have also been prepared by using Se_2Cl_2 instead of SeO_2; in this case the reaction is very exothermic and the addition of reagents must be carried out at about 5–10 °C; yields are also somewhat lower.

Compounds *(1)*, *(2)*, and *(3)* form complexes with $CdCl_2$ which are sparingly soluble in water and in most organic solvents. These complexes offer a useful method for purification of the heterocycles because steam distillation of the complex readily regenerates the 1,2,5-selenadiazole ligand.

When the compounds *(1)*, *(2)* and *(3)* are reduced with H_2S at room temperature, elemental selenium is formed rapidly in stoichiometric amounts along with ethylenediamine, propylenediamine, and 2,3-butylenediamine, respectively.

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[*] Dr. V. Bertini
Istituto di Chimica Organica,
Facoltà di Scienze, Università di Pisa
Via Risorgimento, 35
Pisa (Italy)

[1] *L. M. Weinstock, P. Davis, D. M. Mulvey*, and *J. C. Schaeffer*, Angew. Chem. *79*, 315 (1967); Angew. Chem. internat. Edit. *6*, 364 (1967).

[2] *V. Bertini* and *P. Pino*, Ital. Pat. Appl. 32911A/67 (March 8th, 1967).

[3] Maximum with fine structure,

Spectroscopic Substituent Constants of Phosphorus-containing Groups[1]

By *G. P. Schiemenz* [*]

The spectroscopic constants $\delta\lambda_0$ of the Doub-Vandenbelt equation (a)[2] describe approximately the mesomeric effect of a substituent. Values of $\delta\lambda_0 = 41.1$ to 42.0 and 44.5 to 45.7 for the phosphinyl- and phosphonium-phosphorus, respectively, in the dimethylanilines *(1a)* to *(4a)* containing such substituents can be calculated by means of eqn. (a) from the position of the primary band in the required solvent water[2] with $\delta\lambda_0^{N(CH_3)_2} = 61.1$[3]; the values obtained indicate a $-M$ effect approximately the same as for cyano ($\delta\lambda_0 = 43.9$) and the carboxylate group ($\delta\lambda_0 = 44.7$)[2]. These values, however, being obtained from the spectra of only a few compounds, are not very certain.

It should be possible to obtain more reliable results, as has been done for the Hammett constants[4], by a least squares calculation on the data of a series of phosphine oxides and phosphonium salts substituted systematically by +M groups. However, the monofunctional derivatives *(1)* and *(2)* cannot be used for this purpose because with "electronically weak" substituents X the absorption of the group p-X–C_6H_4 is masked by that of the two phenyl groups[5]. This disturbance does not occur with the trisubstituted compounds *(3)* and *(4)*. Although, within the series *(3)* and *(4)*, the group $-P(O)Ar_2$ (or $-P^{\oplus}(CH_3)Ar_2$) that is regarded as substituent in the compound X–C_6H_5 does not remain constant, we have found previously[3,5] that the absorption of a p-X–C_6H_4 group is only slightly dependent on the presence of even "electronically strong" substituents on other aromatic rings.

p-X–C_6H_4–$P(O)Ar_2$ p-X–C_6H_4–$P^{\oplus}(CH_3)Ar_2$ $Hal^{\ominus}$

(1), Ar = C_6H_5 *(2)*, Ar = C_6H_5

(3), Ar = p-X–C_6H_4 *(4)*, Ar = p-XC_6H_4

When $\delta\lambda_0$ of the substituents X is plotted against λ_{max} of the primary band of compounds *(3)* and *(4)*, the experimental points all fall close to a straight line, only those for phenolates diverging appreciably (in those cases probably because of the accumulation of charged substituents[2]). After approximation (by the method of least squares) the remaining values give the "excellent"[4] equations (b) and (c), which give $\delta\lambda_0^{PO} = 40.0$ (at $\lambda_0 = 183.1$ nm) and $\delta\lambda_0^{P\oplus CH_3} = 47.1$ (at $\lambda_0 = 175.9$ nm). On normalization to $\lambda_0 = 180$ nm[2] one obtains $\delta\lambda_0^{PO} = 43.1$ and $\delta\lambda_0^{P\oplus CH_3} = 43.0$.

($\delta\lambda_0'$, $\delta\lambda_0''$ are spectroscopic substituent constants, $k = 24.05$, $\lambda_0 = 180$ nm in equation (a)).

$$\lambda_{max} = (\delta\lambda_0' \, \delta\lambda_0'')/k + \lambda_0 \quad (a)$$

$$\lambda_{max} = 1.661 \, \delta\lambda_0^{PO} + 183.1 \quad (b)$$
($r = 0.995$, $s = \pm 2.5$ nm)

$$\lambda_{max} = 1.959 \, \delta\lambda_0^{P\oplus CH_3} + 175.9 \quad (c)$$
($r = 0.998$, $s = \pm 1.8$ nm)

X	$\delta\lambda_0^X$	Phosphine oxide	λ_{max} (nm) in H_2O	Phosphonium salt	Hal	λ_{max} (nm) in H_2O
$(CH_3)_2N$	62.1 [3]	*(1a)*	286	*(2a)*	I	295
$(CH_3)_2N$	62.1 [3]	*(3a)*	288.5	*(4a)*	I	298
$O^{\ominus}$	55.0 [2]	*(3b)*	266	*(4b)*	Cl	271
H_2N	50.0 [2]	*(3c)*	263			
CH_3O	36.8 [2]	*(3d)*	244	*(4d)*	I	247
HO	36.1 [2]	*(3e)*	242	*(4e)*	Cl	246
CH_3	29.6 [2]	*(3f)*	231.5	*(4f)*	I	231.5
Cl	29.3 [2]	*(3g)*	235.5	*(4g)*	I	235.5
H	24.05 [2]	*(3h)*	222.5	*(4h)*	Br	224

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[*] Dr. G. P. Schiemenz
Institut für Organische Chemie der Universität
Olshausenstr. 40–46
23 Kiel (Germany)

[1] Lecture given at the Conference for West German Lecturers, Saarbrücken, April 12th, 1967.

[2] *L. Doub* and *J. M. Vandenbelt*, J. Amer. chem. Soc. *69*, 2714 (1947).

[3] *G. P. Schiemenz*, Tetrahedron Letters *1964*, 2729.

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Tetrachlorophosphonium and Chloro(phenyl)-phosphonium Perchlorates and Hexachloroantimonates

By *A. Schmidpeter* and *H. Brecht* [*]

With many metal and non-metal chlorides PCl_5 gives addition compounds that are to be regarded as tetrachlorophosphonium salts of chloro acids. PCl_4^+ salts of pure oxo acids were, however, previously unknown and were considered incapable of existence[1].

We have found that PCl_5 reacts smoothly with perchloric acid in methylene chloride to yield PCl_4ClO_4; chloro(phenyl)-phosphonium perchlorate was obtained in the same way[2]:

$$(C_6H_5)_nPCl_{5-n} + HClO_4 \rightarrow HCl + [(C_6H_5)_nPCl_{4-n}]ClO_4$$
(1)

$[(C_6H_5)_nPCl_{4-n}]X$		$n = 0$	$n = 1$	$n = 2$	$n = 3$
(1)	M.p. (°C) (decomp.)	95	[a]	117	189
X = ClO_4	^{31}P (ppm) [b]	−87.1	−103.0	−93.2	−65.7 [c]
(2) X = $SbCl_6$	^{31}P (ppm)	[7] −87.9	−102.9	−93.2	−65.0

[a] Decomposes explosively at 70 °C.
[b] ^{31}P shifts in nitromethane or nitroethane with respect to 85 % H_3PO_4.
[c] In methylene chloride.

The products are colorless, crystalline compounds that do not decompose over a considerable period of time at −20 °C but are unstable at room temperature. When heated they decompose more or less violently; the phenyl compounds deflagrate with formation of much soot.

The ^{31}P–NMR signals are shifted downfield compared with the corresponding chlorophosphoranes. When plotted against the number of phenyl groups the values lie to a good approximation on a parabola with its minimum at $n \approx 1.2$. They agree with those of the hexachloroantimonates $[(C_6H_5)_nPCl_{4-n}]SbCl_6$ *(2)* which were prepared for comparison. The position of the ^{31}P signal of a solution of PCl_4ClO_4 in nitromethane is comparable[3] with the signals of $[PCl_4]AlCl_4$ (−86.5 ppm)[4], of $[PCl_4]^+$ in crystalline PCl_5 (−96, −92 ppm)[5,6], and of PCl_2F_3 (−95 ppm)[6]. Compounds *(1)* are thus to be considered as chlorophosphonium perchlorates.

Chlorophosphonium perchlorates:

An equivalent amount of an approximately 1 M solution of anhydrous $HClO_4$ in CH_2Cl_2 is stirred into a solution or suspension of a chlorophosphorane $(C_6H_5)_nPCl_{5-n}$, $n = 0$ to 3, in CH_2Cl_2 at 20 °C. The perchlorates crystallize spontaneously or after cautious concentration. The solubility increases greatly with increase in n.

Chlorophosphonium hexachloroantimonates:

Equimolar amounts of the chlorophosphorane and $SbCl_5$, both in CH_2Cl_2, are combined and the solution is concentrated, if necessary.

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[*] Dr. A. Schmidpeter and Dipl.-Chem. H. Brecht
Institut für Anorganische Chemie der Universität
Meiserstr. 1
8 München 2 (Germany)

[1] *W.L.Groeneveld*, Receuil Trav. chim.Pays-Bas *75*, 596 (1956).

[2] We thank *W. Wässle* and *G. Wandinger* for help with the preparation and analysis of the compounds.

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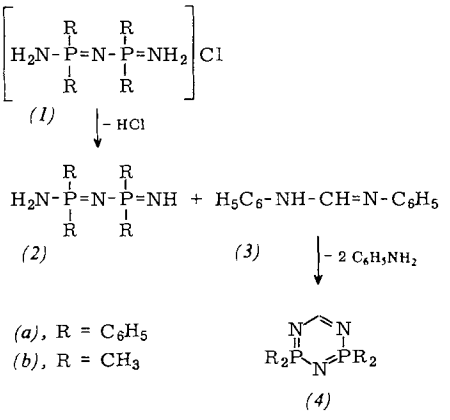
[7] *W. L. Groeneveld* and *A. P. Zuur*, Recueil Trav. chim. Pays-Bas *71*, 1152 (1952).

Synthesis of Phospha- and Diphospha-1,3,5-triazines by Cyclizing Transamination with Aminophosphazenes [1]

By *A. Schmidpeter* and *J. Ebeling* [*]

The methods previously described for the synthesis of diphospha-1,3,5-triazines[2] are not suitable for the preparation of the series *(4)* unsubstituted at position 6. We have now prepared the latter by treating 4-aminodiphosphazenes *(2)* with *N,N'*-diphenylformamidine.

The structure of *(4)* is proved by the NMR spectra [**]: As a result of coupling with the two equivalent phosphorus atoms the signal of the proton at position 6 is split into a triplet with an unusually high coupling constant (see table; the coupling constants J_{PH} of phosphinylmethylamides with the same arrangement of atoms P–N–C–H are between 9 and 15 Hz). The signal is shifted either slightly negatively or positively with respect to the formyl-proton in *(3)* (δ^1H = −8.23). On the other hand, the signal of the proton at position 2 of pyrimidine is at $\delta = -9.26$, although this can be shifted to −7.9 for pyrimidine derivatives. Thus the measured shifts cannot be used to draw conclusions about ring currents.

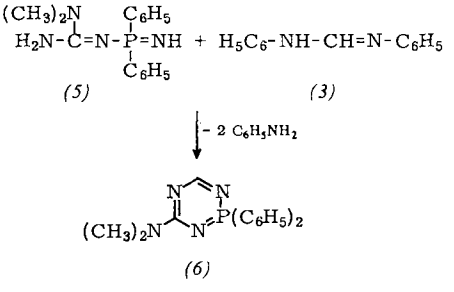


	M.p. (°C)	$\delta^{31}P$	Ring proton		Methyl protons	
			δ^1H	J_{PH} (Hz)	δ^1H	J_{PH} (Hz)
(4a)	242–243	−14.4	−8.43	40.3	—	—
(4b)	121–122 sublimes at 40 °C/0.01 mm	−27.1	−7.57	40.0	−1.40 doublet	14.0

Compound *(4b)* is hygroscopic and dissolves exceedingly readily and without decomposition in water. The solution reacts alkaline (pH = 9).

Compounds *(2a)* (m.p. 182–185 °C, $\delta^{31}P$=−17.7 in methanol) and *(2b)* can be obtained from the reaction of their hydrochlorides[3] with sodium methoxide; this reaction is remarkable insofar as *(2)* are aminophosphazyl-diaryl- and -dialkylphosphine imines and yet triorganylphosphine imines cannot be prepared in this way[4].

Phospha-1,3,5-triazines have hitherto been described only in the form of their imidophosphate or imidothiophosphate tautomers [5]. We obtained 4-dimethylamino-2,2-diphenylphospha-1,3,5-triazine *(6)* by cyclizing transamination with the guanylphosphazene *(5)*.



NMR spectrum of *(6)* in CH_2Cl_2: phosphorus, $\delta = -26.4$, doublet, J_{PH} = 35–40 Hz; ring proton, δ=−8.04, doublet, higher resonance masked by the multiplet of the phenyl protons, J_{PH} = 38 Hz; methyl protons, $\delta = -3.07$, signal broadened by unresolved hyperfine structure.

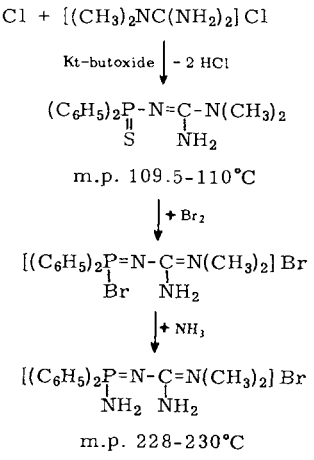
Derkatsch et al. have prepared other phospha-1,3,5-triazines from phosphorus isocyanates[6].

Diphospha-1,3,5-triazines:

A methanolic solution of *(1)* is treated with an equivalent amount of sodium methoxide, filtered from NaCl, and evaporated. The residual *(2)* is melted with an equivalent amount of *(3)* in a vacuum, whereby 2 mol. equiv. of aniline are distilled off. Purification is by recrystallization from benzene or sublimation in a vacuum. Yield: 70–80 %.

4-Dimethylamino-2,2-diphenylphospha-1,3,5-triazine (6):

The hydrobromide of *(5)* is obtained by the stages:



Product recovery is as described for diphospha-1,3,5-triazines. Compound *(6)* crystallizes, from benzene or ether, in flakes, m.p. 146.5–147 °C (yield 78 %).

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[*] Dr. A. Schmidpeter and Dipl.-Chem. J. Ebeling
Institut für Anorganische Chemie der Universität
Meiserstr. 1
8 München 2 (Germany)

[**] Chemical shifts were measured for CH_2Cl_2 or CH_2Br_2 solutions and are given in ppm, and as negative for lower field strengths with respect to 85 % H_3PO_4 or tetramethylsilane.

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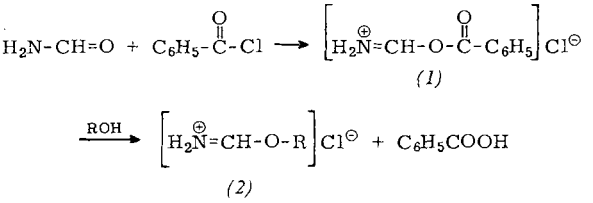
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A Simple Synthesis of Alkyl Formimidates

By *R. Ohme* and *E. Schmitz* [*]

We have found that alkyl formimidate hydrochlorides *(2)* may be prepared by the simultaneous action of benzoyl chloride and alcohol on formamide:



(1)

(2)

The mixed acid anhydride *(1)* may be an intermediate in the reaction since a compound of presumed structure *(1)* has been obtained on reaction of benzoyl chloride with formamide [1]. Such compounds are readily alcoholysed to *(2)* and benzoic acid.

Alkyl formimidate hydrochlorides *(2)* have indefinite melting points. Their structure follows from elemental analysis, thermal decomposition to formamide and alkyl chloride (identified by gas chromatography), and from the following characteristic reactions [2]: (i) with an excess of alcohol they undergo alcoholysis to form the trialkyl orthoformates and ammonium chloride; (ii) treatment with ammonia or amine leads to formamidines in good yields; and (iii) on heating in the presence of tri-*n*-butylamine the 1,3,5-triazines *(3)*, which are useful for many syntheses [3], are obtained in 79 % yield. Compounds *(2)* and *(3)* have hitherto been obtained from anhydrous hydrogen cyanide [4,5] but now become appreciably more easily accessible.

Attempts to carry out the above reaction in which the benzoyl chloride is replaced by other acid halides (*e.g.* sulfonyl chlorides, acetyl chloride, inorganic acid chlorides) proved unsuccessful; either no reaction took place or alcoholysis of the acid halide occurred. Ethanol could be replaced by other primary or secondary alcohols, whereby the corresponding formimidic ester hydrochlorides *(2)* were obtained with the following yields [6]: R = *n*-C_3H_7, 80 %; R = *iso*-C_3H_7, 60 %; R = *n*-C_4H_9, 79 %; R = CH_3, 70 %.

Ethyl formimidate hydrochloride:

A mixture of formamide (45 g) and ethanol (46 g) is added dropwise, and with stirring (over a 45 min period), to a solution of benzoyl chloride (140.6 g) in anhydrous ether (700 ml) at 10 to 20 °C. The whole is stirred for a further, 15 min, and the precipitated hydrochloride is filtered off, washed with anhydrous ether (200 ml), and dried over phosphorus pentoxide. Yield, 109 g (99 %). 1 mole of benzoic acid can be isolated from the filtrate.

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[*] Dr. R. Ohme and Prof. Dr. E. Schmitz
Institut für organische Chemie der Deutschen Akademie der Wissenschaften zu Berlin
An der Rudower Chaussee
X 1199 Berlin-Adlershof (Germany)

[1] *H. Bredereck*, *R. Gompper*, *H. Rempfer*, *K. Klemm*, and *H. Keck*, Chem. Ber. *92*, 329 (1959).

[2] *R. Roger* and *D. G. Neilson*, Chem. Reviews *61*, 179 (1961).

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[5] Cf. [3], pp. 320, and 404.

[6] Patent applied for.

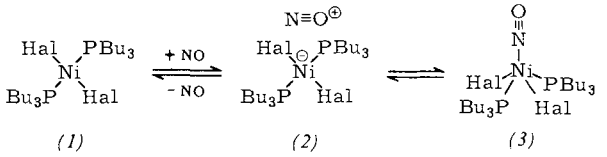
Reaction of Halogeno(phosphine)nickel Complexes with Nitric Oxide

By *H. Brunner* [*]

The reaction of nitric oxide with halogeno(tri-n-butylphosphine)nickels *(1)* is determined by the nature of the halogen. If NO is passed through a solution of $(Bu_3P)_2NiCl_2$ [1] in petroleum ether, benzene, or methylene chloride at room temperature, the IR spectrum of the solution exhibits a band at 2220 cm^{-1}, *i.e.* in the absorption region of the free NO^+ cation. The product, which is also formed in the non-solvating solvent, hexane, would appear to be best formulated as *(2)*. The weak intensity of the NO^+ band indicates that the equilibrium *(1)* ⇌ *(2)* lies largely on the side of *(1)*. When N_2 is passed through the reaction solution the NO bound in the complex is removed along with the dissolved NO, and the starting material *(1)* is recovered.

The IR spectrum of a hexane solution of $(Bu_3P)_2NiBr_2$ [2] that has been treated with NO contains, as well as a band at 2215 cm^{-1}, a further band at 1720 cm^{-1} corresponding to a coordinately bound NO group. Thus, in the case of the bromide, addition of the NO^+ cation follows a rapid reversible electron transfer, yielding *(3)*.

The magnetic moment of 2.0 B.M. found for *(3)* in cyclohexane by the NMR method [3] proves that in *(3)* the noble-

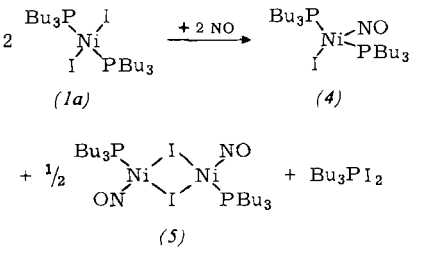


(1) (2) (3)

gas configuration of the Ni is exceeded by one electron. In an attempt to isolate *(3)* NO was lost and *(1)* was re-formed.

The complexes *(1)*, Hal = Cl and Br, cannot indefinitely undergo reversible addition of NO because on prolonged action of NO they are converted into the oxidation products $(Bu_3PO)NiHal_2$ [4].

On reaction of $(Bu_3P)_2NiI_2$ [2] with NO the presence of the intermediates *(2)* and *(3)* cannot be demonstrated although, as the products *(4)* and *(5)* show, they probably represent steps in the reaction.



(1a) (4)

(5)

If the reaction is carried out in hexane, Bu_3PI_2 is precipitated and can be isolated. The IR spectrum of the mixture of *(4)* and *(5)* contains three NO bands, of which one is assigned to *(4)* and the two others to the *cis,trans* isomers [5] of *(5)*. The analytical results and molecular weight of the mixture lie between those of *(4)* and *(5)*.

Chromatographic separation of *(4)* and *(5)* has not been accomplished because of the instability of *(5)*. However, *(5)* is readily converted into *(4)*: if the mixture of *(4)* and *(5)* is treated with PBu_3 the I bridges in *(5)* are broken and after removal of the excess of PBu_3 in a high vacuum at 90 °C analytically pure *(4)* is obtained in 95 % yield (calculated on the $(Bu_3P)_2NiI_2$ *(1)* used). Iodonitrosylbis(tri-n-butylphosphine)nickel *(4)* is a violet compound that is liquid at room temperature and dissolves as the monomer in benzene. Its properties closely resemble those of the compounds $[(C_2H_5)_3P]_2Ni(NO)NO_3$ [4] and $[(C_6H_{11})_3P]_2Ni(NO)I$ [5] which have been prepared by other methods.

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[*] Dr. H. Brunner
Anorganisch-Chemisches Laboratorium
der Technischen Hochschule
Arcisstr. 21
8 München 2 (Germany)

[1] *K. A. Jensen*, Z. anorg. allg. Chem. *229*, 265 (1936).

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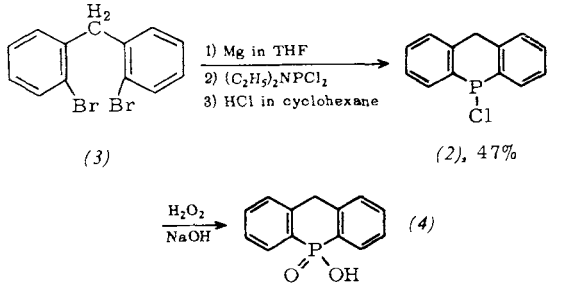
Dibenzo[*b*,*e*]phosphorin

By *P. de Koe* and *F. Bickelhaupt* [*]

With phosphorus, as with other elements of Period 3, the tendency to formation of p_π-hybrid bonds is very slight. Only very recently have derivatives of tervalent phosphorus with coordination number 2 been prepared [1]. We set ourselves the task of synthesizing dibenzo[*b*,*e*]phosphorin (9-phosphaanthracene) *(1)*, the phosphorus analogue of acridine, by removal of HCl from 5-chloro-5,10-dihydrodibenzo[*b*,*e*]-phosphorin *(2)* [2].

We worked out two new methods of preparing *(2)*:

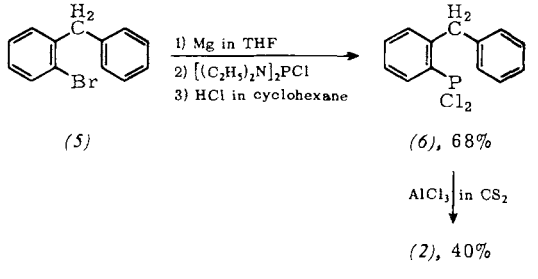
a) A solution of the di-Grignard compound from bis(*o*-bromophenyl)methane *(3)* in tetrahydrofuran was added dropwise to a solution of dichlorodiethylaminophosphine (molar ratio *ca.* 1:1) in tetrahydrofuran at −80 °C. After evaporation of the solvent the residue was extracted with cyclohexane, filtered, and gaseous HCl was passed into the filtrate. The crude product obtained on subsequent evaporation was sublimed and recrystallized from toluene; m.p. (after sublimation) 102–109 °C (lit.: 78–86 °C [2]). To confirm its structure, the product *(2)*, which is very sensitive to hydrolysis, was oxidized in sodium hydroxide solution to *(4)* [2] by hydrogen peroxide.



(3) (2), 47 %

(4)

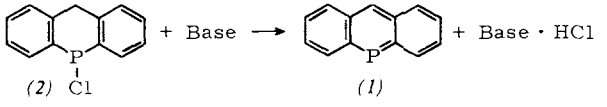
b) Analogously, interaction of the Grignard compound from (*o*-bromophenyl)phenylmethane *(5)* and chlorobis(diethylamino)phosphine in tetrahydrofuran at −80 °C and treatment of the reaction mixture with cyclohexane and HCl as described in a) affords *o*-benzylphenyldichlorophosphine *(6)*, b.p. 142–143 °/0.01 mm, $n_D^{20} = 1.6298$, in 68 % yield. When boiled for 10 h with a slight excess of aluminum chloride in carbon disulfide *(6)* gave *(2)* in 40 % yield [3].



(5) (6), 68%

(2), 40%

Experiments to remove HCl from *(2)* were carried out with various degrees of success with tritylsodium, ethyldicyclohexylamine, triethylamine, and 1,5-diazabicyclo[4.3.0]non-5-ene *(7)* [4] in various solvents, the appearance of the characteristic UV spectrum being considered as indicating formation of *(1)*. We found that a slight excess of *(7)* in toluene or dimethylformamide gave the best results: 76.9 mg of *(7)* was added to 126.5 mg of *(2)* in 10 ml of anhydrous, degassed toluene at −196 °C, the reaction vessel was sealed in a high vacuum, and the mixture allowed to warm to room temperature. The product *(1)* is formed slowly (several hours) in toluene, and the solution obtained is stable for several days. In dimethylformamide formation of *(1)* occurs within an hour but the solution is largely decomposed (UV spectrum) after one day.



(2) (1)

The following observations indicate the formation and structure of *(1)*: When the components are warmed from −196 °C to room temperature the solution gradually becomes

pale yellow; after a short time a white precipitate separates (but not from dimethylformamide), which contains 60–75 % of the hydrochloride of the base. The filtrate gives the UV spectrum reproduced in Fig. 1.

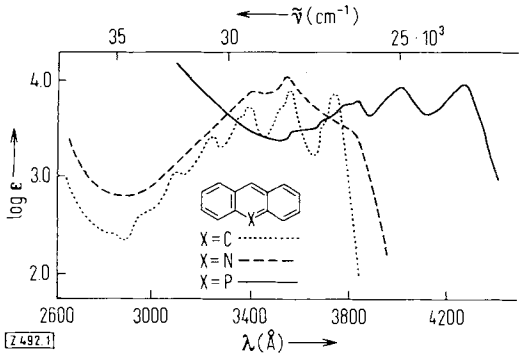


Fig. 1. UV spectra of anthracene (in cyclohexane), acridine (in 95 % ethanol), and *(1)* (in toluene). [The vertical position of the curve for *(1)* is selected arbitrarily.]

Surprisingly, the UV spectrum of the new compound resembles that of anthracene more closely than that of acridine. Apart from the bathochromic shift[1] (long-wave absorption at $\lambda = 429$ mμ, ε unknown) the separations and relative intensities of the maxima show strong analogies to the fine structure of the ^1L_A band of anthracene, possibly owing to the fact that phosphorus and carbon have almost identical electronegativities ($\chi_P = \chi_C = 2.5$)[5], in contrast to the more electronegative nitrogen ($\chi_N = 3.0$).

It has not yet been possible to isolate *(1)*. The UV spectrum disappears immediately on admission of atmospheric oxygen, very rapidly on addition of sodium hydroxide or anhydrous HCl, and slowly on addition of dilute acid or, depending on the solvent, on standing. On either evaporation or cooling to −196 °C the solution appears to decompose (irreversible weakening of the UV bands; evaporation of a filtered solution and washing of the residue with toluene gives an inhomogenous product).

HCl is also very easily split off from *(2)* (molecule ion at $m/e = 232$, intensity 43 %) under the conditions of mass spectroscopy; this gives a stable ion $(1)^+$ ($m/e = 196$, intensity 100 %), which in turn loses phosphorus to give (9-fluorenyl)$^+$ ($m/e = 165$, intensity 57.7 %; corresponding metastable ion at $m/e = 139.1$)[6]. Appearance of $(1)^{2+}$ ($m/2e = 98$, intensity 34 %) is noteworthy.

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[*] P. de Koe and Prof. F. Bickelhaupt
Scheikundig Laboratorium der Vrije Universiteit
de Lairessestraat 174
Amsterdam-Z. (Netherlands)

[1] *G. Märkl*, Angew. Chem. *78*, 907 (1966); Angew. Chem. internat. Edit. *5*, 846 (1966); *G. Märkl*, *F. Lieb*, and *A. Merz*, Angew. Chem. *79*, 59 (1967); Angew. Chem. internat. Edit. *6*, 87 (1967); *K. Dimroth* and *P. Hoffmann*, Chem. Ber. *99*, 1325 (1966).

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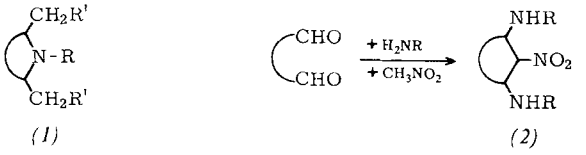
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[6] We thank Prof. *Th. J. de Boer* and Dr. *H. J. Hofman*, Organic Chemical Institute of the University of Amsterdam, for determination of the mass spectrum and for help with its interpretation.

Synthesis of Cyclic 1,2,3-Triamines by the Reaction of Dialdehydes with Nitromethane and Benzylamine [1]

By *F. W. Lichtenthaler*, *T. Nakagawa*, and *A. El-Scherbiney* [*]

The Mannich reaction of 1,4- or 1,5-dialdehydes with primary amines and methylene compounds activated by carbonyl or carboxyl groups gives products of type *(1)* (Robinson-Schöpf synthesis[2]). We have found that cyclic nitrodiamines *(2)* are formed when nitromethane is used as the methylene component – analogous to its double aminomethylation[3].

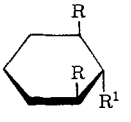


(1) *(2)*

Thus reaction of glutardialdehyde (25 % aqueous solution) with nitromethane and benzylamine in the molar ratio 1:1.5:4 (1 h at 0 °C, 12 h at room temperature) gives all-*trans*-N^1,N^3-dibenzyl-1,3-cyclohexanediamine *(3)* (m.p. 84 to 85 °C) in 60 % yield. The product is precipitated by addition of water and purified by recrystallization from methanol.

If the reaction is carried out stepwise (*i.e.* the nitromethane cyclization product *(4)*[4] is prepared first and then treated with benzylamine) compound *(3)* can be isolated in 75 % yield (calculated on the dialdehyde used).

Catalytic hydrogenation (3 h) of *(3)* over Raney nickel in water gives N^1,N^3-dibenzyl-*trans*-*trans*-1,2,3-cyclohexanetriamine *(5)*, which was isolated as trihydrochloride, m.p. 217–220 °C. On hydrogenation over 10 % palladium/charcoal in methanol/1 N acetic acid (1:1), reduction of the nitro group is accompanied by hydrogenolysis of the *N*-benzyl groups and thus formation of the all-*trans*-cyclohexanetriamine, which was characterized as trihydrochloride *(6)*, m.p. 330 °C, and triacetate, decomp. pt. 329–330 °C.



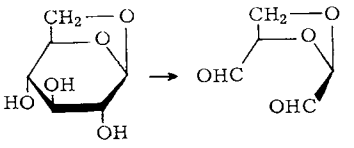
(3), R = C_6H_5-CH_2-NH, R^1 = NO_2
(4), R = OH, R^1 = NO_2
(5), R = C_6H_5-CH_2-NH, R^1 = NH_2
(6), R = R^1 = $NH_2 \cdot HCl$
(7), R = R^1 = NH-CO-CH_3

The all-*trans* configuration of the products *(3)* and *(5)* through to *(7)* is demonstated by the NMR spectra: *(3)* gives a triplet of intensity 1:2:1 at $\tau = 5.93$, which must be assigned to H-2 because of its chemical shift, and whose coupling constant of $J = 10$ Hz proves the axial orientation of the ring protons H-1, H-2, and H-3, *i.e.* the equatorial orientation of the substituents; the CH_3 groups of the triacetate *(7)* give only one signal, at $\tau = 8.10$ (9 H), which proves the steric equivalence of the acetamido groups and their equatorial orientation.

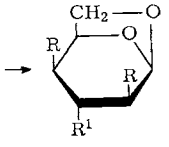
The principle of the reaction can be applied to sugar dialdehydes. Thus the dialdehyde *(9)* that is obtained on oxidation of levoglucosan *(8)* by periodate gives, on reaction with nitromethane and benzylamine (molar ratio 1:2:4), 2,4-bis-(benzylamino)-2,3,4-trideoxy-3-nitro-β-D-idosan *(10)* [yield 53 %, m.p. 121–123 °C, $[\alpha]_D^{20} = 73.5°$ ($CHCl_3$)] which can be isolated by virtue of its insolubility in water and purified by recrystallization from methanol.

Catalytic hydrogenation of the nitro compound over 10 % palladium/charcoal in water (18 h) affords 2,3,4-triamino-2,3,4-trideoxy-β-D-idosan as the trihydrochloride *(11)* [m.p. 189–190 °C (decomp.), $[\alpha]_D^{20} = -48.3°$ (H_2O)], which is converted into the triacetate *(12)*, m.p. 257–258 °C, $[\alpha]_D^{20} = -50°$ (in $CHCl_3$), by warming in acetic anhydride. The D-*ido* configuration of the triamino-anhydro-sugar is shown by the NMR spectrum of *(12)* in [D_6]dimethyl sulfoxide: The anomeric proton gives the expected doublet at $\tau =$

4.76 with a small coupling constant ($J_{1,2}$ = 2 Hz), and the CH_3 groups give a signal at τ = 8.17 whose position proves the presence of three equatorial acetamido groups.



(8) (9)



(10), R = C_6H_5-CH_2-NH, R^1 = NO_2
(11), R = R^1 = $NH_2 \cdot HCl$
(12), R = R^1 = NH-CO-CH_3

Methylamine and aniline are less suitable than benzylamine as amine components, but phenylhydrazine reacts analogously to benzylamine with *(4)*, yielding 2-nitro-*N*^{2},*N*$^{2'}$-diphenyl-*trans*-*trans*-1,3-cyclohexanedihydrazine, m.p. 130 °C (yield 15 %), which can also be obtained (yield 57 %) by treating *(3)* with phenylhydrazine.

Ability to vary the methylene component is shown by reaction of glutardialdehyde with nitroethane and benzylamine to afford *N*^{1},*N*^{3}-dibenzyl-2-methyl-2-nitro-1,3-cyclohexanediamine (yield 56 %, m.p. 98–99 °C) which is also formed (yield 83 %) from benzylamine and the cyclization product of nitroethane and glutardialdehyde [5].

It seems reasonable to classify this reaction, which proceeds similarly to a Mannich condensation, as a three-step process consisting of nitromethane cyclization, dehydration and Michael addition of the amine. Although the easy formation of the nitrodiamine from the nitrodiol, *(4)* → *(3)*, suggests this course, other mechanisms cannot be disregarded (*e.g.* nitromethane cyclization of the double Schiff base formed from dialdehyde and amine or, in certain circumstances, direct displacement of the OH group by the NHR group). Variations in the CH acidity and changes in the reaction conditions could account for the formation of fundamentally different products (compounds of type *(1)*) when carbonyl- or carboxy-activated methylene components are used in the reaction.

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[*] Doz. Dr. F. W. Lichtenthaler, Dr. T. Nakagawa, and Dipl.-Ing. A. El-Scherbiney
Institut für Organische Chemie der Technischen Hochschule
Schlossgartenstr. 2
61 Darmstadt (Germany)

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Simple Methods of Preparing Acetylacetonates

By *G. Stöckelmann*, *A. Kettrup*, and *H. Specker* [*]

Metal acetylacetonates are important in analytical and technical chemistry. We have found that commercial metal salts of 2-ethylhexanoic acid are cheap and excellent starting materials for the preparation of many metal acetylacetonates.

Metal naphthenates and stearates are also suitable. The advantage of these salts, and particularly of the ethylhexanoate, is their good solubility in organic solvents such as petroleum ether, benzene, and chloroform. Consequently the pH control, which is often difficult during synthesis of metal chelates in water or strongly polar solvents, is no longer necessary.

The metal acetylacetonates are precipitated in crystalline form, even at room temperature, on mixing of the β-diketone with the solution of the metal ethylhexanoate in benzene or petroleum ether. We have prepared Fe^{III}, Co^{II}, Co^{III}, Mn^{II}, Zr, Al, Ca, Zn, and Cu acetylacetonates in this way.

The methyl ethylhexanoates were mostly used in their commercial form (solutions in petroleum ether, metal content 8 %). They can, however, also be conveniently obtained from the metal acetates or oxides and the free acid; the acetic acid is removed by distillation and the metal ethylhexanoate, which is usually very viscous, is dissolved in hot petroleum ether; unchanged acetate is filtered off.

Cobalt(II) acetylacetonate:

0.1 mole of cobalt(II) 2-ethylhexanoate is stirred with 0.2 mole of acetylacetone in 100 ml of benzene for 5 min at room temperature under nitrogen. The pink complex is precipitated as crystal flakes in 80 % yield. If the mixture is heated under reflux for 30 min without use of a nitrogen atmosphere, dark green cobalt(III) acetylacetonate is obtained in 70 % yield.

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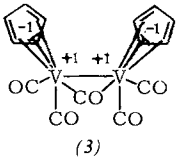
[*] Dipl.-Chem. G. Stöckelmann, Dr. A. Kettrup, and Prof. Dr. H. Specker
Anorganisch-Chemisches Institut der Universität Bochum
Work carried out at:
Institut für Spektrochemie
Bunsen-Kirchhoff-Str.
46 Dortmund (Germany)

Synthesis of Pentacarbonyldicyclopentadienyldivanadium and New Carbonylphosphinecyclopentadienylvanadium Compounds

By *E. O. Fischer* and *R. J. J. Schneider* [*]

We have prepared $Na_2[C_5H_5V(CO)_3]$ *(1)* [1] more simply than before, and in 83 % yield, by shaking a solution of $C_5H_5V(CO)_4$ *(2)* [1] in tetrahydrofuran with 1 % sodium amalgam. If this product is treated with 2 N hydrochloric acid, vigorous evolution of gas occurs and a flocculent green precipitate is formed. Extraction of the precipitate with hexane, chromatography on silica gel, and recrystallization from benzene/hexane (1:1) affords dark green crystals of pentacarbonyldicyclopentadienyldivanadium, $(C_5H_5)_2V_2(CO)_5$ *(3)*, m.p. 99 °C (decomp.), in 78 % yield. No hydride was found.

The ^{1}H–NMR spectrum, the IR spectrum, and the low dipole moment ($\mu_{25\,°C}$ = 1.0 ± 0.1 Debye, in cyclohexane) indicate a binuclear structure with *cis*-configuration, one vanadium-vanadium bond, and one bridging and four terminal CO ligands, as in *(3)*.



(3)

The molecular ion [3] corresponding to the molecular formula $C_{15}H_{10}O_5V_2$ appears in the mass spectrum at *m/e* = 372. Further, the fragment ions arising on stepwise loss of all five CO groups can be detected; an intense peak occurs at *m/e* = 232 $[(C_5H_5)_2V_2^+]$.

If the divanadium compound *(3)* is stirred with tri-*n*-butylphosphine at room temperature for about 20 min, subsequent

	Compound	^{1}H–NMR [a]					νCO (cm^{-1}) in hexane
		π-C_5H_5 τ	CH_2 τ [e]	CH_3 τ [e]	C_6H_5 τ [e]	$J_{P-V-C_5H_5}$ (Hz)	
(2)	$C_5H_5V(CO)_4$	5.70 [b]	–	–	–	–	2031, 1931, 1901
(4)	$C_5H_5V(CO)_3P(C_4H_9)_3$	5.37 [c]	8.60	9.15	–	1	1951, 1874, 1854
(5)	$C_5H_5V(CO)_2[P(C_4H_9)_3]_2$	5.20 [d]	8.40	9.00	–	2	1856, 1762
(6)	$C_5H_5V(CO)_3P(C_2H_5)_2(C_6H_5)$	5.40 [c]	8.10	9.00	2.70	1	1958, 1880, 1851
(7)	$C_5H_5V(CO)_2[P(C_2H_5)_2(C_6H_5)]_2$	5.50 [d]	7.50	8.80	2.67	2	1855, 1762
	$C_5H_5V(CO)_3P(C_6H_5)_3$ [2]	5.50 [c]	–	–	3.03	1	1962, 1884, 1865
(3)	$(C_5H_5)_2V_2(CO)_5$	5.43 [b]	–	–	–	–	2006, 1953, 1905, 1869, 1828
(8)	$(C_5H_5)_2V_2(CO)_4P(C_6H_5)_3$	5.38 [c] 5.98 [b]	–	–	2.85	2	1932, 1871, 1819, 1773 [f]

[a] In C_6D_6 with tetramethylsilane as internal standard. — [b] sharp singlet. — [c] doublet. — [d] triplet. — [e] middle of signal. — [f] in benzene.

distillation of the excess of phosphine in a high vacuum and chromatography on neutral Al_2O_3 with hexane as eluent affords yellow-orange crystals of $C_5H_5V(CO)_3P(C_4H_9)_3$ *(4)* (m.p. 78 °C) and red crystals of $C_5H_5V(CO)_2[P(C_4H_9)_3]_2$ *(5)* (m.p. 68 °C) in a 1:1 ratio and 34 % yield. The structures of both products were proved by IR, NMR, and mass-spectroscopic measurements[3].

$C_5H_5V(CO)_3P(C_4H_9)_3$ can also be prepared, analogously to $C_5H_5V(CO)_3P(C_6H_5)_3$[2], by UV irradiation of a solution of *(2)* and tri-n-butylphosphine in benzene at about 10 °C.

Further, diethylphenylphosphine cleaves *(3)* with formation of yellow $C_5H_5V(CO)_3P(C_2H_5)_2C_6H_5$ *(6)* and red $C_5H_5V(CO)_2[P(C_2H_5)_2C_6H_5]_2$ *(7)*.

However, if *(3)* is stirred with triphenylphosphine in benzene for 70 h, then chromatography on Al_2O_3 with hexane as eluent and crystallization from benzene/hexane (2:1) affords dark green crystals of $(C_5H_5)_2V_2(CO)_4P(C_6H_5)_3$ *(8)*. IR and NMR spectra show that one terminal CO group of *(3)* has been replaced by $P(C_6H_5)_3$. The compounds $C_5H_5V(CO)_3P(C_6H_5)_3$ and $C_5H_5C(CO)_2[P(C_6H_5)_3]_2$ were also formed, but only in traces.

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[*] Prof. Dr. E. O. Fischer and Dipl.-Chem. R. J. J. Schneider
Anorganisch-Chemisches Laboratorium
der Technischen Hochschule
Arcisstr. 21
8 München (Germany)

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[3] We thank Dr. *J. Müller* for the mass-spectroscopic studies.

N,N-Disubstituted Derivatives of *O*-Chloroformylhydroxylamines as Reagents for Peptide Synthesis

By *H. Gross* and *L. Bilk*[*]

Derivatives *(2)* of *O*-chloroformylhydroxylamine can be obtained in good yields by treatment of alkali or trialkylammonium salts of *N*-hydroxysuccinimide *(1a)* or *N*-hydroxyphthalimide *(1b)* in CH_2Cl_2 or CCl_4 with an excess of phosgene at 0 to −5 °C.

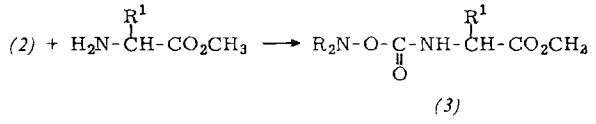
$$R_2NOK + COCl_2 \rightarrow R_2N{-}O{-}COCl$$
(1) *(2)*

(a), $R_2 = OC{-}(CH_2)_2{-}CO$

(b), $R_2 = o\text{-}OC{-}C_6H_4{-}CO$

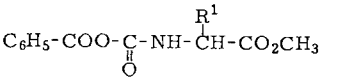
The rather unstable succinimide derivative *(2a)* is isolated as an oil from the filtered solution after removal of the solvent in a vacuum, whereas the stable phthalimide derivative *(2b)* can be obtained in crystalline form.

Amino acid esters react with *(2)* and triethylamine in dioxane at −5 to 0 °C, giving aminooxycarbonyl derivatives *(3)*, which are isolated on evaporating the solvent. Purification may be effected by dissolution of the residue in ethyl acetate, removal of acid and alkaline impurities, evaporation, and recrystallization from ethyl acetate/petroleum ether or methanol/water. These derivatives are relatively stable in both acid and alkaline media. When heated with Na benzoate in dioxane/



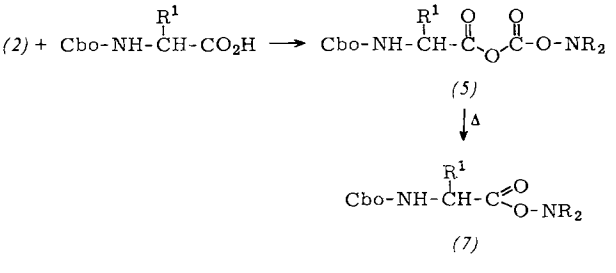
(3)

water (2:1) at 100 °C (90 min) they give the *C*-benzoylurethanes *(4)* in about 75 % yields [isolation and purification as described for *(3)*].

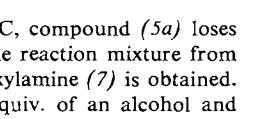


(4)

Acylamino acids with equimolar amounts of *(2)* and triethylamine in tetrahydrofuran afford, within 1 h at −10 °C, good yields of the mixed anhydrides *(5)*, which, on filtration and evaporation of the solution *in* a vacuum, are isolated as crystalline, relatively stable compounds in admixture with triethylammonium chloride. Aminolysis of the succinimide derivative *(5a)* with L-Tyr-OCH_3 in dioxane/water (25:1) gave, within 24 h at −10 to +20 °C, an 81 % yield of Cbo-L-Val-L-Tyr-OCH_3 *(6)*, which was obtained crystalline by the procedure described for *(3)* and recrystallization from ethyl acetate/ether [m.p. 151–153 °C, $[\alpha]_D^{20} = 53.5°$ ($c = 1.07$ in $CHCl_3$); lit.[1], m.p. 144–147 °C, $[\alpha]_D^{24} = 54 \pm 4°$]. The phthalimide derivative *(5b)* reacts analogously with L-Tyr-OCH_3, giving *(6)* in 86 % yield. The mixed anhydrides of type *(5)* do not need to be isolated in these reactions.



(5)



(7)

When warmed for 30 min at 130 °C, compound *(5a)* loses CO_2 and, on recrystallization of the reaction mixture from isopropyl alcohol, the *O*-acylhydroxylamine *(7)* is obtained. Finally, treatment of *(2)* with 2 equiv. of an alcohol and 1.1 equiv. of pyridine in CH_2Cl_2 at −5 to +20 °C gives, within 12 h, 65 to 73 % yields of the *O*-alkoxycarbonylhydroxylamine derivatives *(8)*, which are obtained pure by extraction of the reaction mixture with water, evaporation of the solvent, and recrystallization from ethyl acetate/petroleum ether.

Compound	R_2	R^1	M.p. (°C)	Yield (%)	$[\alpha]_D^{20}$
(2a)	$CO-(CH_2)_2-CO$		oil	75	
(2b)	*o*-$CO-C_6H_4-CO$		87–90 [a]	92	
(3a)	$CO-(CH_2)_2-CO$	$C_6H_5-CH_2$	136–138	64	+2.5° [b]
(3b)	*o*-$CO-C_6H_4-CO$	$C_6H_5-CH_2$	118–120	80	+20.4 [b]
(4)		$C_6H_5-CH_2$	153–156	75–78	
(7)	$CO-(CH_2)_2-CO$	$(CH_3)_2CH$	115–117	46	−25° [c][2]
(8a)	$CO-(CH_2)_2-CO$	t-C_4H_9	98–100	65	
(8b)	$CO-(CH_2)_2-CO$	t-C_5H_{11}	94–96	71	
(8c)	$CO-(CH_2)_2-CO$	$C_6H_5-CH_2$	79–81	70	
(8d)	*o*-$CO-C_6H_4-CO$	t-C_4H_9	118 (decomp.)	73	

[a] M.p. of crude product, [b] $c = 1$ in dimethylformamide,
[c] $c = 2$ in isopropyl alcohol.

$$(2) + R^1\text{-OH} \longrightarrow R_2N\text{-O-C}\overset{O}{\underset{OR^1}{}}$$

(8)

When warmed (95 °C) for 2 h with amino acids in dioxane/0.5 M Na_2CO_3 solution (2:1), these products afford, as was shown by Frankel and co-workers [3] for *(8a)* and *(8c)*, alkoxycarbonylamino acids which are obtained in high yield by evaporation of the solution in a vacuum, adjustment of the pH to 3, extraction with ethyl acetate, and evaporation of the solvent. *(8d)* reacts in the same manner. BOC-amino acids, which are of particular preparative importance, are thus obtained more conveniently than by way of the BOC-hydrazide.

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[*] Doz. Dr. H. Gross
Institut für Organische Chemie
der Deutschen Akademie der Wissenschaften zu Berlin
Rudower Chaussee 5
X 1199 Berlin-Adlershof (Germany)

Dipl.-Chem. L. Bilk
Forschungsabteilung des VEB Berlin-Chemie
Glienicker Weg 180
X 1199 Berlin-Adlershof (Germany)

[1] *W. Rittel, B. Iselin, H. Kappeler, B. Riniker,* and *R. Schwyzer,* Helv. chim. Acta *40*, 618 (1957).

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Erratum

The Authors of the Communication entitled "The Structure of Juvenile Hormone", Angew. Chem. internat. Edit. *6*, 179 (1967) are *H. Röller, K. H. Dahm, C. C. Sweeley,* and *B. M. Trost,* and not *H. Röller, K. H. Dahm, C. C. Sweely,* and *B. M. Trost,* as stated.

CONFERENCE REPORTS

Organometallic and Hydrogen Compounds of Some Transition Metals

By *B. Sarry* [*]

In the absence of air and moisture, anhydrous halides of transition metals react in various ways with ethereal solutions of phenyl-lithium.

Nickel and cobalt halides are reduced to catalytically active metal powders:

$$MX_n + n\ LiPh \longrightarrow M + n\ LiX + \frac{n}{2}\ Ph_2 \qquad (1)$$

Organometallic compounds are not formed, nor are hydrides or hydrido complexes of the metals obtained in the presence of hydrogen. Hydrogen leads merely to the formation of lithium hydride:

$$LiPh + H_2 \longrightarrow LiH + C_6H_6 \qquad (2)$$

This reaction is accelerated by cobalt, whereas nickel acts as catalyst for concurrent hydrogenations.

Tungsten, niobium, and tantalum pentabromides are reduced by phenyl-lithium only as far as the oxidation state +2. Diphenyl derivatives of the metals are formed, which react with the excess of phenyl-lithium present to form organometallic complexes.

$$MBr_5 + 9\ LiPh \xrightarrow{(C_2H_5)_2O}$$

$$[MPh_2(LiPh)_4]\cdot n\ (C_2H_5)_2O + 5\ LiBr + \frac{3}{2}\ Ph_2 \qquad (3)$$

These products are dark brown to black, finely crystalline substances, which are extremely susceptible to oxidation and hydrolysis and are insoluble in petroleum ether, somewhat soluble in ether, and readily soluble in benzene or dioxane. The solvate ether ($n = 3.5$ to 4) is so firmly bound that it is retained even on recrystallization of the complexes from benzene.

Ethereal or benzene solutions of these compounds react with elemental hydrogen – the tungsten compound appreciably faster than the niobium compound – to form organometallic hydrido complexes. This reaction gives the black $WH(LiPh)_2$, which is initially soluble in ether, but which becomes insoluble on precipitation by hydrocarbons. The niobium compound has, so far, yielded two similarly insoluble complexes containing one or two hydride hydrogen atoms, repectively, per niobium atom.

In accord with the position of iron in the Periodic Table, iron(II) chloride can react in either way. Above 0 °C reduction occurs in agreement with equation (1), yielding a mixture of very finely divided pyrophoric iron and ether-insoluble lithium chloride. Reaction at about −15 °C leads to an ether-soluble product which, after separation from the lithium chloride formed simultaneously and from the excess of

phenyl-lithium, can be precipitated by petroleum ether as a dark reddish-brown, powder which is extremely sensitive to air and moisture.

When a phenyl-lithium solution (from bromobenzene) containing lithium bromide is used, the products has the composition $Fe(LiPh)_5 \cdot LiBr$, but when a solution (from diphenylmercury) free from lithium bromide is used the composition is $Fe(LiPh)_5$. It is formed according to the equation:

$$FeCl_3 + 8\ LiPh \longrightarrow Fe(LiPh)_5 + 3\ LiCl + \frac{3}{2} Ph_2 \qquad (4)$$

A small amount of an hydridoiron complex is formed simultaneously which, after isolation, is insoluble in ether. The hydride hydrogen is provided by oxidation of phenyl-lithium to biphenylylenedilithium.

Lecture at Kiel on November 24th, 1966 [VB 50 IE]
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[*] Prof. Dr. Brigitte Sarry
Institut für Anorganische und Analytische Chemie der Technischen Universität
Hardenbergstrasse 34
1 Berlin 12 (Germany)

Chemistry and Stability of Lead(IV) Compounds

By *F. Huber* [*]

The stability and structural relations of Pb(IV) and Pb(II) compounds cannot be explained by means of completion of the 6s orbitals [1,2] ("inert electron pair"). In the third and fourth main groups the decrease in stability of the maximal valency can be correlated satisfactorily with the decrease in covalent bond strength [3] only for the chlorides. A more generally valid rule can be derived by assuming Pb(IV) compounds to provide an intramolecular redox system and by attending more strictly to the ionic contribution to the valence [4].

In contrast to PbF_4, $PbCl_4$ cannot be obtained by direct halogenation of Pb(II) halides; chlorine oxidises only complex-bound $PbCl_2$, presumably in accord with $PbCl_3^{\ominus} + Cl_2 \rightarrow [PbCl_5]^{\ominus}$ and $PbCl_4^{2\ominus} + Cl_2 \rightarrow [PbCl_6]^{2\ominus}$. $PbCl_4$ is then obtained from the isolated hexachloroplumbates(IV), preferably from $[(C_2H_5)_3NH]_2[PbCl_6]$. $PbBr_4$, PbI_4, $M_2[PbBr_6]$, and $M_2[PbI_6]$ (M = cation) have not been prepared; the compounds described in the literature as $[C_9H_7NH]_2[PbBr_6]$ and $[C_9H_7NH]_2[PbI_6]$ [5] are in fact halogenoplumbates(II), which are formed by addition of halogen (set free in the "oxidation" of $Br^{\ominus}$ or $I^{\ominus}$ by Pb(IV)) to the quinolinium cation $C_9H_7NH^+$. $PbCl_4$ forms complexes $PbCl_4 \cdot 2Z$, which are more stable than $PbCl_4$, provided that Z is not susceptible to oxidation [Z = pyridine, quinoline, or $(C_6H_5)_3PO$]. Complexes with amines, $(C_6H_5)_3P$, ethers, *etc.*, decompose more or less rapidly, and partially even below 0 °C. Similar relations between stability and susceptibility of the cation to oxidation can be demonstrated for hexachloroplumbates(IV). Aminolysis of $PbCl_4$ occurs through an intermediate, for which the formula $[NH_4]_2[PbCl_4(NH_2)_2]$ has been derived. $PbCl_4$ reacts with PCl_5 to give $[PCl_4]_2[PbCl_6]$, and with $SbCl_5$ to give a complex, presumably $[PbCl_2][SbCl_6]_2$.

The ease of preparation and the stability of organolead complexes depend on the number and nature of the anionic groups X bound to Pb, and on the nature of the organic groups R. Donor-acceptor complexes of PbR_4 are unknown, and those of R_3PbX are unstable; nevertheless, complexes of various compositions can be obtained from R_2PbX_2, *e.g.* with pyridine, ethylenediamine, and 3-azapentamethylenediamine. The coordination number (CN) 6 is usual in these cases, and CN 5 is unusual; there are indications of CN 8, *e.g.* in the complex $[(C_6H_5)_2Pb(en)_3]I_2$.

The compound $R_2PbHal_2 \cdot 4\ C_5H_5N$ can be regarded as the ionic complex $[R_2Pb(C_5H_5N)_4]Hal_2$.

Stereoisomeric chelates $R_2Pb(ox)_2$ (Hox = 8-hydroxyquinoline) can be prepared from R_2XPbox by reaction with NH_3 or with NH_3 and Hox. In R_2XPbox the coordination number depends on the nature of the ligands, on the concentration, and on the temperature; in solution CN is often 5, and in the solid state presumably 6.

The compounds $RPb(ox)_3$ avoid CN 7 since two of the ox groups are bidentate and the third one is unidentate. Attempts to obtain compounds of the type $M[R_2PbX_3]$ gave halogenoplumbates(II) $M[PbX_3]$, with elimination of the alkyl group R as ethane (R = CH_3) or alkane/alkene mixtures (R = C_2H_5 *etc.*).

Lecture at the Humboldt University, Berlin, on November 18th, and at the Freie Universität, Berlin, on November 21st, 1966 [VB 51 IE]
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[*] Priv.-Doz. Dr. F. Huber
Institut für Anorganische Chemie und Elektrochemie der Technischen Hochschule
Templergraben 55
51 Aachen (Germany)

[1] *H. G. Grimm* and *A. Sommerfeld*, Z. Physik *36*, 36 (1926).

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[5] *A. Classen* and *B. Zahorski*, Z. anorg. allg. Chem. *4*, 100 (1894).

Boron Azides and Boron Imides

By *P. Paetzold* [*]

Thermal or photolytic decomposition of diorganylboron azides leads to the formation of rearrangement products in high yields. The decomposition may be formulated as in eq. (a), where $n = 2$ for R = aromatic ligand; or $n = 3$ for R = aliphatic ligand; $(RNBR)_n$ = rearrangement product.

$$R_2BN_3 \longrightarrow N_2 + \frac{1}{n} (RBNR)_n \qquad (a)$$

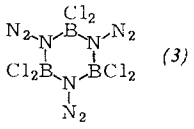
The tetraaryl-1,3,2,4-diazadiboretidines *(1)*, $n = 2$, which are isoelectronic with cyclobutadienes, are extremely sensitive to oxidation. Kinetic measurements of the decomposition of diarylboron azides show that they are the more stable the better electron-donors the aryl groups are, although *Saunders* and *Ware* observed the opposite relation for decomposition of triarylmethyl azides [1]. On decomposition of azides of the type $(C_6H_5)RBN_3$ the aryl group R migrates the more readily (relative to the C_6H_5 group) the more strongly it attracts electrons and the bulkier it is according to the following series: *m*-trifluoromethylphenyl > *o*-tolyl > α-naphthyl > phenyl > *p*-chlorophenyl > *p*-tolyl. The kinetic measurements and the migratory tendencies accord with a synchronous mechanism for the diorganylboron azide rearrangement.

Bis(dialkylamino)boron azides are more stable thermally than the diorganylboron azides; when heated to 270 °C they give indefinite resins. Photolysis leads, in accord with eq. (b), to the formation of rearrangement products in good yields, namely, to tetrakis(dialkylamino)-1,3,2,4-diazadiboretidines *(2)* that are susceptible to oxidation and on hydrolysis give, *inter alia* 1,1-dialkylhydrazines.

$$2\ (R_2N)_2BN_3 \longrightarrow 2\ N_2 + (R_2N{-}BN{-}NR_2)_2 \qquad (b)$$

Its vibrational spectra indicate that trimeric dichloroboron azide has a structure with a planar BN six-membered ring *(3)* and contains *N*-diazonium groups. When this compound is

heated in the absence of a solvent at *ca.* 200 °C, Cl migrates from B to the N_α atom of the N_3 group, N_2 is split off, and hexachloroborazole is formed.



(3)

If diphenylboron azide is heated with benzonitrile phenylimide as 1,3-dipolar agent, the phenylboron phenylimide, $C_6H_5-B\equiv N-C_6H_5$, that is formed as intermediate, acts as a dipolarophile and undergoes a 1,3-dipolar cyclization to yield a B-containing five-membered ring compound (1,2,4,5-triazaboroline); this reaction provides the first evidence for occurrence of a boron imide.

Boron imides stable at room temperature are obtained when aromatic amines such as *p*-anisidine, *p*-thioanisidine, or 2,4,6-trimethylaniline are treated with pentafluorophenylboron dichloride in boiling toluene [reaction (c)]. These compounds undergo a 1,3-dipolar reaction with benzonitrile *N*-oxide or phenyl azide, even at room temperature, which

$$F_5C_5-BCl_2 + ArNH_2 \longrightarrow C_6F_5-B\equiv N-Ar + 2\ HCl \qquad (c)$$

leads to heterocyclic five-membered ring compounds (1,2,4,5-oxadiazaborolines; tetrazaborolines) in almost quantitative yield. The BN stretching vibrations are IR-inactive but appear as intense bands in the Raman spectrum just above 1700 cm^{-1}. Unexpectedly, $C_6H_5BCl_2$ and $C_6H_5NH_2$ yield a monomeric boron imide with an IR-inactive but Raman-active BN stretching vibration at 1658 cm^{-1}.

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[*] Priv.-Doz. Dr. P. Paetzold
Institut für Anorganische Chemie der Universität
Meiserstrasse 1
8 München 2 (Germany)

[1] *W. H. Sounders* and *J. C. Ware*, J. Amer. chem. Soc. *80*, 3328 (1958).

New Compounds with Apatite or Garnet Structure

By *H. Schwarz* [*]

Ternary compounds $M^{II}_3(X^VO_4)_2$ have the same structure when M^{II} = Sr or Ba and X^V = P, As, V, or Cr. Isomorphous replacement of the cations, in accordance with a general formula $M^{II}_{3-x}M^{I}_x(X^VO_4)_{2-x}(X^{VI}O_4)_x$, leads, when $x = 2$, to double compounds of the type $M^{II}M^{I}_2(X^{VI}O_4)_2$ which, without exception, have the structure of the parent when X^{VI} = Cr, Se, or S, M^I = K, NH_4, Rb, or Tl, and M^{II} = Sr, Pb, or Ba (Ba only when X^{VI} = Cr) [1]. The compounds can generally be obtained by a thermal route or by precipitation from very concentrated $M^I_2X^{VI}O_4$ solutions. In agreement with this it was found for some more extensively studied $M^I_2X^{VI}O_4/M^{II}X^{VI}O_4$ systems that only the 1:1 double salts exist and that there are no regions of solid solution.

A second type of coupled replacement leads, from $Sr_3(PO_4)_2$, to a series of unusual apatites. If the P^{5+} in the parent $Sr_3(PO_4)_2$ is replaced by Si^{4+} and at the same time Sr^{2+} is partially replaced by La^{3+} $[Sr_{9-x}La_x(PO_4)_{6-x}(SiO_4)_x]$, a surprising change in structure occurs. From $x = 4.5$ $[Sr_{4.5}La_{4.5}(PO_4)_{1.5}(SiO_4)_{4.5}]$ to $x = 6$ $[Sr_3La_6(SiO_4)_6]$ only a single phase, which has the apatite structure, occurs; when $x = < 4.5$ the products are a mixture of $Sr_3(PO_4)_2$ and the apatite phase for $x = 4.5$. $Sr_3La_6(SiO_4)_6$ itself is the $y = 0$ member of a mixed-crystal series $Sr_{3-y}La_{6+2y/3}(SiO_4)_6$ that exists from $y = 1$ to $y = -1$. Here are for the first time compounds of apatite structure that have defects in the cation part of the lattice. Similar compounds *(1)* and *(2)* exist in the binary system La_2O_3/SiO_2, but here there are long series of mixed crystals of type *(1a)* and *(2a)* that extend up to the ternary silicate apatites *(1b)* and *(2b)* having filled cationic

(1)	$La_{8\frac{2}{3}}(SiO_4)_6O$
(1a)	$Sr_{4-y}La_{6+2y/3}(SiO_4)_6O$; $4 \geqslant y \geqslant 0$
(1b)	$Sr_4La_6(SiO_4)_6O$
(2)	$La_{9\frac{1}{3}}(SiO_4)_6O_2$
(2a)	$Sr_{2-y}La_{8+2y/3}(SiO_4)_6)_2$; $2 \geqslant y \geqslant 0$
(2b)	$Sr_2La_8(SiO_4)_6O_2$

parts of the lattice. In sum the ternary system $SrO/La_2O_3/SiO_2$ contains an extensive region of mixed crystals with the apatite structure.

Except for the natural berzeliites [2], the garnets *(3)* have hitherto presented no example with a quinquevalent element in the tetrahedral sites, which is surprising since in other respects there are many relationships between silicates and phosphates, arsenates, and vanadates. After unsuccessful experiments with various phosphate systems, we were able to prepare a series of arsenate *(3a)* and vanadate *(3b)* garnets, and our first attempts with fluoride systems led to synthesis of the cryolithionite *(3c)*. At higher temperatures the products decompose in various ways; for instance, after formation of a tetragonal phase at 850 °C, $Na_3Fe_2As_3O_{12}$ decomposes at 900 °C with loss of As_2O_3 and O_2 and formation of α-Fe_2O_3 and Na_3AsO_4.

(3)	$\{A_3\}$	$[B_2]$	(C_3)	O_{12}	
(3a)	$\{NaCa_2\}$	$[M^{II}_2]$	(As_3)	$O_{12}\}$	M^{II} = Mg, Co, or Ni
	$\{M^{II}Ca_2\}$	$[LiM^{III}]$	(As_3)	$O_{12}\}$	
	$\{Na_3\}$	$[M^{III}_2]$	(As_3)	$O_{12}\}$	M^{III} = Fe or Cr
(3b)	$\{Na_3\}$	$[M^{III}_2]$	(V_3)	$O_{12}\}$	
	$\{Ca_2In\}$	$[Li_2]$	(V_3)	O_{12}	
(3c)	$\{Na_3\}$	$[Al_2]$	(Li_3)	F_{12}	
(4)	$\{M^{III}_3\}$	$[M^{III}_2]$	$(\square_3)$	$(OH)_{12}$	
(4a)	$\{Ca_3\}$	$[M^{III}_2]$	$(\square_3)$	$(OH)_{12}$	M^{III} = Al or Cr
(4b)	$\{Sr_3\}$	$[M^{III}_2]$	$(\square_3)$	$(OH)_{12}$	M^{III} = Al, Ga, Fe, or Cr

To set alongside calcium hydroxoaluminate $Ca_3[Al(OH)_6]_2$ which was earlier recognized as a defect garnet structure *(4)* [3], we have obtained a series of further "hydrogarnets" *(4a)* and *(4b)* by two methods; precipitation from solution can generally be used; but the second method, in which anhydrous oxometalates $3M^{II}O.M^{III}_2O_3$ are treated with steam under pressure gives purer products. As an example of the often complex process of thermal decomposition of such "hydrogarnets" we may mention the decomposition of $Ca_3Al_2(OH)_{12}$ which affords $3CaO{\cdot}Al_2O_3$ only above 900 °C and by way of two intermediate stages.

Inorganic Colloquia at Göttingen on January 23rd, 1967, and at Giessen on February 10th, 1967 [VB 60 IE]
German version: Angew. Chem. *79*, 584 (1967)

[*] Priv.-Doz. Dr. H. Schwarz
Institut für Anorganische Chemie
der Technischen Hochschule
Englerstr. 11
75 Karlsruhe (Germany)

[1] *H. Schwarz*, Z. anorg. allg. Chem. *344*, 41, 214 (1966); *345*, 230 (1966).

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New Results in the Chemistry of Chromium

By *H. L. Krauss* [*]

1. Chromium peroxides

$CrCl_3$ or $CrCl_3$·aq in tetrahydrofuran reacts with an excess of concentrated H_2O_2 to form first $CrCl_3$·3THF and then a deep blue chromium(VI) peroxide. The blue compound is spectroscopically identical with "CrO_5", which is quite stable in THF. The substance shows the same broad absorption maximum at 580 nm in water, ether, alcohol, and THF.

Electrophoresis of "CrO_5" in $THF/H_2O/H_2O_2$ with $LiClO_4$ as conducting salt showed, surprisingly, that the blue compound is anionic. It is assumed that the anions CrO_6H^- and CrO_5X^- [1,2] are present, their absorption being identical with that of CrO_5 (at the same pH).

Decomposition of "CrO_5" in water (pH = 1) with an excess of H_2O_2 [eq. (a)] or of chromate [eq. (b)] gives different amounts of oxygen but with the same rate of reaction:

$$Cr_2O_7^{2-} + 5\ H_2O_2 + 8\ H^+ \rightarrow 2\ Cr^{3+} + 9\ H_2O + 4\ O_2 \quad (a)$$

$$Cr_2O_7^{2-} + 3\ H_2O_2 + 8\ H^+ \rightarrow 2\ Cr^{3+} + 7\ H_2O + 3\ O_2 \quad (b)$$

The rates of reactions (a) and (b) are determined by attack of the protons; the rate of decomposition is thus dependent on the proton concentration. The apparent catalytic decomposition of H_2O_2 is explained by a redox reaction between chromium peroxide and hydrogen peroxide.

2. Surface Chemistry of Chromium

In continuation of work concerned with chromium(VI) and chromium(III) compounds on the surface of amorphous aluminum silicates with various Si/Al ratios the magnetic and the optical behavior have been studied at various temperatures, oxygen partial pressures, and concentrations. In all cases it was possible to distinguish chromium chemisorbed on the surface from that retained in capillaries.

Only the surface chromium has catalytic activity, *e.g.* for polymerization of ethylene. With corresponding supply of oxygen and on "activation" at 400 to 600 °C the oxidation number of surface chromium always lies between 5 and 6, the highest value (5.95) being achieved on pure SiO_2·aq. Comparison of quantitative ESR measurements with the analytical findings shows that the paramagnetic components appearing in surface chromium cannot be identical with chromium(V). It is assumed that the ESR-active species consists of chromium(III) ions in special crystal environments; the band form leads to the same conclusion.

The redox reactions were studied optically by use of a high-temperature cell for reflection measurements in the visible and near-IR region. This work gave complete agreement with the analytical results concerning the reduction-reoxidation sequence in the activation process. Chromium(VI) is present as dichromate in the active material. The catalytic reaction with ethylene was also studied optically. The initial step clearly consists in reduction of the surface chromium(VI), which leads to formation of the catalytically active centers.

Lecture at Kiel on December 15th, 1966 [VB 63 IE]
German version: Angew. Chem. 79, 538 (1967)

[*] Prof. Dr. H. L. Krauss
Anorganisch-chemisches Laboratorium
der Technischen Hochschule
Arcisstr. 21
8 München 2 (Germany)

[1] *W. P. Griffith*, J. chem. Soc. (London) *1962*, 3948.

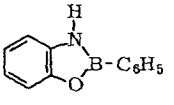
[2] *D. G. Tuck*, J. chem. Soc. (London) *1965*, 5753.

Reactions of Boron Compounds with Metal Chelates and Chelating Agents

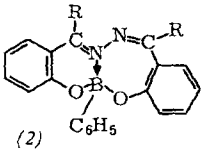
By *F. Umland* [*]

Phenylboric acids, Ph_2BOH and $PhB(OH)_2$, react with chelating agents to form chelate rings with quadri- or triligating boron. From consideration of the bond angle between the ligands on the boron and the bond angle in the ring it is to be expected that quadriligating boron will be favored in five-membered ring chelates because of the tetrahedral angle (≈ 105 °; cf. bond angle in the ring 108 °), whereas triligating boron (120 °) should be favored in six-membered-ring chelates. Five-membered diphenylboron chelate rings occur with, *e.g.*, 8-hydroxyquinoline or nitrosophenylhydroxylamine [1]. Quasiaromatic systems, however, always lead to great stability, independently of the bond angles. Thus the diphenylboron chelate of *o*-aminophenol splits off benzene, with formation of 2-phenyl-1,3,2-oxazaboroline *(1)*.

Very stable quasi-aromatic six-membered ring compounds of Ph_2BOH are obtained with chelating agents such as salicylaldehyde or the corresponding azomethines [2]. The hydroxydiphenylboron-salicylaldehyde chelate is suitable as a reagent for primary amines; NH_3, NH_2OH, and NH_2NH_2 also react. Loss of benzene and formation of boric acid derivatives occur only when a more condensed ring system can be obtained, *e.g.*, with hydrazine, giving *(2)*. Free boric acids also give chelates of these types [3].

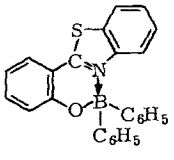


(1)



(2)

However, when *o*-aminothiophenol is used as amine component, a diphenylboron chelate *(3)* of the benzothiazole is formed with evolution of hydrogen.



(3)

The Ph_2B^+ group may replace the proton of metal chelates of the bis(dimethylglyoxime)nickel(II) type, $Ni(DMGH)_2$, containing an intramolecular hydrogen bridge [4]. A special study was made of whether analogous cationic complexes with triligating boron can be prepared. So far the following types are known: $[Ni(DMG)_2(BOH)_2]_3[B_3O_6]_2$ with a boroxole anion, $[Ni(DMG)_2Py_2(BOH)_2]Cl_2$, and $[Ni(DMG)_3(BPh)_2]$. Attempts to introduce elements other than boron into $Ni(DMGH)_2$ succeeded with Sn^{VI}, the trinuclear complex [(HDMG)Ni(DMG)$SnCl_2$(DMG)Ni(DMGH)] being formed.

Lecture at Marburg on February 3rd, 1967 [VB 64 IE]
German version: Angew. Chem. 79, 583 (1967)

[*] Prof. Dr. F. Umland
Anorganisch-chemisches Institut der Universität
Hindenburgplatz 55
44 Münster (Germany)

[1] *F. Umland* and *C. Schleyerbach*, Angew. Chem. *77*, 169 (1965); Angew. Chem. internat. Edit. *4*, 151 (1965).

[2] *F. Umland* and *C. Schleyerbach*, Angew. Chem. *77*, 426 (1965); Angew. Chem. internat. Edit. *4*, 432 (1965).

[3] *F. Umland* and *B. K. Poddar*, Angew. Chem. *77*, 1012 (1965); Angew. Chem. internat. Edit. *4*, 958 (1965).

[4] *F. Umland* and *D. Thierig*, Angew. Chem. *74*, 388 (1962); Angew. Chem. internat. Edit. *1*, 333 (1962).

Optical Behavior of Solutions of Sodium in Ammonia at High Pressures

By *U. Schindewolf*[*]

Solutions of Na in NH_3 have a lower density and a greater compressibility than pure ammonia. This is attributed to the solvated electrons that are formed on dissociation of the Na ($Na \rightarrow Na^+ + e^-_{sol}$). The solvated electrons are situated inside cages formed of NH_3 molecules. The apparent molar volume of the dissolved Na (60 to 70 ml/mole; cf. pure Na 23 ml/mole) gives a value of 3.25 Å for the radius of the solvated electrons.

The dilute solutions are deep blue (absorption maximum at 1.5 μ; maximal extinction coefficient 4×10^4 l mole^{-1} cm^{-1}) owing to strong light absorption in the red to near infrared spectral region. The absorption is attributed to transition of the electrons from the 1s to the 2p state in a hydrogen-like potential, paralleling the light absorption of F-centers (electrons at anion sites in ionic crystals). The transition energy is, to a first approximation (square well potential), inversely proportional to the square of the radius of the cage containing the electrons. Quantum mechanical calculation using the radius given above for the solvated electron is in agreement with the transition energy found.

The increase in compressibility of the solutions suggests that solvated electrons are more compressible than pure ammonia. Because of the relation between the radius of the solvated electrons and the energy of the electron transition it should be possible to estimate their compressibility from the increase in shift of the absorption maximum towards shorter wavelengths with increasing pressure.

The absorption spectra of dilute $Na-NH_3$ solutions at pressure up to 2000 atm and at temperatures −60 and +20 °C were studied by using a high-pressure cell. Owing to the strong absorption of the solutions the light path was kept below 10^{-2} cm.

The results of these investigations confirm the hypotheses: compression of the solvated electron by pressure shifts the absorption maximum towards shorter wavelengths (1000 Å/1000 atm); on the other hand, increase in temperature shifts the absorption maximum towards longer wavelengths (1000 Å/40 °C). The latter shift can be interpreted as due to thermal expansion of the solvated electrons.

These measurements lead to values of the compressibility (6.5×10^{-5} atm^{-1}) and thermal expansion (3.0×10^{-2} deg^{-1}) of the solvated electrons that are greater than those of pure ammonia (4.0×10^{-5} atm^{-1} and $1\times9\cdot10^{-2}$ deg^{-1}, respectively). Solvated electrons thus contrast with normal solvated ions, whose compressibilities and thermal expansions are smaller than those of the solvating medium.

Lecture at Marburg (Germany) on January 20th, 1967 [VB 65 IE]
German version: Angew. Chem. 79, 585 (1967)

[*] Doz. Dr. U. Schindewolf
Institut für Kernverfahrenstechnik
der Technischen Hochschule
75 Karlsruhe (Germany)

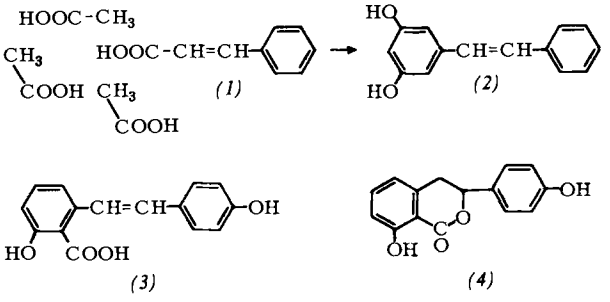
Biosynthesis of Aromatic Systems

By *G. Billek*[*]

Aromatic natural products are formed almost exclusively by (i) condensation of acetate and malonate units (polyacetate rule[1]) or (ii) through intermediate stages of carbohydrate metabolism, by way of shikimic, chorismic, and prephenic acid (shikimic acid route[2]). Examples of the latter are the aromatic amino acids phenylalanine and tyrosine and their deamination products cinnamic and *p*-coumaric acid. It has been found for stilbenes of vegetable origin that both routes can contribute together to the formation of aromatic natural products.

More than half of the 14 stilbene derivatives that are now known as constituents of higher plants have been studied in regard to their biosynthesis[3]. The syntheses proceed along analogous routes in very different types of plant, namely, condensation of a cinnamic acid *(1)* with three acetate units, leading, on loss of a carboxyl group, to 3,5-dihydroxystilbene (pinosylvin) *(2)*. Hydroxylated cinnamic acids (*p*-coumaric, 2,4-dihydroxycinnamic, caffeic, and isoferulic acid) yield the correspondingly substituted 3,5-dihydroxystilbenes resveratrole (3,5,4′-trihydroxy-), oxyresveratrole (3,5,2′,4′-tetrahydroxy-), piceatannol (3,5,3′,4′-tetrahydroxy-), and rhapontigenin (3,5,3′-trihydroxy-4′-methoxy-stilbene).

Biosynthesis of hydrangeic acid *(3)* and hydrangenol *(4)* proceeds without loss of a carboxyl group but with intermediate reduction.



Benzoic acids, which are widely distributed in higher plants, are not formed, as previously assumed, by aromatization of dehydroshikimic acid or of shikimic acid, but by degradation of cinnamic acids[4]. In the biosynthesis of hydroxylated benzoic acids the substitution pattern can be determined at the cinnamic acid stage since conversions such as ferulic acid → vanillic acid, and *p*-coumaric acid → *p*-hydroxybenzoic acid, are known. On the other hand, for biosynthesis of gentisic acid the route cinnamic acid → benzoic acid → salicylic acid → gentisic acid has been demonstrated, *i.e.* in some cases hydroxylation occurs only at the benzoic acid stage[5].

Lecture at Hamburg (Germany) on February 24th, 1967 [VB 67 IE]
German version: Angew. Chem. 79, 586 (1967)

[*] Doz. Dr. G. Billek
Unilever-Forschungslaboratorium
Behringstr. 154
2 Hamburg 50 (Germany)

[1] *A. J. Birch*, Fortschr. Chem. org. Naturst. *14*, 186 (1957); *F. Lynen* and *M. Tada*, Angew. Chem. *73*, 513 (1961).

[2] *D. B. Sprinson*, Adv. Carbohydrate Chem. *15*, 235 (1960).

[3] *G. Billek* and *H. Kindl*, Mh. Chem. *92*, 493 (1961); *93*, 814 (1962); *G. Billek* and *W. Ziegler*, *ibid. 93*, 1430 (1962); *G. Billek* and *A. Schimpl*, *ibid. 93*, 1457 (1962).

[4] *H. Kindl* and *G. Billek*, Österr. Chem.-Ztg. *63*, 290 (1962); Mh. Chem. *95*, 1044 (1964).

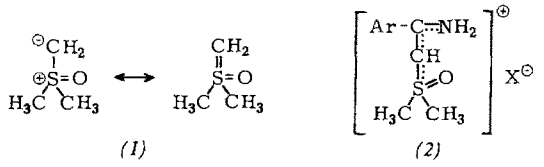
[5] *G. Billek* and *F. P. Schmook*, Mh. Chem., in press.

Chemistry of Sulfur Ylides

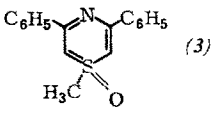
By *H. König*[*]

Whereas cinnamonitrile, like α,β-unsaturated ketones, is converted into phenylcyclopropanecarbonitrile by dimethyloxosulfonium methylide *(1)*, cinnamanilide affords only a little of the cyclopropane derivative along with much 1,3-diphenylpyrrolidone. The nature of by-products from other α,β-unsaturated amides permits conclusions to be drawn about the reaction mechanism. Reaction of a carbonyl or imine group with *(1)* occurs with methylene transfer and formation of heterocycles containing three-membered rings.

With aromatic nitriles prototropy leads to conjugated vinylsulfonium salts *(2)*. Benzonitrile gives also the novel heterocycle *(3)*.

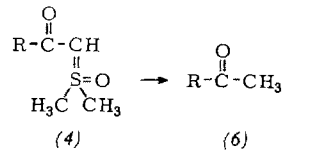


(1) *(2)*

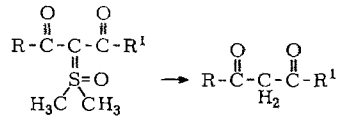


(3)

Isocyanates are not converted into the α-lactams by *(1)*, but form stable crystalline sulfur ylides of type *(4)* or *(5)*, which on desulfurization, *e.g.* by nickel, afford the carbonyl or 1,3-dicarbonyl compounds *(6)* and *(7)*. Simultaneous action of an electrophilic and a nucleophilic reagent on the ylides leads to derivatives of these carbonyl compounds with loss of dimethyl sulfoxide.



(4) *(6)*



(5) *(7)*

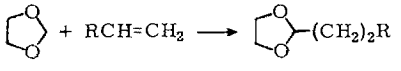
According to the nature of the group R, thermolysis of compounds *(4)* occurs either by reversal of the reaction by which they were formed, or – on copper catalysis – with loss of ketocarbene.

Lecture at Ludwigshafen (Germany), on January 13th, 1967 [VB 70 IE]
German version: Angew. Chem. 79, 538 (1967)

[*] Dr. H. König
Badische Anilin- & Soda-Fabrik, Hauptlaboratorium
67 Ludwigshafen (Germany)

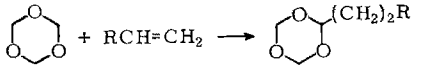
SELECTED ABSTRACTS

The light-induced addition of cyclic acetals to terminal olefins without ring cleavage has been described by *D. Elad* and *I. Rosenthal*. 1,3-Dioxolane and 1,3,5-trioxane gave mainly the



(1)

R = C_5H_{11}, C_6H_{13}, C_8H_{17}

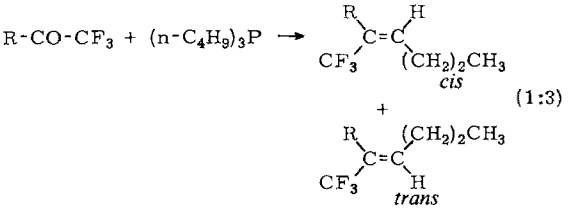


(2)

1:1 adducts *(1)* and *(2)* (yield about 20%). The reaction is carried out by exposure of a mixture of olefin and acetal to UV radiation or to sunlight in the presence of acetone./Chem. Commun. *1966*, 684 / –Ma. [Rd 611 IE]

The stoichiometry of GTP-cleavage during protein biosynthesis was measured by *F. Lipman* and co-workers. In the presence of the complex ribosome/mRNA/aminoacyl-tRNA, GTP and an enzyme system are necessary, as well as a thiol and ammonium ions, for peptide formation. The enzyme system could be purified until the GTPase-activity almost disappeared. In previous experiments the GTP-cleavage was *ca.* 500 times higher than the number of peptide bonds formed. Above a level of a GTPase activity in the region of the peptide bond forming activity it could be demonstrated that one GTP molecule is cleaved per peptide bond formed. The enzyme system could be resolved into three components: T_s (relatively stable), T_u (very heat labile) and G (including the GTPase activity). Hitherto, two components (A and B or I and II) were known. The experiments were conducted with the systems of *Escherichia coli* and *Pseudomonas fluorescens*; the poly-U dependent polyphenylalanine biosynthesis was observed. The enzymatic components of the two microorganisms proved interchangable. / Proc. Nat. Acad. Sic. U.S.A. *55*, 212 and 1562 (1966) / –Hö. [Rd 633 IE]

The reactions of aryl trifluoromethyl ketones with trialkylphosphines have been investigated by *D. J. Burton, F. E. Herkes*, and *K. J. Klabunde*. These investigators found that heating a mixture of the above substances in boiling n-hexane for 20 h resulted in replacement of the carbonyl oxygen atom by an alkylidene group, thus yielding trifluoroolefins. Octanal, benzaldehyde, and acetophenone do not react under these conditions. In the trifluoromethyl ketones, however, the electrophilic character of the carbonyl oxygen atom is increased by the electron-attracting effect of the CF_3–C group. Triphenylphosphine does not react.

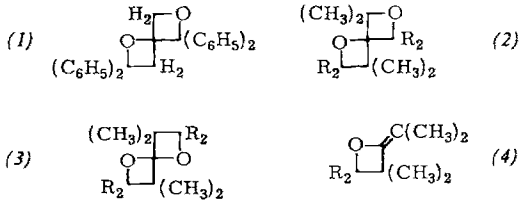


(1:3)

cis + *trans*

This is the first example of a ketone reacting with a trialkylphosphine to yield an olefin. R = C_6H_5, yield 43%; R = *p*-CH_3–C_6H_4, yield 64%. / J. Amer. chem. Soc. *88*, 5042 (1966) / –Ma. [Rd 639 IE]

The photoaddition of carbonyl compounds to allenes has been investigated by *D. R. Arnold* and *A. H. Glick*. The addition of radiation excited CO compounds, to allenes yields the hitherto unknown 2-alkylideneoxetanes as well as the 1,5- and 1,6-dioxaspiro[3.3]heptane ring systems. Compound *(1)* is

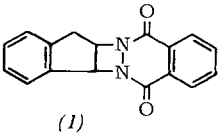


(1) *(2)* *(3)* *(4)*

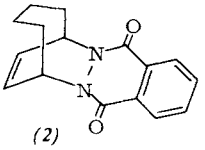
a: R = C_6H_5; *b*: R = CH_3

produced on irradiation of a benzene solution of benzophenone and allene with a high-pressure Hg lamp. Compounds *(2a)*, *(3a)*, and *(4a)*, in yields of 43, 22, and 12 % respectively, result from benzophenone and tetramethyl allene under the same conditions. Acetone and tetramethylallene give *(2b)*, *(3b)*, and *(4b)* in 8, 51, and 27 % yields. All the cycloaddition products can be formed by attack of the oxygen of the carbonyl n, π^* state on the central carbon atom of the allene. / Chem. Commun. *1966*, 813 / –Ma. [Rd 640 IE]

The 1,2-cycloaddition of an azo group to an olefin has been observed by *O.L.Chapman* and *S. J. Yominianni*. Phthalizine-1,4-dione reacts with indene to form the adduct *(1)*, m.p. 256–258 °C (decomp.), yield 58 %. Phenanthrene probably gives a similar product by 9,10-addition. 1,3-Cyclooctadiene adds phthalizine-1,4-dione to give *(2)*, m.p. 314–315 °C, yield 60 %. Compound *(2)* is the first Diels-Alder adduct of



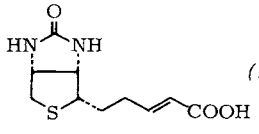
(1)



(2)

1,3-cyclooctadiene. The strong dienophilic character of phthalazine-1,4-dione is demonstrated by the fact that the reaction proceeds at *ca.* 0 °C. / J. org. Chemistry *31*, 3861 (1966) / –Ma. [Rd 641 IE]

The Edman degradation of peptides which are bound to carriers is the subject of a report by *R. A. Laursen*. The peptide, the N-terminal group of which is protected by methyl isothiocyanate, is activated by *N,N'*-carbonyldiimidazole in dimethylformamide, coupled to a substituted polystyrene carrier, and cyclized to the thiazolinone with trifluoroacetic acid. The solid phase is subsequently separated and the degradation repeated. The thiazolinone, which is formed from the terminal amino acid and which is present in the



(1)

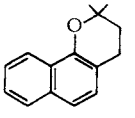
filtrate, is then analysed. The peptide residue on the carrier is treated with HCl and the aminoacids may be identified in the hydrolysate. / J. Amer. chem. Soc. *88*, 5345 (1966) / –Ma. [Rd 645 IE]

The variation of melting temperature with pressure has been expressed by *E. A. Kraut* and *G. C. Kennedy* as a simple relationship of the form

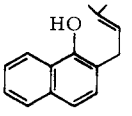
$$T_m = T_m^0(1 + C\Delta V/V_0)$$

where T_m^0 is the temperature of melting and V_0 is the volume at 1 atm. $\Delta V/V_0$, the isothermal compression, is $(V_0 - V)/V_0$ and varies from zero at 1 atm to one at infinite pressure. C is a constant for a given material. For substances which do not undergo a polymorphous change at pressures within the range used in the experiment, the melting temperature, as given by the above equation, may be extrapolated up to values of *ca.* 0.5 for the isothermal compression. Polymorphous transitions may be recognized as breaks in the curve of melting point against compression. The validity of the expression was tested for various metals, sodium chloride, and ice. / Physic. Rev. [2] *151*, 668 (1966) / –Hz. [Rd 646 IE]

A biogenetically important component of teak wood is 2,2-dimethylbenzo[*h*]chroman *(1)*, as has been found by *H. W. Sandermann* and *M. H. Simatupang*. The isolation of *(1)* (m.p. of the picrate: 135–137 °C) supports an earlier hypothesis, according to which 2-(4-methylbut-2-enyl)-1-naphthol *(2)* is a precursor of the various prenyl(= 4-methylbut-2-enyl)-



(1)



(2)

substituted naphthoquinones, of tectol, of dehydrotectol, and possibly also of the 2-methylanthraquinones. Thus the prenyl residue is probably introduced at a 2-naphthol stage, and not at a naphthoquinone stage. / Naturwissenschaften *54*, 118 (1967) / –Jg. [Rd 689 IE]

Trisodium hexahydridoaluminate was obtained in a fairly pure state (approximately 95 %) by *M. Mamula* and *T. Hanslik* by the reaction of a suspension of sodium and aluminum (atomic ratio 3:1) with hydrogen gas (approx. 5 to 150 atm; reaction rate substantially independent of pressure) at 140–200 °C in toluene or hexane in the presence of a little triethylaluminum:

$$3Na + Al + 3H_2 \longrightarrow Na_3AlH_6$$

Trisodium hexahydridoaluminate is a gray-white powder (d = 1.48), which ignites spontaneously in air or with H_2O or alcohols. The (thermal) decomposition curve indicates that the substance is uniform. Some of its reactions are:

$$Na_3AlH_6 + 2Al + 3H_2 \xrightarrow[p_{H_2} \approx 75\,atm]{140-160\,^\circ C} 3NaAlH_4$$

$$Na_3AlH_6 + 2AlH_3 + 3LiCl \longrightarrow 3LiAlH_4 + 3NaCl$$

$$Na_3AlH_6 \xrightarrow{> 200\,^\circ C} 3NaH + Al + 1.5\,H_2$$

$$Na_3AlH_6 + 6/(4-x)\ R_xSiCl_{4-x} + L \longrightarrow 6/(4-x)\ R_xSiH_{4-x} + 3NaCl + AlCl_3 \cdot L$$

(L = ether, tertiary amine)

/ Collect. czechoslov. chem. Commun. *32*, 884 (1967) / –Jg. [Rd 690 IE]

Geschiche der Chemie seit dem Wiederaufleben der Wissenschaften bis an das Ende des 18. Jahrhunderts (The history of chemistry from the scientific renaissance to the end of the 18th century) by J. F. Gmelin. 3 volumes, with viii, 777; 790, and II, 1288 pages and index (unpaginated, 96 pages). Reprographic reprint of the Göttingen edition 1797/1798/1799. Georg Olms Verlagsbuchhandlung, Hildesheim 1965; DM 398.–.

Geschichte der Chemie (History of Chemistry), by *H. Kopp*, 4 volumes, with XIX, 456; X, 428; XII, 373, and XVI, 446 pages. Repropraphic reprint of the Braunschweig edition 1843/1844/1845/1847. Georg Olms Verlagsbuchhandlung, Hildesheim 1966; DM 232.–.

The discussion of these two works together reveals, apart from the subject, an interesting relation between the authors. *Johann Friedrich Gmelin* (1748–1804), Professor of Medicine and Philosophy at Göttingen, was the father of *Leopold Gmelin* (1788–1853), the originator of the "Handbuch der theoretischen Chemie" (1817/1819), which in its 5th edition (1852/1853) was renamed "Handbuch der anorganischen Chemie". *Leopold Gmelin*, as Professor of Chemistry at Heidelberg, was the teacher of *Hermann Kopp* (1817–1892), who at the age of 26 started to publish his famous history of chemistry, which is still regarded as a standard work.

J. F. Gmelin's history forms Part 8 of a "History of the Arts, and Sciences, by a Group of Learned Authors", which was to be an encyclopedia of the development of the natural sciences up to the beginning of the 18th century. A few years earlier, *Johann Christian Wiegleb*'s three-volume "Geschichte des Wachsthums und der Erfindungen in der Chemie in der neuren Zeit" (1790/1791) and "... in der ältesten und mittlern Zeit" (1792), which contains a wealth of facts, had been published. Gmelin was aware of the complex and often contradictory material that had to be molded into a history. In the introduction to the first volume he wrote "Of all the sciences and arts that have engaged the human mind, few have undergone such frequent and rapid changes through the ages, and have had to overcome so many difficulties in their formation, elucidation, and perfection from their earliest infancy up to our own times, as chemistry". The author therefore maintains in the preface that the historian cannot achieve any useful purpose unless he is aware of the significance of the science with which he is dealing. On the other hand, he should not "allow himself to be carried away by passionate love of the subject to such an extent that the attributes to it unfounded exclusive privileges for the education of mankind and for the perfection of other sciences and arts".

In accordance with his intention "to remain true to fact in this description of the fortunes of chemistry", he unfolded before his contemporaries a comprehensive picture of chemistry as it appeared to him with the chemical knowledge of that time. His information, arranged chronologically rather than by subject, is substantiated by numerous references to the earlier and to contemporary literature. However, this work is nowadays generally regarded as having little permanent interest, and is because of the many errors that it contains often disposed of in a few words. This is most unjust in the reviewer's opinion, since the work provides a veritable mine of early views and opinions for the present-day historian.

In the development scheme of historiography given by *H. Breysig* in 1931, *Gmelin*'s work would undoubtedly belong to the purely factual phase, though the facts were subjected to a certain critical evaluation. *Johann Bartholomä Trommsdorff*'s "Versuch einer allgemeinen Geschichte der Chemie" (Erfurt 1806) and *Thomas Thomson*'s two-volume "History of Chemistry", which was published in London in 1830/1831 and is described by *J. R. Partington as* "still of value", since it also makes extensive reference to the original sources, also belong to this phase.

The second phase, classificatory historiography, began with *Alexander von Humboldt*'s five-volume work, "Kosmos, Entwurf einer physischen Weltbeschreibung" (Stuttgart 1845/1862), which also formed the highlight of this phase. In the first volume of this monumental interpretation of knowledge of natural science, the author says that the purpose of such a description is "to recognize the unit in the multiplicity; to embrace all that recent discoveries hold out to us about the particular; to examine and sift the details without being overcome by their weight". Thus this work paved the way for a turning point in the approach to history, *i.e.* the replacement of a listing of facts by their classification and the extraction from them of ideas serving as a basis for new work.

The first work of this type on the history of chemistry was probably *Ferdinand Hoefer*'s two-volume "Histoire de la chimie depuis les temps les plus reculés jusqu'à notre époque" (Paris 1842/1843). By the use of the Greek and Latin manuscripts available at the "Bibliothèque Nationale" in Paris, this author was able to present, in many respects, a better picture of the earlier period of chemistry than *Kopp*, though, as *Berthelot* was also to do later, he made many errors of interpretation. *Kopp*'s history of chemistry will therefore be generally regarded as more reliable.

Kopp gives a reason that is very common even today for the compilation of his history, which arose from notes that had become so comprehensive "that it seemed to be useful to arrange and publish them". Thus in the preface to the first volume he says, "The decision.... to publish this work was largely influenced by the fact that the history of chemistry seems to have been a much neglected field of research in recent decades". This was only natural, since these years were marked by the work in the new field of synthetic organic chemistry, and successes and progress counted for much more than retrograde understanding.

However, *Kopp* regarded this understanding and the discovery of relationships as important. "Past historians", he wrote, "attempted to report all the achievements of all chemists in one order, *i.e.* in chronological order. Owing to the volume and diversity of the material, however, a work arranged in this manner, though possibly complete in other respects, can only contain a confusion of unrelated discoveries".

Up to our own time, *Kopp*'s work remained the comprehensive work on the history of chemistry. Supplemented later by the "Entwicklung der Chemie in der neuren Zeit" (München 1873), „Beiträge zur Geschichte der Chemie" (3 parts, Braunschweig 1869/1875), and "Alchemie in älterer und neuerer Zeit" (Heidelberg 1886), it was the only comprehensive work, apart from Hoefer's, that referred to the original sources. Smaller works such as *Ernst von Meyer*'s "Geschichte der Chemie von den ältesten Zeiten bis zur Gegenwart" (Leipzig 1889 and later editions) was largely based on this history by *Kopp*.

Parallel to the development in chemistry itself, "specialization" began in chemical historiography even before the turn of the century. Though at first still leading to books covering an entire field, such as "Geschichte der organischen Chemie von ältester Zeit bis zur Gegenwart" by *Edvard Hjelt* (Braunschweig 1916) or the "Geschichte der organischen Chemie" by *Carl Graebe* (Berlin 1920), historical research moved into ever narrower sectors, the results of which were published in journals and monographs.

As a result of this specialization, it naturally became necessary to correct many of *Kopp*'s data, but there was at first no author to be found to write such a modified general history. It was only in 1961, 120 years after the publication of *Kopp*'s work, that *J. R. Partington*'s "History of Chem-

istry" began to appear (four volumes, the last of which is still to be published).

Have therefore, in view of these developments, works such as those by *Gmelin* and *Kopp* become superfluous? For the reader interested in a given event in the development of chemistry, *Partington* may be more suitable, since it presents the current state of knowledge. However, for those with a deeper interest in the problems of the history of chemistry, it will still be necessary to return to the earlier publications, since *Gmelin* and *Kopp* present the knowledge of their time in a lucid form. The publishers therefore have good reason to include these two works in their reprint program.

W. Ruske [NB 559 IE]

Grundlagen der Polarographie (Principles of Polarography) by *J. Heyrovský* and *J. Kůta*. Translated by *H. Bažantová*. Edited in German by *K. Schwabe*. Akademie-Verlag, Berlin 1965. 1st Edit., xvii, 592 pp., 256 figures. DM 73.–

The book presents a comprehensive survey of the theoretical principles of and the general information that can be obtained by classical direct-current polarography, with reference to its applications in electrochemical kinetics and the physical chemistry of solutes. Polarography in these fields has undergone a remarkable and decisive development in the past two decades.

The authors are successful in their aim of explaining the basic theoretical aspects without losing themselves in details of the mathematical derivations, which easily can be found in the original literature cited. The style is fluid and clear, so that the theoretical problems of polarography, which often are not entirely free from complications, are made accessible even to the novice. The experienced worker will also find this an indispensable and frequently consulted reference work. This applies, not only to specialists in polarography, but to electrochemists in general and all those concerned with the application of electrochemical techniques. The present volume, which reflects more than 40 years' experience of the originator of polarography and his co-worker *Kůta*, can therefore be recommended to a wide circle of readers. It is to be hoped that this book will lead to a more intensive use of the versatile possibilities of the polarographic method. The present work clearly refutes the view that polarography is unsuitable for fundamental problems. Provided that there is freedom of choice concerning the electrode material, as is usually the case in fundamental problems, the opposite is in fact true, and polarographic methods become the method of choice.

The Czech edition has been added to and brought up to date in the German translation, which takes into account the literature up to the beginning of the 1960's. The subject matter is divided into 22 chapters, which deal with the following topics: physics of the dropping-mercury and mercury-jet electrodes, influence of the resistance of the electrolyte, theory of the diffusion current and kinetically controlled limiting currents, the theory of reversible and irreversible steps including their behavior in the case of complexes and semiquinones, the evolution of hydrogen and its catalysis, adsorption and inhibition, maxima, the uses of the hitherto much neglected Kalousek switching circuit and the theory of the resulting currents, and oscillographic polarography, with special emphasis on the *Heyrovský* version. The appendix contains a useful table of half-wave potentials of inorganic and many organic depolarizers in a series of supporting electrolytes. The reviewer would have welcomed a more thorough treatment of the double-layer effect. The results for the dissociation and recombination kinetics of weak acids also require a much more critical discussion than the footnote to Table 17/3.

Finally, it should be pointed out that the numerous novel polarographic techniques, which open up formerly closed fields to electrochemical kinetics and offer a wealth of new information, are almost completely absent. Alternating-current, square-wave, and pulse polarography are mentioned only briefly, and while the increased instrumental demands are stressed no list is given of the far-reaching possibilities thus gained. No mention is made of second-order techniques (such as Faraday rectification, the use of higher harmonics, and intermodulation methods). The treatment of oscillographic pulse methods is also too short.

The German edition unfortunately contains more printing errors than such an important book should. The presentation and binding are good. *H. W. Nürnberg* [NB 556 IE]

An Introduction to Electron Paramagnetic Resonance. By *M. Bersohn* and *J. C. Baird*. From the series "Frontiers in Chemistry". W. A. Benjamin, Inc., New York-Amsterdam 1966. 1st Edit., xi, 274 pp., 110 figures, $15.00.

After a general introduction, the authors devote about 120 pages (Chapters 3 to 10) to hyperfine structure, relaxation, g factors, quantitative measurements, organic radicals, triplets, inorganic compounds, and double-resonance; a further 40 pages (Chapters 11 and 12) deal with applications in chemistry and biology. The appendix gives a more quantitative presentation of the interactions in the two-spin system, and the book ends with a list of the coupling constants of 130 selected organic radicals and radical ions.

The book is intended for chemists and biologists having no prior knowledge of the subject. The picture presented is very general, since *e.g.* the following topics are covered in a total of about 30 pages: inorganic radicals, metal complexes, nonconductors, metals, Mössbauer effect (1½ pages!), Overhauser effect, ENDOR, optical pumping, and level crossing.

A conspicuous feature of the whole book and particularly of the tables (g factors, pp. 70/71, and coupling constants, pp. 238–270), is the complete disregard of all but English-language literature. The physical chemist will sometimes be disappointed by the lack of accuracy. Thus in the discussion of the intensities of the HFS components (p. 80), the incorrect, but convenient, and hence commonly used counting rule is described in detail for the H_2^+ ion, but the reader is not told that two protons combine to give a singlet and a triplet, though this is explained in an elementary and laborious manner for the case of electrons (p. 108).

On the whole, the reviewer has gained the impression that the authors were pressed for time. However, despite the shortcomings mentioned above, the book will undoubtedly find a wide circle of readers and contribute to the growth of interest in this modern field. *K. H. Hausser* [NB 570 IE]

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Investigation of Inorganic Systems at High Temperature by Mass Spectrometry

BY J. DROWART AND P. GOLDFINGER [*]

High-temperature mass spectrometry (hitherto at temperatures between 1000 and 2500 °K and at pressures between 10^{-3} and 10^{-12} atm) has already made possible the identification of many previously unknown and unpredicted diatomic and polyatomic molecular species. The present paper deals with the investigation of many oxides, of halides, and of carbon molecules and intermetallic molecules. An apparatus for the production and investigation of molecular beams is described. Knudsen cells permit the production of molecular beams under equilibrium conditions; in special cases the "double-oven" type of Knudsen cell is used. Thermodynamic and kinetic quantities such as ΔH_T^0 values, dissociation energies, and ionization cross sections of the species investigated are given.

1. Introduction

Thermodynamic investigations by mass spectrometry of high temperature systems were started by *Chupka* and *Inghram* [1] and by *Honig* [2] about fifteen years ago with the study of the vaporization of carbon. Thereafter the studies extended rapidly to other elements [3,4], to intermetallic compounds [5], to oxides [6, 7, 8], sulfides, selenides, and tellurides [5], to halides [9–13], hydroxides [14], and nitrates [15].

This method has become one of the most powerful tools for the study of gas-solid or gas-liquid equilibria at high temperatures. Hundreds of condensed systems in equilibrium with their vapor have since been studied and their mode of evaporation [a] established. Gaseous molecules, many of which had been previously studied by spectroscopic methods only or were unknown and quite unexpected, were identified and their dissociation or atomization energies obtained from their equilibrium pressures. These results have led to an appreciably modified picture of the stability of gaseous inorganic molecules and to the knowledge of many new molecular species.

During the past few years, high temperature mass-spectrometric studies have been extended to the study of the mechanism and kinetics of vaporization and condensation processes and to the investigation of

[*] Prof. J. Drowart and Prof. P. Goldfinger
Laboratoire de Chimie Physique Moléculaire
Université Libre de Bruxelles
Bruxelles (Belgium)

[1] *W. A. Chupka* and *M. G. Inghram*, J. chem. Physics *21*, 371, 1313 (1953); J. physic. Chem. *59*, 100 (1955).

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[a] The expression "mode of evaporation" is used here to describe the entirety of the overall chemical reactions observed. The detailed sequence of processes or steps of these reactions is referred to as mechanism.

chemical reactions of gases and solids [16]. In these fields, this technique is leading to the accumulation of important new data.

The method consists in: isolating a representative sample of the gaseous phase of the system investigated in the form of a molecular beam; forming ions from the neutral species present in this beam; mass analysing the ions in the spectrometer and measuring their intensity; identifying the ions and thus determining the neutral species from which they were formed; calculating the flux of neutral species in the molecular beam from the ion intensity and then deriving thermodynamic and kinetic quantities from the flux.

Comprehensive reviews [17,18] have been written which give the details of the technique, calculations, and tables of results. In the present paper, the various steps of the method outlined above are described and a brief summary is given of the contributions which the technique has made to our knowledge of gaseous inorganic molecules.

2. Experimental Details

The apparatus used for this particular application of the molecular beam technique consists of a) a molecular beam source and collimating system; b) an ionization source; c) a mass spectrometer; d) an ion-collector; e) a vacuum envelope in which the components (a–d) are placed and in which a low pressure can be maintained so that the mean free path is several times the greatest distance to be traveled by any particle (*i.e.* from the ion source to the collector).

A molecular beam is defined [19] as "a large number of molecules moving practically collision free in a highly evacuated space in straight and almost parallel trajectories". Such a beam emerges from a metal vessel (Fig. 1) with a small aperture of area s, usually called a Knudsen cell, which contains the gas or vapor to be studied. The atoms or molecules whose velocity vectors point towards the orifice effuse and continue to travel along straight lines. By placing one or more apertures in front of the orifice it is possible to select a fraction of the effusing molecules to form the beam proper. Collisions in the beam occur only on those rare occasions when a molecule overtakes a slower moving one. Monomolecular decay of complex molecules excited above their dissociation limit is also a rare occurrence and any optical transitions do not modify the chemical nature of the species. For these reasons such a beam is a truly representative sample of the system investigated.

Collisions between molecules in the effusion orifice may be avoided by maintaining the mean free path λ of the molecules in the cell large compared to the diameter d of the orifice. When $\lambda \simeq d$ transition to hydrodynamic flow ($\lambda \ll d$) takes place, which is usually avoided in the type of work described here (see, however, [20]).

When the ratio between the area of the effusion orifice s and that of the vaporizing substance S is small, the equilibrium between the gas and the condensed phase will not be perturbed by the effusion. If necessary this can be verified by measuring the rate of effusion as a function of the ratio s/S at constant temperature. When the orifice has a negligible thickness compared to its diameter, elementary kinetic theory of gases shows that the total number of molecules effusing per unit time, Z, is given [21] by

$$Z = nus/4 \qquad (1)$$

($n = p/kT$: the number density (molecules cm^{-3}) in the cell, $u = (8kT/\pi m)^{1/2}$: the average velocity; p = pressure; k = Boltzmann's constant; T = absolute temperature; m = mass).

Their intensity distribution is proportional to the cosine of the angle between the paths of the molecules and the normal to the orifice, in an analogous manner to Lambert's law for radiation emitted from a light source. When the orifice has a finite thickness x, both the rate of effusion and the angular distribution [22] are a function of x/d.

An alternate way of producing molecular beams consists in collimating the molecules freely vaporizing from the surface of the sample studied. This technique has been widely applied by Langmuir [23] and is usually referred to by his name.

To ensure the establishment of equilibrium between the condensed and the gaseous phase, Knudsen cells have been employed as molecular beam sources in a large proportion of the investigations discussed here; where the interest lay in the kinetics and reaction mechanism, the Langmuir method was used [16].

A typical apparatus is given in Fig. 1 which shows the Knudsen cell, radiation shields, and the heating element. For the study of equilibria between a condensed phase and a permanent gas, cells with a "gas-inlet" have been used [24] while for the study of the equilibria

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in unsaturated vapors, measurements have been performed in "double-oven" [25] type Knudsen cells. Recently, electrochemical Knudsen cells have been employed [26].

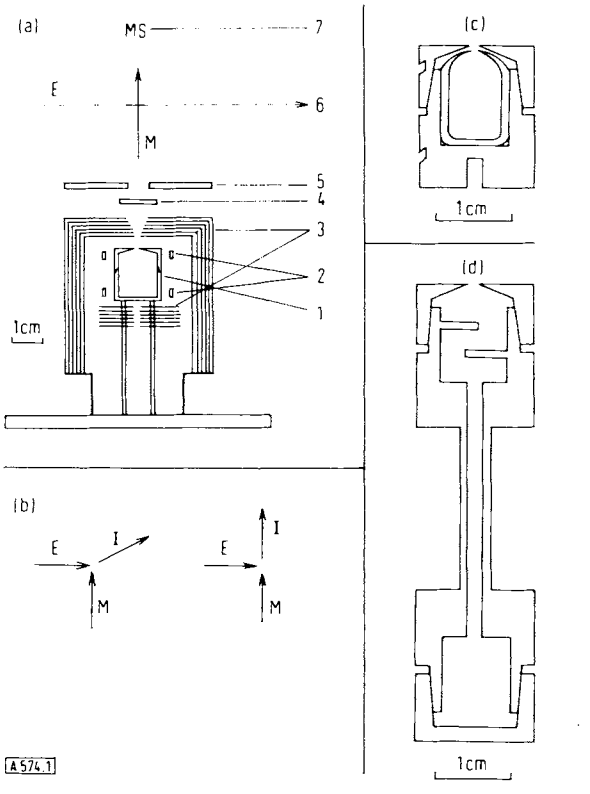


Figure 1. Knudsen Cell

(a) Assembly
(1) Knudsen cell; (2) Heating elements; (3) Radiation shields; (4) Movable shutter; (5) Entrance slit to ion source (can be water or liquid nitrogen cooled) (6) Electron beam; (7) Mass analyser.

(b) Shows mutuallv perpendicular molecular (M), electron (E), and ion (I) beams or alternatively parallel molecular (M) and ion (I) beams and vertical electron (E) beam.

(c) Detail of Knudsen cell in which a refractory ceramic or metallic crucible may be inserted and which has a number of holes for sighting with an optical pyrometer or for inserting thermocouples.

(d) Double Knudsen cell.

The cells, which are usually made from molybdenum, tantalum, or tungsten, may contain refractory metallic or ceramic liners to avoid reaction of the species with the cell material. The choice of the appropriate container materials is a serious problem at high temperatures; it can be facilitated when phase diagrams are available, but often proceeds empirically. The selection is then facilitated by the fact that gaseous reaction products or variations in activity resulting from alloy or compound formation are easily observed with the mass spectrometer.

Heating is generally performed by radiation up to temperatures of about 1000 °C and by electron bombardment at higher temperatures. Arc imaging techniques [27] and lasers [28] have also been used.

Thermocouples are used for temperature measurement in the lower range; optical pyrometers, usually monochromatic, sighting into black-body holes [b] or directly into the effusion orifice are employed at higher temperatures. Provision can be made to check temperature uniformity throughout the Knudsen cell. In the authors' opinion the reproducibility and accuracy of temperature measurements is essentially the same in the mass spectrometric system as in the classical, analogous apparatus for measuring pressures by the Knudsen, torsion, or Langmuir methods. In the temperature interval 1000–2500 °K, in which most of the measurements are performed, the temperature uncertainty is estimated to be about 1%.

The molecular beam leaving the cell is defined by an aperture in the radiation shields (see Fig. 1). A movable beam defining slit placed in front of the ion source enables one to measure the intensity distribution in the molecular beam, in order to ascertain the correct geometrical origin of the species identified in the mass spectrometer (Fig. 1 and 2) and to detect perturbing phenomena such as the creeping of liquids onto the lid of the cell or their migration through the walls *e.g.* by interboundary migration. It further permits one to distinguish the ions formed by electron impact on the vaporizing species from those produced from the background gases.

Different geometric arrangements of the molecular, electron, and ion beams have been used. In most applications, the electron beam is parallel to the entrance slit of the spectrometer and the molecular beam perpendicular to it. The ion beam can then be either coaxial with or perpendicular to the molecular beam (Fig. 1). In practice no significant differences in operation or in the results have been observed.

The ionization method is selected so as to give as faithful a picture as possible of the neutral molecules in the molecular beam and simultaneously the highest possible sensitivity. Therefore, ionization by electron impact and identification of the positive ions have been applied. Since in most cases an energy spread of a few tenths of one eV is permissible in establishing the main features of the ionization efficiency curves which are to be discussed, ion sources of conventional types [29] have been used. A retarding potential difference [30] source has been used [31] in applications where the interest lay more in the accurate study of the ionization efficiency curve of high temperature species than in the measurement of partial pressures and where, therefore, monoenergetic electrons are required, the obtention of which results in a marked loss of intensity.

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[26b] *D. Detry, J. Drowart, P. Goldfinger, H. Keller,* and *H. Rikkert,* Z. physik. Chem. [Frankfurt], in press.

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[28] *R. E. Honig* and *J. R. Woolston,* Appl. Physics Letters *2,* 138 (1963); *R. E. Honig, ibid. 3,* 8 (1963); *J. Berkowitz* and *W. A. Chupka,* J. chem. Physics *40,* 2735 (1964).

[b] A cavity with a large depth to diameter ratio is a satisfactory "black-body". The measurement of surface temperatures when using Langmuir conditions requires a knowledge of the emissivity.

[29] *H. Ewald* and *H. Hintenberger*: Methoden und Anwendung der Massenspektroskopie. Verlag Chemie, Weinheim/Bergstr. 1953; *G. B. Barnard*: Modern Mass Spectrometry. Institute of Physics, London 1953; *M. G. Inghram* and *R. J. Hayden*: Mass Spectroscopy. Nuclear Sci. Ser. Rep. 14. Nat. Acad. Sci. – Nat. Res. Council, Washington D.C. 1954; *J. H. Beynon*: Mass Spectrometry and its Uses in Organic Chemistry. Elsevier, Amsterdam 1960; *R. I. Reed,* Mass Spectrometry. Academic Press, London-New York 1965; *C. Brunnee* and *H. Voshage,* Massenspektrometrie. K. Thiemig K.G., München 1964.

[30] *R. E. Fox, W. M. Hickam, T. Kjeldaas jr.,* and *D. J. Grove,* Physic. Rev. *84,* 859 (1951); Rev. Sci. Instruments *12,* 1101 (1955); *C. A. McDowell*: Mass Spectrometry. McGraw Hill Book Co., New York 1963, p. 524.

[31] *N. C. Blais* and *J. B. Mann,* J. chem. Physics *33,* 100 (1960); *J. B. Mann, ibid. 40,* 1632 (1961).

Surface ionization, which is extremely sensitive, is only applicable to elements or molecules with low ionization potentials and is hence too specific. Field ionization[32] which has promising characteristics has not hitherto been applied. Recently, interesting results obtained with photoionization have been published[33].

Mass analysis has been performed in general with single focusing magnetic instruments. The characteristics of such instruments and their mode of operation have been discussed in monographs on mass spectrometry[29]. Because of better accessibility to the source and a greater ease of installing multipliers, 60° instruments have been preferred. Since 1960, time-of-flight mass spectrometers have also been applied[34]. In the sector instruments, the resolving power and detection limit have in general been better than in the time-of-flight mass spectrometers. With the assemblies described hitherto in the literature the overall pressure range accessible extends from about 10^{-3} to 10^{-12} atm in the Knudsen cell. The upper pressure limit is set by the dimension of the effusion orifice. Usually these have been 0.1 to 1 mm in diameter. The use of smaller diameters or very narrow slits as effusion orifices leads to difficulties which increase markedly with temperature. The lower limit is, generally speaking, fixed by interference with background gases and by the sensitivity of the mass spectrometer. In the former case, the pressure should be decreased below the usual value of some 10^{-6} to 10^{-7} torr; alternatively double focusing instruments can be used for which the increased resolving power enables one to separate the inorganic ions of interest here from the mostly organic ions formed from the background gases. When the limitation is set by the sensitivity of the mass spectrometer, the now available quadrupole[35] (or monopole) instruments which combine the advantage of high sensitivity and relatively high resolving power may be used. High intensity ion sources[36] and focusing lenses[27,37] present further possibilities.

3. Identification of Species

For species identification, the complete mass spectrum must be evaluated over the greatest possible temperature range. The spectrum is checked at the mass numbers corresponding to all possible combinations of the elements and their isotopes present in the system (including the container materials and possible impurities), ascertaining whether their intensity is affected by the movable beam defining slit. It is simultaneously verified that the intensity distribution of the neutral molecule in the molecular beam is normal (see Fig. 2). Ions formed from the vaporizing species are so singled out from those due to the ionization of background gases. The higher the resolving power, the greater will be the observable effect of differences in packing fraction[c] between inorganic ions and hydrocarbon ions.

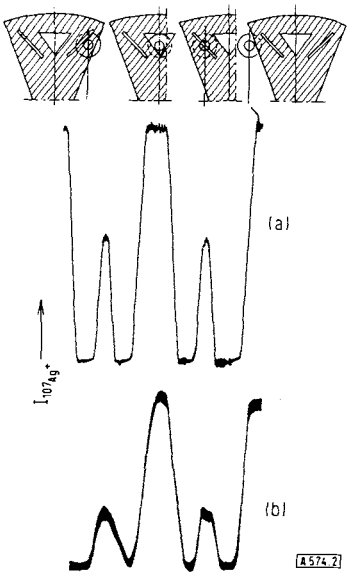


Figure 2. Measurement of the intensity distribution in the molecular beam.

Normal (a) and distorted (b) intensity profiles obtained when rotating the beam defining slit across the molecular beam. Note slopes in the profiles, width and height of peak, flat or rounded valley when narrow slits cross. The upper part of the figure represents positions of the beam defining slit corresponding to the intensity on the recording.

Since most elements have several isotopes and since there is little overlapping between mass numbers, the measurements of the isotopic distribution and beam profile will leave little ambiguity concerning the identification of the ions. The measurement of their appearance potential will often remove remaining difficulties.

In the type of application discussed here, the nature and concentration of the neutral molecules is deduced from the ions identified and an understanding of the ionization phenomena[38–42] leading to their forma-

[c] The packing fraction is defined as $(M-A)/A$ where M is the exact mass and A the corresponding whole mass number, both in atomic mass units. In the ^{12}C scale, the difference $M-A$ is *e.g.* 7825×10^{-6} for H, 0 for ^{12}C, -5085×10^{-6} for ^{16}O, -52052×10^{-6} for ^{48}Ti and $+ 50760 \times 10^{-6}$ a.m.u. for ^{238}U. Therefore the exact mass of ^{48}Ti, 47.947867, is different from that of $^{12}C_4$, 48.0 exactly, by 0.1%.

[32] *R. Gomer* and *M. G. Inghram*, J. chem. Physics *22*, 1279 (1954); J. Amer. chem. Soc. *77*, 500 (1955); *M. G. Inghram* and *R. Gomer*, Z. Naturforsch. *10a*, 863 (1955); *H. D. Beckey* in: Advances in Mass Spectrometry. Vol. 2, Pergamon Press, London 1963, p. 1; Vol. 3, p. 35; *D. Beckey* in *R. I. Reed*: Mass Spectrometry. Academic Press, London-New York 1965.

[33] *J. Berkowitz* and *W. A. Chupka*, J. chem. Physics *45*, 1287 (1966).

[34] *D. White, A. Somer, P. N. Walsh*, and *H. W. Goldstein* in *R. M. Elliott*: Advances in Mass Spectrometry. Vol. 2, Pergamon Press 1963, p. 110; *M. B. Panish*, J. chem. Physics *34*, 1079 (1961).

[35] *W. Paul* and *H. Steinwedel*, Z. Naturforsch. *8a*, 448 (1953); *W. Paul* and *H. Raether*, Z. Physik *140*, 262 (1955); *C. Brunnée* in *R. I. Reed*: Mass Spectrometry. Academic Press, London-New York 1965. *U. v. Zahn*, Rev. Sci. Instruments *34*, 1 (1963).

[36] *R. Weiss*, Rev. Sci. Instruments *32*, 397 (1961).

[37] *C. F. Giese*, Rev. Sci. Instruments *30*, 260 (1959).

[38] *H. D. Hagstrum* in: Mass Spectrometry in Physics Research. Nat. Bur. Standards (U.S.A.), Circular 522, 193 (1950); Rev. mod. Physics *23*, 185 (1951).

[39] *F. H. Field* and *J. L. Franklin*; Electron Impact Phenomena. Academic Press Inc., New York 1957.

[40] *G. H. Wannier*, Physic. Rev. *90*, 817 (1953); *100*, 1180 (1956); *S. Geltman, ibid. 102*, 171 (1956); *112*, 176 (1958).

[41] *J. D. Morrison*, J. appl. Physics *28*, 1409 (1957); J. chem. Physics *40*, 2488 (1964); 12e Conseil de Chimie Solvay, Interscience Publishers, New York *1962*, p. 397.

[42] *J. H. Dunn* and *L. J. Kieffer*, Physic. Rev. *132*, 2109 (1963); *D. Rapp, P. Englander-Golden*, and *D. D. Briglia*, J. chem. Physics *42*, 4081 (1965).

tion and not from typical mass spectra of standard samples.

All neutral gaseous species are ionized by impact with electrons. At about three to five times the ionization potential, the ionization cross section goes through a flat maximum, where its value from the lightest atoms to the heaviest molecules increases quite regularly by about a factor of fifty [d] (Table 1). In most cases, the parent ion, *i.e.* the molecular ion formed without fragmentation, will be 5 to 20 times more intense than fragment ions derived from the same molecule. Typical exceptions are molecules containing strongly electronegative atoms or groups, where the predominating ion is that formed by the loss of this atom or group. In order to identify a neutral precursor, parent and fragment ions must be distinguished; consideration of the ionization phenomena and of chemical and thermodynamic arguments enables one to make this distinction.

The basis of the ionization efficiency and appearance potential measurements is illustrated qualitatively in Fig. 3 (for a more detailed discussion, see [41]). The minimum energy at which direct ionization

$$A(g) + e \rightarrow A^+(g) + 2\,e \qquad (2)$$

takes place is the ionization potential IP of atom A. For a molecule, the minimum energy for the process

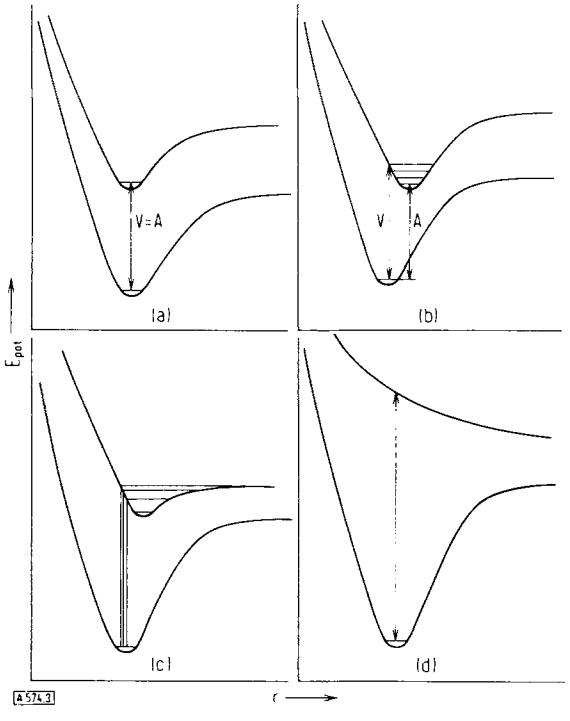


Figure 3. Potential energy curves showing: equal vertical (V) and adiabatic (A) ionization potential $V = A$ (a); $V \neq A$ (b); vertical ionization leading to, or nearly to, dissociation, with parent and fragment ions present (c); upper potential energy curve repulsive, with ionization always accompanied by fragmentation (d).

[d] Therefore ions corresponding to all species present in a gaseous mixture in widely different concentrations are observed in the mass spectrometer. This is the reason for the unique advantages of mass spectrometry in the analysis of gases. In contrast, optical absorption or emission probabilities may vary by several powers af ten from one gaseous species to another.

$$AB(g) + e \rightarrow AB^+(g) + 2\,e \qquad (3)$$

is either the adiabatic or the vertical (Fig. 3) ionization potential depending on whether or not the Franck-Condon principle, which is applicable to this process, allows the minimum of the AB^+ potential energy curve to be reached.

The minimum energy AP (appearance potential) at which fragmentation, *i.e.* the process

$$AB(g) + e \rightarrow A^+ + B(g) + 2\,e \qquad (4)$$

occurs, is given by

$$AP \geqslant IP(A^+) + D(AB) \qquad (5)$$

where the inequality results from the fact that both A^+ and B can have kinetic energy (or kinetic plus internal energy in the case where A or B represent di- or polyatomic species) [42].

Especially for process (2), theory [40], and experiment [41,43], indicate that the efficiency increases linearly with the excess energy as long as the process corresponds to a transition from one well defined lower to a similarly well defined upper state; the ionization efficiency curve will therefore have the form illustrated in Fig. 4 when the vapor contains both species A and AB so that processes (2) and (4) can occur simultaneously.

The straight line a–b corresponds to the direct ionization of A, while the difference between the line b–c and the extrapolated line a–b corresponds to the production of A^+ ions from AB molecules. In such cases it is still possible to measure the pressure for A in presence of large amounts of AB by maintaining the energy below that corresponding to point b.

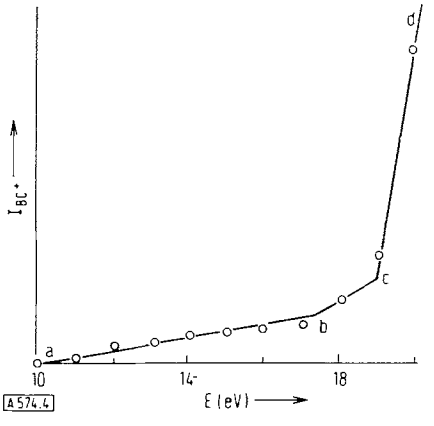


Figure 4. Ionization efficiency curve for the ion BC^+; a–b corresponds to $BC \rightarrow BC^+$; b–c and c–d correspond to $B_2C \rightarrow BC^+ + B$ and $BC_2 \rightarrow BC^+ + C$ respectively.

The difference $E_b - E_a$ should correspond approximately (relation (5)) to the dissociation energy of the bond AB. In view of difficulties in obtaining accurate dissociation energies in this manner, it has usually been preferred to obtain these data from thermodynamic calculations (Sections 5 and 6).

In the case of an atomic ion, the correctness of the identification can be easily verified by checking whether the measured ionization potential IP(A) corresponds to the spectroscopic value. Rydberg series

[43] *L. J. Kieffer* and *G. H. Dunn*, Rev. mod. Physics *38*, 1 (1966).

for molecules have been observed in few cases only. Comparison with isoelectronic molecules, for which the ionization potential is known spectroscopically or from mass spectrometry, will then be useful [39,44]. It has further been observed that the ionization potential of a molecule with no free valence electrons is about equal to the average of the ionization potentials of the constituent atoms. For molecules with free valence electrons, it tends to be closer to the ionization potential of the more metallic element.

If the potential energy curve of the molecular ion is repulsive (or only the repulsive branch is accessible in the Franck-Condon region) (Fig. 3c and 3d), the ion A^+ is formed with kinetic energy. Measurement of the latter then confirms the occurence of such processes [45].

In the case of polyatomic molecules, the excess energy can appear in internal degrees of freedom and the parent ion may be metastable. If the rate constant for dissociation of the initial ion (mass m_i, charge n_i) to fragment ions (mass m_f, charge n_f) is such that decay occurs in the region between the ion source and the analyser, it can be observed by the presence in the spectrum of peaks at an apparent mass [29] m_{app},

$$m_{app} = n_i m_f^2 / m_i n_f^2. \qquad (6)$$

Whereas there are numerous such examples for hydrocarbons, few are known presently in high temperature chemistry.

Alternative modes of ionization [38,39,46], such as

$$AB(g) + e \rightarrow A^+ + B^- + e \qquad (7)$$

have a different [41] ionization efficiency curve from that shown in Fig. 4. If this process is suspected to occur, a search for the ion B^- should be made; the cross section for this reaction is small.

For M_2 species with very low relative intensities, it is useful to verify that the peak observed is not due to second order phenomena such as charge exchange reactions [47] of the type (8)

$$M^{++} + X \rightarrow M^+ + X^+ \qquad (8)$$

which take place in the analyser, where X is a residual gas. According to (6), such reactions give rise to an apparent mass $2m_i$, which can not be distinguished from that of M_2^+ except by the isotopic distribution. Such processes are avoided by working at ionizing electron energies below the second ionization potential of M.

Other reactions which should be considered are ionization reactions caused by excited metastable A* atoms [47,48]

$$A^* + A \rightarrow A_2^+ + e \qquad (9)$$

where A* is produced by electron impact. Again, a different efficiency curve will be obtained since the process $A + e \rightarrow A^* + e$ is a resonance process.

Ion attachment reactions [49]

$$A^+ + 2\,A \rightarrow A_2^+ + A \qquad (10)$$

may also be mentioned, although the density in the source is in general too low for three body collisions. Yet another possibility is that of ion/molecule reactions [50] as in eq. (11).

$$\begin{aligned} A^+ + B_2 &\rightarrow AB^+ + B \\ A + B_2^+ &\rightarrow AB^+ + B \end{aligned} \qquad (11)$$

In this case the ionization efficiency curve for AB^+ should parallel that for A^+ or B_2^+ and may further be a function of the potentials in the ion source. If A or B_2 are permanent gases, it is useful to vary their pressure.

Independent chemical and thermodynamic arguments are sometimes necessary in the identification of the neutral precursor of an observed ion. Such arguments involve consideration of the variation of temperature, of crystalline modification, comparison of equilibrium and nonequilibrium conditions, and modification of the composition of the system. A number of examples most easily illustrate the use of such arguments. The ratio of the ion intensities for C^+ and C_3^+ varies from 2.3 to 8.0 between 1820 and 2700 °K [51]; at 2400 °K the ratio varies from 6 for vaporization from a Knudsen cell to 1.5 for vaporization from a polycrystalline filament [52,27]; this shows that C^+ and C_3^+ have different neutral precursors, namely C and C_3. The variation with temperature of the intensity of the ions LiI^+ and Li_2I^+ formed from the vapor in equilibrium with crystalline LiI is almost parallel [53], the change for Li_2I^+ is, however, double that for LiI^+ at the melting point; this demonstrates that Li_2I^+ is formed from a neutral molecule which is a dimer of the molecule from which LiI^+ is formed. Since the change forLiI^+

[44] *R. W. Kiser*: Table of Ionization Potentials. Office of Technical Services, Dept. of Commerce, Washington 25, D. C., 1960; *V. I. Vedeneiev, L. V. Gurvitch, V. N. Kondratiev, V. A. Medvedev,* and *E. L. Frankevitch*: Dissociation Energies of Chemical Bonds, Ionization Potentials and Electron Affinities. Academy of Sciences, USSR, Moscow 1962.

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[48] *J. A. Hornbeck* and *J. P. Molnar*, Physic. Rev. *84*, 621 (1951); *M. Pahl*, Z. Naturforsch. *18a*, 1276 (1963); Ergebn. exakt. Naturwiss. *34*, 182 (1962); *P. M. Becker* and *F. W. Lampe*, J. chem. Physics *42*, 3857 (1965).

[49] *R. A. Johnson, B. T. McClure*, and *R. B. Holt*, Physic. Rev. *80*, 376 (1950); *A. V. Phelps* and *S. C. Brown, ibid. 86*, 102 (1952).

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[51] *J. Drowart, R. P. Burns, G. DeMaria*, and *M. G. Inghram*, J. chem. Physics *31*, 1131 (1959).

[52] *W. A. Chupka* and *M. G. Inghram*, Mém. Soc. roy. Sci. Liege, 4e Serie, *15*, 373 (1954).

[53] *L. Friedman*, J. chem. Physics *23*, 477 (1955).

corresponds to the known heat of melting, LiI^+ and Li_2I^+ are formed from the neutral molecules LiI and Li_2I_2 respectively[45,54,55]. The intensities I of the ions $Ge_2O_2^+$ and $Ge_3O_3^+$ vary proportionally to $I^2(GeO^+)$ and $I^3(GeO^+)$ respectively when dismutations GeO(amorphous) → 1/2 GeO_2(glass) + 1/2 Ge(crystalline) → 1/2 GeO_2(hexagonal) + 1/2 Ge(crystalline) occur in the condensed phase. The variation in intensity, *i.e.* partial pressure of the ion GeO^+ yields thermodynamic data for GeO(amorphous) and GeO_2(glass) relative to those for GeO_2(hexagonal), which agree with the literature data. GeO^+ is therefore formed from the molecule GeO and $Ge_2O_2^+$, and $Ge_3O_3^+$ from Ge_2O_2 and Ge_3O_3 respectively[56].

The ratios of intensities for S_6^+, S_7^+, and S_8^+ are markedly different for rhombohedric, amorphous, and Engel's sulfur showing again that they are formed from different neutral precursors[57].

Mass spectrometric measurements on the polyatomic sulfur and selenium molecules have also been performed with electrochemical Knudsen cells[26b]. Such measurements are based on the use of the galvanic cell Pt, Ag/AgI/Ag_2S (or Ag_2Se), Pt, where AgI, a purely ionic conductor, is used as solid junction. When such cells are polarized the reaction

$$Ag_2S\,(\text{or } Ag_2Se)\,(\text{solid}) \rightarrow 2\,Ag\,(\text{solid}) + S_x/x\,(\text{or } Se_x)\,(\text{gas}) \quad (12)$$

occurs. Since Ag_2S and Ag_2Se have a small homogeneity range, it can be shown that the chemical potential μ of sulfur and silver in the compound are related by eq. 13, with good approximation, to the Gibbs free energy of formation of the compound and the chemical potentials μ^0 in the standard state.

$$\mu_S - \mu_S^0 = \Delta G(Ag_2S) - 2(\mu_{Ag} - \mu_{Ag}^0) \quad (13)$$

Therefore the pressure of S_x in equilibrium with a given composition is related to its pressure in equilibrium with pure sulfur by eq. (14).

$$p_{S_x} = p_{S_x}^0 \text{ exp. } x(\mu_S - \mu_S^0)/RT \quad (14)$$

If $p_{S_x}^{'}$, the decomposition pressure above Ag+Ag_2S, is chosen as reference pressure, eq. (14) becomes eq. (15).

$$p_{S_x} = p_{S_x}^{'} \text{ exp. } 2xEF/RT \quad (15)$$

(R = gas constant, E = EMF of the cell, F = Faraday constant, T = absolute temperature).

From eq. (20), the ion intensity $I^+(S_x)$ measured after mass analysis is given by eq. (16). The measurement

$$I^+(S_x)T \sim \text{exp. } 2xEF/RT \quad (16)$$

of $I^+(S_x)$ as a function of E at constant temperature thus permits the determination of x. Between 200 and 400 °C and within large limits of E, x = 2, 6, 7, and 8 respectively were measured for S_2^+, S_6^+, S_7^+, and S_8^+. These ions are therefore parent ions. At low values of E, x = 3, 4, and 5 for S_3^+, S_4^+ and S_5^+, were obtained whereas at high values of E, x tends towards higher values for these three ionic species: at low activity of sulfur they are parent ions, afterwards fragment ions.

The ratio AlO^+/Al_2O^+ changes from about 0.5 for the vapor above Al_2O_3 to less than 0.001 for that above the system Al + Al_2O_3. AlO^+ and Al_2O^+ thus result from the ionization of different molecules, actually AlO and Al_2O[58,58a].

In the system BaO/H_2O, the ion $BaOH^+$ was observed[59]. The ion intensity $I(BaOH^+)$ is proportional to $I(H_2O^+)$ at high water pressures and proportional to its square root at low pressures corresponding to the gas phase equilibria (17).

$$BaO + H_2O \rightleftharpoons Ba(OH)_2 \quad (17)$$
$$BaO + 1/2H_2O \rightleftharpoons BaOH + 1/2\,O$$

Therefore the ion $BaOH^+$ is formed from the molecules BaOH and $Ba(OH)_2$ by electron impact. The contribution of each molecular species to the common ions could be obtained quantitatively and confirmed by the study of other equilibria involving BaO, BaOH, $Ba(OH)_2$, H_2O, H_2, and O_2.

In the system $NaF{\cdot}ZrF_4$[60] (or $LiF{\cdot}BeF_2$[61]) the ternary gaseous molecules decompose under electron impact giving mainly Na^+ and ZrF_3^+ and other fragment ions. They were identified by comparing the mass spectra for the pure components and for mixtures of different activities.

4. Pressure Determination

The density (flux/velocity) in a molecular beam issuing normally from a Knudsen cell of orifice area s[e] and crossing an electron beam, at right angles at a distance L, is given by eq. (18).

$$n_s = 2\,n_c s/3\,\pi^2 L^2 \quad (18)$$

Here n_c is the number of molecules per cm^3 in the cell.

For ions formed by electron impact, the intensity I^+ measured on the collector

$$I^+ = n_s i^- l \sigma_i \eta_i \gamma_i \quad (19)$$

[54] *L. N. Gorokhov*, Doklady Akad. Nauk SSSR *142*, 113 (1962); *P. A. Aksihin, L. N. Gorokhov*, and *L. N. Sidorov*, Vestnik Moskovskogo Univ., Ser. Math., Mechan., Astronom., Fiz. Chim. No. 6, 194 (1959).

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[60] *L. N. Sidorov* and *P. A. Akishin*, Ž. fiz. Chim. *151*, 581 (1963).

[61] *A. Büchler* and *J. L. Stauffer*, Thermodynamics, Vol. 1. Internat. Atomic Energy Agency, Vienna 1966, p. 271.

[e] It is assumed here that s is the area of a knife edge orifice or that correction has been applied for its thickness [22].

i^- is the intensity of the ionizing electrons, l their effective path, σ_i is the ionization cross section for the process considered for electrons of the energy used, η_i is the transmission of the mass spectrometer *i.e.* the ratio of number of ions formed to those collected after mass analysis, which may be a function of the mass of the ion. In many cases this mass discrimination [29] is not very important and may be assumed to be negligible or corrected for. γ_i is the gain for the ion i when collected on a secondary electron multiplier (when using a simple collector $\gamma_i = 1$).

Inserting the gas law $P = nkT$ in eq. (18) and (19) yields eq. (20).

$$I_i^+ T = P_i \cdot A \cdot \sigma_i \gamma_i = P_i S_i \tag{20}$$

S_i can be called the sensitivity and A combines all instrumental factors assumed independent of mass and nature of species.

The sensitivity factor S_i can be measured by combining the Hertz-Knudsen equation [21] for weight loss (G_i) by effusion of the species of molecular mass m_i (t = time)

$$P_i = G_i(2\pi kT/m_i)^{1/2}/st \tag{21}$$

with eq. (19), which yields

$$S_i = 44.33\ M_i^{1/2}\ (s/G_i)\ \Sigma I_i T^{1/2} \Delta t \tag{22}$$

M_i is now the molecular weight in a.m.u. of species i, S_i being obtained in the units (ion intensity × °K/atm).

This sensitivity determination is usually performed by vaporizing a weighed sample in the mass spectrometer and measuring ion intensities and temperatures over a period $\Sigma\ \Delta t$. The pressure determination by this method is very similar to the classical Knudsen method when only one species is present or predominates, or when the condensed phase decomposes congruently.

When several species are present in comparable amounts, eq. (20–22) can be written for all relevant species. It is, however, necessary in this case to know their relative ionization cross sections and multiplier gains. The same is true when the sensitivity of the instrument is determined by vaporizing a known amount of another substance (*e.g.* Ag), applying eqn. (22), and calculating other pressures by the relation(23).

$$P_i = P_{Ag}\ \frac{I_i T_i \sigma_{Ag} \gamma_{Ag}}{I_{Ag} T_{Ag} \sigma_i \gamma_i} \tag{23}$$

It is of course also possible to perform sensitivity calibrations using data on pressure dependent equilibria obtained from other sources; dissociation equilibria (*e.g.* $O_2 \rightleftharpoons 2\ O$) have been used for this purpose as well as decomposition pressures (*e.g.* $M_2O_3(s) \rightarrow 2\ M(g) + 3/2\ O_2$) or vapor pressure data; the use of known pressures at triple points (*e.g.* solid-liquid-gas for Ag or Au) is especially favorable. In electrochemical cells, the pressure can be readily derived from the galvanic current. In kinetic applications, the measurement of absolute fluxes may be more complex. However, it should in general be possible to apply relation (23) using the flux corresponding to the vapor pressure of the condensed element studied as a reference.

Multiplier yields are obtained by direct calibration. This is done by measuring the ratio of intensities received on the multiplier and on a simple collector which can be inserted in, and removed from, the ion path. Further experimental interpolation regularities can be used [62].

Ionization cross sections at the maximum of the ionization efficiency curve (σ_{max}) or their ratios have in general been taken from theoretical calculations of *Otvos* and *Stevenson* [63] for atoms; for molecules, the additivity of σ_{max} was postulated by the same authors. These ionization cross sections were calculated [63,63a] on the basis of a theoretical treatment by *Bethe*, which suggests that the ionization cross section of an atomic electron with quantum numbers (n,l) is approximately proportional to the mean square radius of the electron shell. With hydrogen-like wave functions the latter is given by

$$\bar{r}_{n,l}^{-2} = a_0^2\ n'^4 (Z - S_{nl})^{-2} - 1 + {}^3/_2 \left(1 - \left\{\frac{l(l+1) - {}^1/_3}{n'^2}\right\}\right) \tag{24}$$

n' is an effective quantum number and S_{nl} the screening constant.

Ionization cross sections at low energies σ_E are usually estimated by assuming that the cross section varies linearly up to the maximum with the excess energy above the appearance potential AP, *i.e.*

$$\sigma_E = \sigma_{max}(E - AP)/(E_{max} - AP) \tag{25}$$

When, E_{max} cannot be measured directly because of fragmentation of more complex molecules, the additional approximations are usually made that either $(E_{max} - AP)$ is approximately constant or that $E_{max} = n$AP. Eq. (25) then becomes eq. (25′).

$$\sigma_E = \sigma_{max}(E - AP)/(n-1)AP \tag{25'}$$

An alternate, classical theory has been developed by *Gryzinski* [64]. The cross section for ionization of a single electron of the jth electronic shell containing N_j electrons is there given by

$$\sigma_j = 6.56 \times 10^{-14} (N_j/U_j^2)\ g(x) \tag{26}$$

$$g(x) = X^{-1}[(X-1)/(X+1)]^{1/2}\{1 + {}^2/_3\ (1 - 1/2x) \ln [2.7 + (X-1)^{1/2}]\}$$

where $X = E/U_j$, E being the energy of the ionizing electron and U_j the ionization potential of the jth shell.

This theory justifies the postulated additivity of atomic cross sections since σ_j is proportional to N_j and deviations from the additivity caused by the dependence of σ_j on U_j^{-2}. It further gives an explicit dependence of the cross section on the energy. Cross sections,

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Table 1. Calculated and experimental ionization cross sections for atoms.

Element	$\sigma^{[63]}$ (Å²) [a]	$\sigma_j^{[65]}$ (Å²) (60eV)	$\sigma_{exp}^{[66]}$ (Å²)
H	0.33	0.76	0.67 [42]
He	0.23	0.41	0.30 [42]
Li	2.8	3.3	3.1 (50 eV) [67]
Be	2.1	2.9	3.15; 2.50
B	1.7	3.2	1.74
C	1.4	2.8	(2.07 ± 0.05)
N	1.3	2.4	1.4 [42]
O	1.1	3.2	1.6 [42]
F	0.62	2.4	
Ne	0.58	1.7	0.45 [42]
Na	4.8	3.8	4.1 (50eV) [67]
Mg	5.3	4.0	
Al	5.1	4.9	
Si	4.8	4.9	
P	4.6	4.4	
S	4.3	5.5	4.63
Cl	3.9	4.5	4.15
Ar	3.6	3.7	2.7; 3.4 [42]
K	12.9	5.6	5.9 (50eV) [67]
Ca	14.0	6.0	5.4 [65]
Sc	12.7	6.9	
Ti	12.2	7.8	13.2 ± 2.6
V	11.9	8.6	
Cr	9.3	10.9	7.8
Mn	10.0	11.8	
Fe	9.3	13.0	9.8 [65]
Co	8.7	12.9	11.4 [65]
Ni	8.1	14.3	9.6 [65]
Cu	6.1	12.9	5.3 [65]
Zn	5.3	7.9	5.03 ± 0.45
Ga	6.0	7.3	
Ge	6.1	5.8	
As	6.2	5.0	
Se	6.1	6.0	7.18
Br	6.0	5.3	
Kr	5.8	4.7	4.8 [42]
Rb	19.4	6.5	6.8 (50eV) [67]
Sr	21.4	7.0	6.0 [65]
Y	19.8	6.0	
Zr	19.9	8.8	
Nb	19.2	11.6	
Mo	17.5		
Tc	16.0		
Ru	14.7		
Rh	13.5		
Pd	8.4		
Ag	11.6	11.4	10.1 [65]
Cd	7.3		8.54 ± 0.33
In	8.3		
Sn	8.6	7.9	20.9
Sb	8.7		
Te	8.5		10.46
Xe	8.0	6.0	5.0; 7.3 [42]
Cs	24.4	8.4	8.8 (50eV) [67]
			5.3 (50eV) [68]
Ba	26.0		8.7 [65]
Au		12.4	11.6
Hg	9.10	9.8	5.4; 6.8 [42]
Tl	10.0		6.0 [65]
Pb	10.4		
U	18.5		16.6 [71]

[a] The original relative values were divided by 3 and expressed in Å² [66].

calculated by either approach [63,65], and experimental values [43,66,67] are compared in Table 1. Except for the alkali metals, the two methods of calculation lead to values in essential agreement with each other and with experimental results.

For solids AB vaporizing simultaneously to gaseous AB and $(AB)_2$, ratios of cross sections can be obtained [25,54,55] by the use of double oven type Knudsen cells in which $(AB)_2$ is thermally dissociated. One obtains the equation,

$$\sigma_{(AB)_2}/\sigma_{AB} = \frac{\sqrt{2}\,(I'_{(AB)_2}\sqrt{T'} - I_{(AB)_2}\sqrt{T})}{(I_{AB}\sqrt{T} - I'_{AB}\sqrt{T'})} \qquad (27)$$

I' and I represent intensities measured at temperatures of the upper cell T' and T respectively, the temperature in the lower cell remaining constant. The subscripts 1 and 2 refer to monomer and dimer respectively.

For stoichiometric solids AB vaporizing according to

$$AB(s) \rightarrow A(g) + \left(\frac{1-x}{2}\right) B_2 + xB(g) \qquad (28)$$

eq. (28), relative cross sections σ_A/σ_B and σ_A/σ_{B2} can be obtained [69] simultaneously from the relation (29)

$$\frac{I_A}{I_{B_2}} = \left[\frac{M_A}{M_B}\right]^{1/2} \frac{I_B}{I_{B_2}} \frac{\sigma_A}{\sigma_B} + 2\left[\frac{M_A}{M_{B_2}}\right]^{1/2} \frac{\sigma_A}{\sigma_{B_2}} \qquad (29)$$

if x varies sufficiently with temperature. If not, double oven type cells can be used to promote the thermal dissociation of B_2. Similar equations can be established

Table 2. Experimental ratios for ionization cross sections [66].

Molecules	$\sigma_i(1)/\sigma_i(2)$	Molecules	$\sigma_i(1)/\sigma_i(2)$	Ref.
H_2/H	1.44	$(RbCl)_2/RbCl$	1.43	
N_2/N	1.93	$(KReO_4)_2/KReO_4$	0.68	[73]
O_2/O	1.80	S_2/In_2S	1.0	
S_2/S	1.44	$NaF/ZrF_4/NaZrF_5$	1/1.8/2.5	
Se_2/Se	1.64	$Zn/BS_2/B_2S_2/B_2S_3$	1/1.5/2.0/2.0	
	0.59 [72]			
Te_2/Te	1.68	Li/Li_2O	1.6	
$(LiCl)_2/LiCl$	1.15; 0.83	$S_2/S_6/S_7/S_8$	1.0/1.4/1.7/1.0 (14eV)	[26b]
$(LiBr)_2/LiBr$	1.42; 1.84	YO/Y	0.68	[74]
$(LiI)_2/LiI$	1.04	LaO/La	0.60	
$(NaF)_2/NaF$	1.24			
$(NaCl)_2/NaCl$	1.58	UO_2/UO	0.82	[75]
$(NaI)_2NaI$	0.86			
$(KF)_2/KF$	1.27	US/U	1.16	[71]
$(KCl)_2/KCl$	1.57	$Te_2/SiTe$	1.4	[76]
$(KI)_2/KI$	1.66			

for well defined stoichiometric decompositions other than (28). Such studies [25,55,69,70] have shown that the ionization cross section of homonuclear diatomic molecules and of dimeric heteronuclear molecules is about 1.5 times that of the monomer (Table 2) rather

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than ≈ 2 as implied by the additivity rule. For simple heteronuclear molecules the latter rule leads to a fair approximation in most cases. For more complex molecules the additivity rule may overestimate the ionization cross section by up to a factor of two. However high these uncertainties may seem, it may be emphasized that, in calculating thermochemical data, they lead to inaccuracies which are not larger than those introduced by other parameters (see below).

The assumption has hitherto been made that ionization cross sections are temperature independent. In the absence of low lying excited states, this assumption is justified for atoms and probably for simple molecules with high vibrational frequencies, since the Boltzmann distribution then results in relatively little variation of the population of different vibrational levels. For polyatomic molecules with low vibrational frequencies, transition probalities and fragmentation pattern may change with temperature.

In discussing the accuracy of pressure determinations, three cases can be distinguished: that of a largely predominating component, that of a minor component and that of components of comparable importance.

1) The first case is equivalent to a conventional Knudsen experiment monitored by the spectrometer and the evaluation of the pressures becomes independent of cross sections and multiplier yields when eq. (20)–(22) are applied. Accuracy and reproducibility are then the same as in the conventional experiment and pressures can be measured with an accuracy of 5 to 20%. There are, however, a number of advantages in the mass spectrometric method: high speed, minor components can be detected, and, if necessary, corrections can be applied. Perturbations, such as creeping or interboundary migration of the condensed phase, chemical reactions with the container or residual gases, impurities, alloy formations, phase transitions, and disproportionation reactions are readily observed. The evolution of a non-stoichiometric compound to its congruently vaporizing composition and the modification of the latter with temperature can be followed.

2) The pressure of a minor component as obtained from relation (23) depends usually on an estimate of $\sigma\gamma$ ratios which can be made within a factor of 1.5 to 3, depending on the availability of data on analogous molecules with which comparisons can be made. Although this uncertainty may seem high, it must be realized that in many cases such species cannot be identified by other methods.

3) For components of comparable importance, the uncertainty in pressure data may approach one or the other of the above cases, depending on the possibility of performing $\sigma\gamma$ measurements by changing the composition of the vapor by modifications in the thermodynamic conditions.

5. Calculation of Thermochemical and Kinetic Quantities

Apart from the identification of molecular species and the measurement of their relative concentrations, great interest lies in the calculation of their free energies, enthalpies, and entropies of formation. In kinetic studies, one wishes to obtain reaction orders and activation energies from which reaction mechanisms are to be deduced.

Reaction enthalpies, ΔH_T^0, at temperature T can be obtained by the second law of thermodynamics (Clausius-Clapeyron or van't Hoff equation):

$$\Delta H_T^0 = -R \, \mathrm{d} \ln K_p / \mathrm{d}(1/T) \qquad (30)$$

$K_p = \pi P_i^{n_i}$ is the equilibrium constant of the reaction; n_i are the stoichiometric coefficients and R is the gas constant.

In kinetic studies, (30) (with k = rate constant instead of K_p) is the Arrhenius equation.

The advantage of relation (30) lies in the fact that only temperatures and variations of equilibrium constants are needed. It is assumed to a first approximation that ΔH_T^0 is constant in the temperature range in question, or that its variation with temperature has been calculated as described in standard textbooks of thermodynamics. In mass spectrometric measurements, combination of eq. (20) and eq. (30) gives the relationship (31) provided that the ionization cross sections σ_i are temperature independent.

$$\Delta H_T^0 = -R \, \mathrm{d} \ln \pi (I_i^+ T)^{n_i} / \mathrm{d}(1/T) \qquad (31)$$

An alternative method consists in the use of the third law of thermodynamics, which requires a knowledge of the absolute value of K_p

$$\begin{aligned} \Delta H_T^0 &= \Delta G_T^0 + T\Delta S_T^0 \\ \Delta H_0^0 &= \Delta G_T^0 + T\Delta S_T^0 - \Delta(H_T^0 - H_0^0) \\ &= \Delta G_T^0 - T\Delta \left(\frac{G_T^0 - H_0^0}{T} \right) \end{aligned} \qquad (32)$$

$\Delta G_T^0 = -RT \ln K_p$; the superscript ^{0} indicates that the magnitude is taken in the standard state and subscript 0 or T indicates the temperature.

In this method entropies or free energy functions $(G_T^0 - H_0^0)/T$ are calculated from specific heat data or, for gaseous molecules, from molecular parameters discussed below by the use of statistical mechanical relations [77].

If measured thermodynamic data and molecular parameters are not available, satisfactory estimates of specific heat and standard entropy can be made in many cases for condensed phases [77]. For gaseous molecules interatomic distances can be estimated from atomic radii derived from crystallographic data [78]. Vibration frequencies can be estimated by comparison with isoelectronic molecules, or from vibration frequencies of other molecules containing the same group [79].

Correlations have been made between vibration frequencies, interatomic distancies, and dissociation energies [79,80]. Probable structures for tri- and polyatomic molecules can be

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found by comparison with known molecules of similar type or from rules such as those relating total number of valence electrons and structure [81]. For molecules with low numbers of valence electrons, the electronic ground state can be predicted and the approximate position of low lying excited states estimated [79]. For molecules formed from atoms with large numbers of electrons; especially transition metals, quantum mechanical calculations become necessary [82]. For polyatomic molecules, where experimental data are largely missing, simplified approximations have also been proposed [83,84].

With accurate spectroscopic or calorimetric data, the uncertainties in free energy functions are ±0.1 to 0.5 and 0.5 to 1.0 clausius^{-1} for a gaseous and a condensed phase respectively. With estimated data these uncertainties are rated to increase in simple cases to about 2–3 clausius. It may be pointed out that, in many cases, variations of the estimated free energy function with temperature will be closer to the real ones than the absolute values.

Assuming the different uncertainties independent of one another, the relative uncertainty in third law calculations can be written as follows:

$$\delta\Delta H/\Delta H = [(RT\delta \ln K_p/\Delta H)^2 + (T\delta\Delta S/\Delta H)^2 + (\delta/T/T)^2]^{1/2}$$

or (33)

$$\delta\Delta H/\Delta H = \{[\delta(\Delta S - R\ln K_p)/(\Delta S - R\ln K_p)]^2 + (\delta T/T)^2\}^{1/2}$$

where the symbol δ designates both fortuitous errors and possible systematic errors, the latter being treated as accidental.

In second law calculations the relative uncertainty is:

$$\delta\Delta H/\Delta H = [(\delta\Delta \ln K_p/\Delta \ln K_p)^2 + (\delta T_1/T_1)^2 + (\delta T_2/T_2)^2 + (\delta\Delta T/\Delta T)^2]^{1/2} \quad (34)$$

When ΔH is large, usually only a relatively small temperature interval ΔT is accessible to measurement and the dominant contribution to the uncertainty comes from the last terms in (34) which are of the order of $\sqrt{2}\delta T/\Delta T$. In the third law (eq. 33) the corresponding uncertainty $\delta T/T$ is much smaller. For low values of ΔH, the importance of the temperature uncertainty decreases and second law measurements may lead to quite accurate results, provided $\Delta \ln K_p$ is measured with sufficient accuracy. In that case ΔH^0_T can be inserted in eq. (32) to obtain entropy values. In third law calculations, the first two terms which represent an absolute, not a relative error in eq. (32) are always present; they are therefore more important in the case of low ΔH values. However, low ΔH values are usually differences between the high values of bond dissociation energies and the uncertainty should be considered relative to these large values rather than compared with the small ΔH values which are measured.

If satisfactory free energy functions are available, third law calculations will lead to a relative error of about 1% (temperature component) to which an absolute error of about 1 to 5 kcal must be added. An advantage of the third law method is that it gives for all points a ΔH value at a single reference temperature, usually 0 or 298 °K. The method thus facilitates consistency analysis of individual points of a given series as well as different series from the same or different laboratories. Further, the third law is the only method that can be applied when observations on a given species are possible only within a narrow temperature range; such restrictions apply often in mass spectrometric measurements. In the second law, the relative error will be 2 to 5% if a sufficiently large pressure and temperature range can be covered; the uncertainty can, however, increase drastically if this is not the case.

The question "should one apply the second- or third-law approach" is often raised. Undoubtedly one should use both. Naturally each case should be judged according to the discussion sketched above in order to determine what weight to give to one or the other.

6. Results [17, 18]

As mentioned in the introduction, the first result [1, 2] of the application of mass spectrometry to high temperature chemistry was the determination of the heat of vaporization of monoatomic carbon from graphite. Simultaneously these investigations led to the spectacular discovery that at the temperature studied (about 2500 °K) the main components of carbon vapor, in order of decreasing importance, are C_3, C, and C_2; C_4, and C_5 are minor components. Polyatomic species were also discovered in the vapor of other group 4 elements and their mixtures or compounds. Thus polyatomic molecules and their thermodynamic properties are now known for the elements of the 4th, 5th, and 6th group of the periodic table (Table 3) [f].

Table 3. Atomization energies of polyatomic molecules (kcal/mole).

Element	C [51]	Si [3]	Ge [3]	Sn [3]	S[26b, 57]	Se [72]	P [85, 86]	As [86]	Sb [85, 86]	Bi [87]
M_3	320.8±25	173±10	153±10	120±10	164±2.0	124 (850 °K)	—	—	—	88±4
M_4	439.5±6	275±10	240±10	220±10	230±2.5	—	286.0±2.0	251±3	202±3	142±4
M_5	610±6	—	—	—	300±3.2	229 (500 °K)	—	—	—	—
M_6	—	—	—	—	371±3.7	286 (475 °K)	—	—	—	—
M_7	—	—	—	—	434±4.2	336 (500 °K)	—	—	—	—
M_8	—	—	—	—	501±4.6	386 (500 °K)	—	—	—	—

A number of homonuclear diatomic molecules (Table 4), and intermetallic molecules (Table 5), knowledge of which was scanty or non-existent, have

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Table 4. Dissociation Energies D_0^0 of homonuclear diatomic molecules (kcal/mole) [88,89].

H_2																
Li_2 25.0 ± 1.2	Be_2 (14)											B_2 65.5 ± 5.5	C_2 142.3 ± 3.4	N_2 225.1 ± 0.5	O_2 117.96 ± 0.04	F_2 36.8
Na_2 17.3 ± 0.7	Mg_2 (7)											Al_2 46 ± 5	Si_2 74 ± 5	P_2 116.0	S_2 101.0 ± 1.0	Cl_2 57.4
K_2 11.8 ● 1.2	Ca_2 (5)	Sc_2 38.0 ± 5	Ti_2 58	V	[90,91] Cr_2 36 ± 7	Mn_2 18	Fe	Co_2 39 ±6	Ni_2 54.5 ± 5	Cu_2 45.5 ± 2.2	Zn_2 (6)	Ga_2 32 ± 5	Ge_2 64 ± 5	As_2 90.8	Se_2 72.94 ± 0.05	Br_2 45.5
Rb_2 10.8 ± 1.2	Sr	Y_2 37.3 ± 5	Zr	Nb	Mo	Tc	Ru	Rh	Pd_2 ⩽33	Ag_2 37.6 ± 2.2	Cd_2 2.1 ± 0.5	In_2 19.5 ± 2.5	Sn_2 45.8 ± 4	Sb_2 70.6 ± 1.5	Te_2 55 ±2	I_2 35.6
Cs_2 10.4 ± 1.0	Ba	La_2 57.6 ± 5	Hf	Ta	W	Re	Os	Ir	Pt	Au_2 51.5 ± 2.2	Hg_2 1.4 ± 0.07	Tl_2 (14)	Pb_2 23 ± 5	Bi_2 47.0 ±2.0 [87]	Po	At

Table 5. Dissociation energies of intermetallic molecules [88].

Molecule	D_0^0 (kcal/mole)	Molecule	D_0^0 (kcal/mole)
NaK	14.3± 0.7	AgSn	31.6± 5
NaRb	13.1± 1.5	AuSi	81
KHg	1.08± 0.05	AuSn	57.5± 4
CsHg	1.10± 0.05	AuPb	30
CuAg	40.7± 2.2	AuCr	50.4± 3.5
CuAu	54.5± 2.2	AuPd	33.3± 5
AgAu	47.6± 2.2	CdIn	32
AuBe	73	ZnIn	7.7
AuMg	61	HgTl	0.7
AuCa	57	BSi	68 ± 6
AuSr	88	InSb	35.4± 2.5
AuBa	66	YLa	47.3± 5
AuAl	70	GeSi	71 ± 5
AuGa	46	GeNi	66.4± 4 [91]
CuSn	41.4± 4	PbBi	31 ± 5

been studied. Their dissociation energies lie in the range of 30 to 60 kcal/mole; nevertheless, their concentration is always low. This can be readily understood in the light of the vaporization processes of an element [92]:

$$M_{sol.\ or\ liq.} \rightarrow M_{gas} \quad (35)$$

$$2\ M_{sol.\ or\ liq.} \rightarrow M_{2\ gas} \quad (36)$$

The corresponding free energy changes can be written as

$$\Delta G_{T,1} = -RT \ln P(M) = \Delta H_{T,1} - T\Delta S_{T,1}$$

$$\Delta G_{T,2} = -RT \ln P(M_2) = \Delta H_{T,2} - T\Delta S_{T,2} \quad (37)$$

and

$$\Delta G_{T,1-2} = \Delta G_{T,1} - \Delta G_{T,2} = -RT \ln P(M)/P(M_2) =$$
$$(\Delta H_{T,1} - \Delta H_{T,2}) - T\Delta S_{T,1-2} = D_T(M_2) - \Delta H_{T,1} - T\Delta S_{T,1-2} \quad (38)$$

The subscripts 1 and 2 refer to the process corresponding to the monoatomic and diatomic species. $D_T(M_2)$ is the dissociation energy of M_2.

Equation (38) is the description of this system corresponding to the pressure independent reaction

$$M_{2,g} \rightarrow M_s + M_g \quad (39)$$

in which the temperature alone determines all partial pressures. This is in contrast to the more usual homogeneous system

$$M_{2,g} \rightleftarrows 2\ M_g \quad (40)$$

in which at a given temperature the partial pressures are only determined, when the total pressure is fixed.

Eq. (38) and (39) have two characteristic parameters:

a) ΔS is negative and small; for homonuclear diatomic molecules about −10 e.u. (in the range of 1000 to 2000 °K).

b) The enthalpy term may be positive or negative. In the former instance $P(M_2) > P(M_1)$; this is the case for the "classical", "low temperature" molecules of the elements of the right hand side of the periodic table. In the latter instance $P(M_2) < P(M_1)$ but $P(M_2)/P(M_1)$ increases with temperature: it is therefore appropriate to call them "high temperature molecules" in the present context [92c].

Eq. (38) can also be used to define "high temperatures" [92b]

$$T = (\Delta H_{T,1} - \Delta H_{T,2})/\{\Delta S_{T,1-2} - R \ln P(M_1)/P(M_2)\} \quad (41)$$

The definition (41) thus depends not only on the properties (ΔH and ΔS) of the system but also on the sensitivity limit of the analytical device. For the mass

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Table 6. Dissociation energies of gaseous monoxides (kcal/mole).

Li 77 ± 5 [95]	Be 106 ± 3 [95]	H 101.30 [89]										B 191.0 ± 3.5 [96]	C 256.16 [89]	N 150.1 ± 1.0 [89]	O 117.96 ± 0.04 [89]	F 36.4 ± 1 [89]
Na 71 ± 5 [95]	Mg 86 ± 5 [97]											Al 115 ± 5 [95]	Si 190.4 ± 1.5 [95]	P 143 H10 [89]	S 123.5 ± 0.3 [89]	Cl 36.2 ± 0.1 [89]
K 70 ± 5 [95]	Ca 93 ± 5 [97]	Sc 160.5 ± 2.0 [75]	Ti 158 ± 5 [95]	V 147.5 ± 2.5 [75]	Cr 101 ± 7 [98]	Mn 84 ± 5 [99]	Fe 91 ± 5 [99]	Co 86.5 ± 5 [100]	Ni 86 ± 5 [101]	Cu 60 ± 5 [99]	Zn	Ga 90.2 ± 3.5 [58a]	Ge 156.4 ± 1.5 [56]	As 114.1 [89]	Se 100 ± 3 [102]	Br 55.3 [89]
Rb	Sr 102 ± 5 [97]	Y 170.4 ± 2.5 [75]	Zr 181 ± 5 [95]	Nb 180 ± 2.5 [103]	Mo 116 ± 15 [104]	Tc	Ru	Rh 100 ± 10 [105]	Pd 67 ± 5 [105]	Ag	Cd	In 76 [106]	Sn 126.5 ± 2.0 [107]	Sb 74 ± 9 [89]	Te 90 ± 3 [102]	I
Cs	Ba 131.8 ± 1 [108]	La 190.3 ± 2.5 [75]	Hf 183 ± 6 [109]	Ta 194 ± 10 [110]	W 155 ± 10 [95]	Re	Os	Ir 84 ± 5 [111]	Pt	Au	Hg	Tl	Pb 88.4 ± 1.4 [112]	Bi 92 ± 23 [113]	Po	At
Fr	Ra	Ac	Th 198 ± 5 [114]	Pa	U 181.2 ± 3.2 [75]	Np 172 ± 5 [114]	Pu 172 ± 5 [114]	Am	Cm							
		Ce 188.6 ± 3.5 [75]	Pr 180.8 [115, 116]	Nd 171.1	Pm	Sm 141.6	Eu 132.8	Gd 172.5	Tb 173.7	Dy 150.8	Ho 150.8	Er 151.9	Tm 137.8	Yb 91.0	Lu 166.3	

spectrometer this limit is about $1:10^5$; for the molecules mentioned above, with $\Delta H \geqslant 30$–60 kcal, "high temperatures" therefore lie at 1000 to 2000 °K and higher.

Eq. (35–38) can be easily generalized[93] for polyatomic homonuclear molecules and di- and polyatomic heteronuclear molecules. In such cases alternative processes to (35) and (36) take place, *e.g.*

$$1/2\ AB(s,l) \rightarrow 1/2\ A(g) + 1/2\ B(g) \quad (42)$$

$$AB(s,l) \rightarrow AB(g) \quad (43)$$

Instead of eq. (38), other pressure independent free energy equations are obtained. In each case the possibility of observing a molecule AB is favored by a high value of the dissociation energy, but the enthalpy term is descreased by the enthalpy corresponding to the atomization of condensed AB (eq. 41), possibly by that of dissociation of B_2 and/or vaporization of A. For the entropy term similar values are expected as for (37). It thus appears that, in addition to the entropy, the importance of which has been stressed in a number of recent papers[94], the value of the enthalpy difference in an equation corresponding to (38) determines the possibility of observing molecular species.

The existence and the dissociation energy of nearly all gaseous monoxides have now been established (Table 6). Of interest is the trend in the dissociation

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Table 7. Atomization energies of gaseous suboxides [a].

Molecule	Atomization Energy (kcal/mol)	Reference
H_2O	219.3 ± 0.5	[89]
N_2O	263.6 ± 0.5	[89]
F_2O	101.5 ± 0.5	[89]
Cl_2O	96.6 ± 0.5	[89]
S_2O	210 ± 15	[118]
Li_2O	175 ± 7	[95]
Be_2O	230 ± 10	[119]
Sr_2O	194 ± 6	[97]
Ba_2O	224 ± 17	[120]
Al_2O	245 ± 7	[58]
Ga_2O	210 ± 4	[121]
In_2O	178 ± 4	[106]
Sc_2O	245 ± 11	[122]
Y_2O	258 ± 8	[122]
La_2O	266 ± 8	[122]

[a] Corresponding to the reaction $M_2O(g) \rightarrow 2\,M(g) + O(g)$.

Table 9. Atomization energies of gaseous trioxides.

Molecule	$MO_3(g) \rightarrow M(g) + 3O(g)$ Atomization Energy (kcal/mole)	Ref.
SO_3	336	[89]
ClO_3	168	[89]
CrO_3	341 ± 20	[98]
MoO_3	415 ± 10	[104]
WO_3	443 ± 10	[104]
UO_3	514 ± 9	[75]
ReO_3	445 ± 10	[125]
IrO_3	322 ± 10	[111]

oxides such as B_2O_3 [126], Mo_2O_5, Mo_3O_8 [127], V_2O_4, V_4O_8, V_4O_{10}, V_6O_{12}, V_6O_{14} [128], Re_2O_7 [125] have been characterized. They emphasize the frequent occurence of several valencies and differing degrees of association in gaseous compounds.

Table 8. Atomization energies of gaseous dioxides [123] (kcal/mole).

$MO_2(g) \rightarrow M(g) + 2O(g)$

Spectroscopic data [124] indicate that TaO_2 is non-linear in the ground state and hence that Walsh's rule [81] is also applicable to d electrons. According to this rule, molecules with 16 and less or 21 or more electrons are linear, the others non-linear. The atomization energies based on third law calculations given by [123] have therefore been reduced by 6 kcal/mole for the V, Cr, Mn, and Fe groups.

H: 163.6 ± 1 [97]												B 322 ± 10 [95]	C 381.9 ± 0.5	N 221.9 ± 0.1	O 142.2 ± 0.5	F 101.5 ± 0.5
Li	Be															
Na 158 ± 10	Mg											Al	Si 298 ± 10	P 270 ± 25	S 254.4 ± 0.5	Cl 121.6 ± 0.5
K	Ca	Sc	Ti 313 ± 5	V 290 ± 10	Cr 221 ± 15 [98]	Mn 220 ± 25	Fe	Co	Ni	Cu	Zn	Ga	Ge	As	Se 201 ± 5	Br
Rb	Sr	Y	Zr 345	Nb 341 ± 5 [104]	Mo 270 ± 10 [126]	Tc 255 ± 15	Ru 225 ± 15	Rh 204 ± 5 [105]	Pd	Ag	Cd	In	Sn	Sb	Te 215 ± 7	I
Cs	Ba	La	Hf 360 ± 20	Ta 343 ± 15	W 296 ± 7 [126]	Re	Os 255 ± 20	Ir 219 ± 10 [111]	Pt 211 ± 5	Au	Hg	Tl	Pb	Bi	Po	At
Fr	Ra	Ac	Th 388 ± 5 [114]	Pa 360 ± 20	U 352 ± 4 [75]	Np 325 ± 10 [114]	Pu 309 ± 10 [114]	Am	Cm							

energies of the monoxides of the first transition series, which shows a doubly humped curve with a minimum when the d shell is half filled. An analogous curve is found for the rare earth oxides. In both cases the trend in dissociation energy of the oxide and the heat of sublimation of the metal show a striking similarity. This also applies to bonding energies in solid carbides, silicides, nitrides, and oxides and to force constants of halides [93, 117]. Besides the monoxides, suboxides (Table 7), dioxides (Table 8), trioxides (Table 9) and

Several binary oxides yield appreciable amounts of gaseous dimers and polymers. Polymerization energies (Table 10) per added monomer approach the heat of sublimation of the latter.

The equilibrium mode of evaporation of oxides is consequently strongly dependent on differences in

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Table 10. Polymerization energies of gaseous oxides.

Molecule	$(MO_x)_y(g) \rightarrow yMO_x$ Polymerization Energy (kcal/mole)	Ref.
$(LiO)_2$	92±8	[129]
$(BeO)_2$	159±10	[130]
$(BeO)_3$	336±10	
$(BeO)_4$	485±15	
$(BeO)_5$	635±15	
$(BeO)_6$	791±20	
$(BaO)_2$	89±11	[120]
$(BO)_2$	110±10	[126,96]
$(AlO)_2$	135±5	[58]
$(YO)_2$	108±11	[122]
$(LaO)_2$	86±10	[122]
$(SiO)_2$	53±10	[131]
$(GeO)_2$	45±3	[56]
$(GeO)_3$	89±5	
$(SnO)_2$	67±4	[107]
$(SnO)_3$	137±5	
$(SnO)_4$	208±5	
$(PbO)_2$	63±5	[112]
$(PbO)_3$	126±6	
$(PbO)_4$	202±10	
$(PbO)_5$	253±20	[112]
$(PbO)_6$	320±30	
$(MoO_3)_2$	110±10	[132,133]
$(MoO_3)_3$	215±15	
$(MoO_3)_4$	298±20	[132,134,135]
$(MoO_3)_5$	384±20	[134]
$(WO_3)_2$	115±20	[133,135,104]
$(WO_3)_3$	226±20	
$(WO_3)_4$	306±30	

stability of the lattice and of the numerous possible gaseous molecules [17,93].

In general the stability of sulfides, selenides, and tellurides is lower than that of oxides; therefore the mode of vaporization is simpler. In most cases the gas phase contains a high proportion of dissociation products. The gaseous molecules which have been observed are limited to the monochalcogenides or their polymers, and a few dichalcogenides. The trends are parallel for oxides, sulfides, selenides and tellurides with a marked decrease in dissociation energy in this sequence [90,93]. However, an exception is boron sulfide which gives highly polymeric and complex gaseous molecules [136].

Carbides vaporize mainly by decomposition. In a number of cases, MC_2 and also MC_4 [137] molecules have been observed as minor components. Parallel trends in dissociation energies M–C_2 and M–O have been observed [138,139]; the analogy between C_2 and O has been pointed out [138].

Borides, silicides, nitrides, phosphides [17,86] *etc.* decompose upon vaporization [140]. Halides, hydroxides, and cyanides usually give gaseous products, which contain the same units as the lattice, or polymers [139]. In several instances dimers and trimers are the major products.

Ternary halide molecules of the type LiCl·NaCl, LiF·AlF_3, and others, behave similarly.

The study of mixtures or compounds formed from two binary compounds confirms and extends the types of gaseous ternary compounds known by classical methods; ternary halides and oxyhalides may also be mentioned in this context. Metaborates [141] and perrhenates [73] yield gaseous monomers and dimers; molybdates and tungstates [142] yield monomers; the corresponding acids [127,143] have been studied.

Systematic studies of whole groups of ternary compounds are lacking. It may, however, be pointed out that the thermochemical relations [93] for binary compounds AB (eq. 42, 43) enable one to rationalize the present observations when A and B are considered to represent binary molecules constituting the ternary compound.

In kinetic applications, rates of evaporation and vaporization and condensation coefficients have been obtained for a number of elements and compounds [16, 58a,144].

The investigation of the reaction between oxygen and molybdenum [16], tungsten [16], and tantalum [16], as well as of those of halogens with nickel [16] and yttrium [16] has made it possible to identify the gaseous species formed and the influence of time, temperature, and flux of impinging gaseous molecules on their rate of formation. Data on residence time and angular distribution of reflected molecules or reaction products have been obtained by molecular beam techniques combined with mass spectrometric detection for some of these and other reactions [16].

7. Outlook

Present gaps in the knowledge of certain types of molecules, *e.g.* the homonuclear diatomic molecules of most transition and rare earth elements can, presumably, be reduced by extending the sensitivity of the

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method and its ability to cope with higher temperatures and pressures [20].

In the condensed phase, thermodynamic data have been obtained mainly for stoichiometric compounds. The present techniques readily permit one to study phase diagrams and thermodynamic properties as functions of composition of non-stoichiometric compounds [75, 145, 146]. Likewise, other aspects of heterogeneous reactions and of the mechanism and kinetics of vaporization, *e.g.* in electrochemical cells, can be studied.

Problems of electronic and molecular structure of gaseous molecules can not be solved directly by mass spectrometric techniques. The use of this technique for detecting and identifying species in magnetic and electric molecular beam experiments has, however, already given interesting results [147]. The simultaneous study of gaseous phases by mass spectrometry and by optical spectroscopy, including microwave and matrix techniques [148], are also promising developments, as is the molecular structure determination by electron diffraction [149].

Many problems and systems mentioned here are regularly covered and discussed in review articles [150].

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Aromatic Fluorine as a Chemical Label for Detecting Reaction Mechanism[**]

BY H. SUSCHITZKY [*]

BASED ON WORK CARRIED OUT WITH I. K. BARBEN, M. BELLAS, P. MILES, AND R. K. SMALLEY

This article explains how nucleophilically activated fluorine can be used for the detection of ion-pair formation during the decomposition of various aryl radical generators. Thus a concurrent dual mechanism for the breakdown of certain aryl radical sources can be experimentally demonstrated by fluorine labeling. The bearing of this information on the mechanism of diazo coupling is also discussed.

In addition, labeling with aromatic fluorine is applied to the thermolysis of aryl azides, the aminolysis of 3-aryl-4-bromosydnones, and the hydrolysis of 3-arylsydnone imines. Finally some mechanistic problems are posed which may possibly be solved by this labeling technique.

I. Principle of the Method

Nucleophilic replacement of suitably activated fluorine in an aromatic structure usually occurs more readily than that of any other group or atom [1]. Foremost in this activating tendency is undoubtedly the diazonium ion $-N_2^{\oplus}$, which can render aromatic fluorine (and to a lesser extent other halogens or a nitro group) so labile that the latter can be lost inadvertently during a synthesis by being displaced in the presence of even a weak nucleophilic reagent. *Bunnett* and *Zahler* [2] have called this annoying property of a diazonium group the "nuisance effect" and the aptness of the metaphor will be appreciated by anyone who has experienced this phenomenon. An instance of such an unwanted

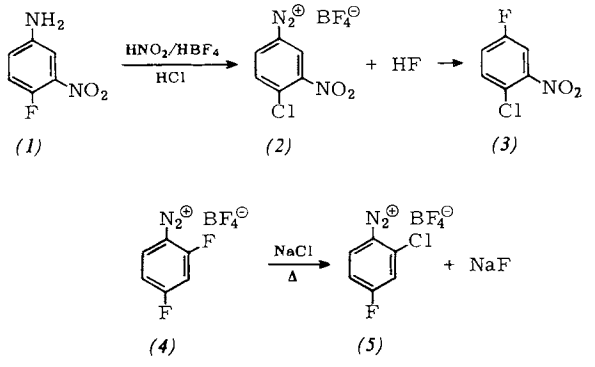
[*] Dr. H. Suschitzky
Department of Chemistry and Applied Chemistry,
University of Salford, Salford 5,
Lancashire (England)

[**] Extended version of a lecture presented at the 3rd International Fluorine Symposium, Munich, September 1965.

[1] *J. F. Bunnett*, Quart. Rev. *12*, 1 (1958).

[2] *J. F. Bunnett* and *R. E. Zahler*, Chem. Revs. *49*, 273 (1951).

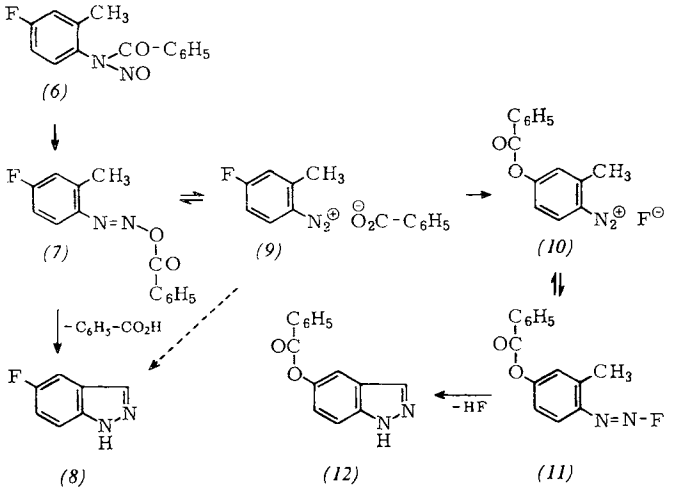
fluorine displacement is the loss of the fluorine atom from 4-fluoro-3-nitroaniline *(1)* which occurs during diazotization in hydrochloric acid [3] to give unexpectedly the chloro compound *(3) via* the intermediate *(2)*. Another example is the formation of the chlorodiazonium salt *(5)* when the dry 2,4-difluorobenzenediazonium fluoroborate *(4)* is heated to its melting point (which lies below its decomposition temperature) in the presence of sodium chloride [4]. Even a hydrochloric acid solution of diazotized *o*- or *p*-fluoroaniline will eventually give a positive test for fluoride ions indicating fluorine-chlorine exchange [3]. Examples of the effect of a diazonium ion on the ease of replacement of other groups, are also well known [5].



In the above reactions *(1)* → *(3)* and *(4)* → *(5)*, aromatic fluorine has in a sense acted as a chemical label since it records the presence of the diazonium ion by appearing as easily detectable ionic fluorine (HF) in the reaction mixture. This information is obviously superflous in the cases mentioned. However, a situation could be envisaged in which the intermediacy of a diazonium ion, or any other group that causes aromatic fluorine to be anionically labile, is only postulated or even unsuspected. Under these circumstances the conversion of covalent (aromatic) into ionic fluorine would clearly be of value in diagnosing the mechanism involved. Some of the results, which we obtained from experiments in which aromatic fluorine was used as a "chemical marker", are discussed in the subsequent sections. It is hoped that other workers will be stimulated to apply this simple and novel method to suitable problems.

II. Mechanism of Indazole Formation

The idea of probing into the mechanism of a reaction by fluorine labeling suggested itself to us in the course of making 5-fluoroindazole by Jacobson's method [6, 7], which entails the spontaneous decomposition of the *N*-nitrosobenz-*o*-toluide *(6)* in benzene [see Scheme 1].



Scheme 1. The preparation of 5-fluoroindazole.

The expected 5-fluoroindazole *(8)* was obtained together with an approximately equal quantity of a fluorine-free substance which proved to be 5-benzoyloxyindazole *(12)*. Fluoride ions were detected [*] in the reaction mixture [8]. Halogen replacement did not occur with the *meta* isomer (F *meta* to $N(NO)COC_6H_5$ in *(6)*) and the behavior of fluorine in the *ortho* position was not tested as the required nitroso compound could not be prepared.

Huisgen and *Nakaten* [9] have shown that the Jacobson indazole synthesis involves a rate-determining rearrangement of the nitroso compound to a diazoester (*e.g. (6)* → *(7)*) before cyclization. In this context the ready replacement of the fluorine in the *para* position is rationally explained if the covalent diazoester *(7)* dissociates into the ion pair *(9)*. Fluorine replacement by the anion $C_6H_5CO_2^{\ominus}$ is then strongly facilitated because the charged diazonium group $-N_2^{\oplus}$ activates the fluorine towards nucleophilic attack. Thereby a new ion pair *(10)* is formed in which the previously covalent fluorine has taken on the role of anionic partner. Aromatic, covalent fluorine has been changed into a fluoride ion and thus has functioned as a sensitive chemical label since it has revealed the unsuspected and transient formation of a diazonium ion pair during indazole cyclization in benzene. Moreover, fluorine is found to be specific in providing this mechanistic information since the chloro or bromo analogue of *(6)*, F = Cl or Br, yields exclusively the corresponding halogenoindazoles *(8)*, F = Cl or Br.

The existence of ion pairs raises the obvious question whether it is the covalent *trans*-diazoester, *e.g. (7)*, as previously postulated [9], or the diazonium ion pair, *e.g. (9)*, which is involved in the ring closure to give the indazole. *De Tar* [10] has investigated the cyclization

[3] *H. Suschitzky*, unreported result.

[4] *G. C. Finger* and *R. E. Oesterling*, J. Amer. chem. Soc. *78*, 2593 (1956).

[5] *H. Suschitzky* in: Advances of Fluorine Chemistry. Butterworths, London 1965, Vol. IV, p. 12.

[6] *I. K. Barben* and *H. Suschitzky*, J. chem. Soc. (London) *1960*, 672.

[7] *P. Jacobsen* and *L. Huber*, Ber. dtsch. chem. Ges. *41*, 660 (1908).

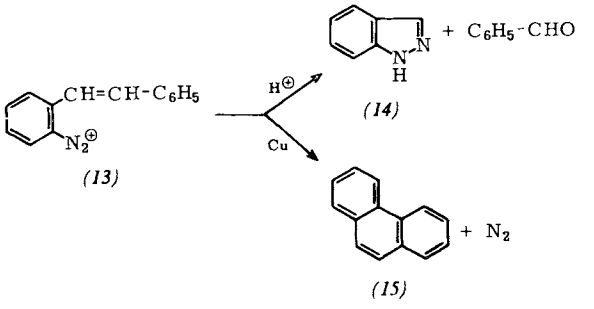
[*] Fluoride ions can be conveniently detected by means of the zirconium alizarin test; *F. Feigl:* Spot Tests. Elsevier, New York 1954, Vol. II, p. 67.

[8] *I. K. Barben* and *H. Suschitzky*, J. chem. Soc. (London) *1960*, 2735.

[9] *R. Huisgen* and *H. Nakaten*, Liebigs Ann. Chem. *586*, 84 (1954).

[10] *D. F. De Tar* and *Y. W. Chu*, J. Amer. chem. Soc. *76*, 1686 (1954).

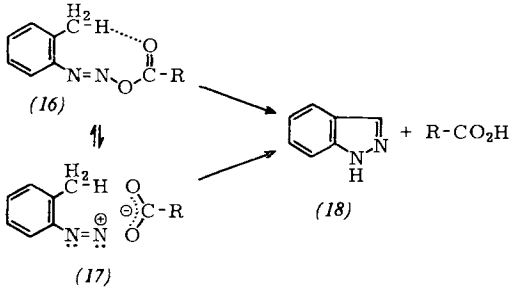
of *cis-o*-diazostilbene *(13)* and shown that indazole *(14)* is formed under conditions favoring a heterolytic process (aqueous acid) and that phenanthrene *(15)* is the main product from homolysis (copper powder). To this extent it is feasible that the cyclization step in



(13) *(14)* *(15)*

the Jacobson synthesis is also ionic in nature [see Scheme 1: *(9)* → *(8)*]. The ionic route accounts satisfactorily for the ease of internal coupling between diazo and methyl group since the diazonium ion can activate its coupling partner by a powerful +I effect. Moreover, the closeness of the carboxylate ion would promote cyclization by providing a suitable acceptor for the methyl proton which is released during ring closure.

The elegant, kinetic studies which led *Huisgen*[9] to postulate a four-center concerted mechanism within the covalent *trans*-diazoester *(16)* → *(18)* do not



(16) *(17)* *(18)*

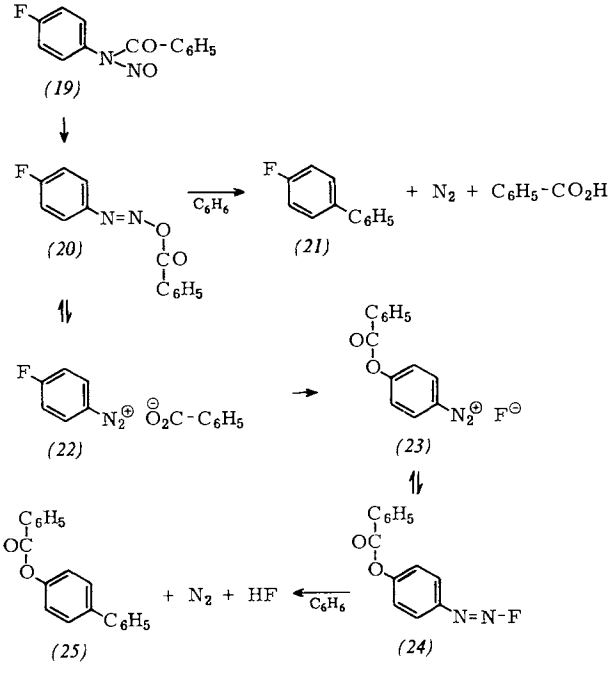
necessarily invalidate our ionic reaction scheme for indazole formation *(17)* → *(18)*. It must be realized that association of two ions to form either the covalent *trans*-diazoester *(16)* or the intimate ion pair *(17)* is a gradual and continuous process and the two species *(16)* and *(17)* would be indistinguishable if it were not for fluorine labeling.

An obvious objection to the ionic mechanism of cyclization is the lack of indazole formation from *o*-methyl substituted diazonium compounds in aqueous mineral acid. It is, however, feasible that an activated methyl-group will undergo internal coupling only if closely associated with a proton accepting base, a situation realized in an ion pair. The fact that various nitro- and polynitro-indazoles can be made from the appropriate nitrobenzene-diazonium salts in aqueous mineral acid[11] supports the postulated mechanism: it is well known that in aqueous solutions such diazonium compounds exist to a considerable extent in their covalent form, which must be in equilibrium not only with "free" ions but also with tightly held ion pairs.

[11] *E. Nölting*, Ber. dtsch. chem. Ges. *37*, 2556 (1904); *H. D. Porter* and *W. D. Peterson*, Org. Syntheses, Coll. Vol. III, p. 660.

III. Decomposition of Fluorine Substituted Acylarylnitrosamines

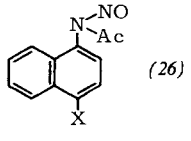
It was a logical step to extend the application of fluorine labeling to acylarylnitrosamines without an *ortho* methyl substituent[8] since these compounds are known to break down homolytically in non-polar solvents to provide aryl radicals. A benzene solution of *N*-(4-fluorophenyl)-*N*-nitrosobenzamide *(19)* kept at room temperature gave the expected 4-fluorobiphenyl *(21)* by homolytic aromatic substitution of the *p*-FC_6H_4 radical in the solvent (C_6H_6) and an equal amount of 4-benzoyloxybiphenyl *(25)*. Corresponding



(19) *(20)* *(21)* *(22)* *(23)* *(24)* *(25)*

Scheme 2. Decomposition of *N*-(4-Fluorophenyl)-*N*-nitrosobenzamide.

results were observed with fluorine in the *ortho*-position and also with other acyl groups, and fluoride ions were present in each reaction mixture. Fluorine *meta* to the *N*-nitroso group, or any other halogen in *ortho* or *para* position, was not expelled. In the naphthalenes *(26)*, X = F, Cl, or Br, however, chlorine as well as bromine suffered replacement[12] in conformance with the higher reactivity of activated halogen in this ring system[13].

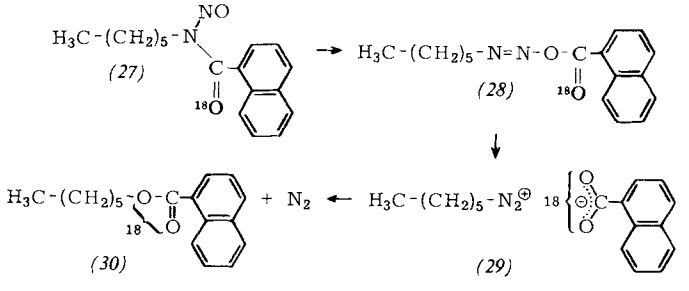


(26)

These results are again rationally accommodated within the accepted reaction scheme by interpreting

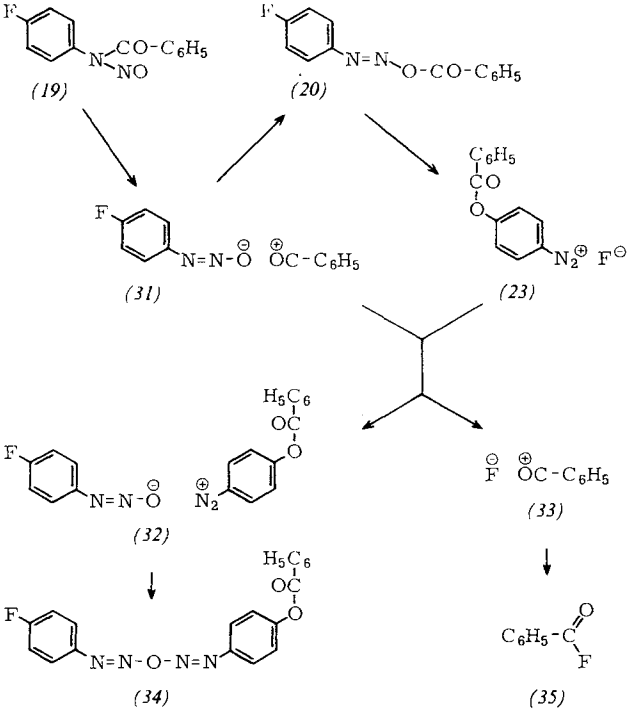
[12] *P. Miles* and *H. Suschitzky*, Tetrahedron *18*, 1369 (1962).
[13] *H. J. Van Opstall*, Recueil Trav. Chim. Pays-Bas *52*, 901 (1933).

the appearance of fluoride ions as evidence for the heterolysis of the covalent diazoester *(20)* into an ion pair *(22)*. At this stage the fluorine is rendered labile towards nucleophilic attack by the anionic partner [$C_6H_5CO_2^{\ominus}$ in *(22)*], and the steps leading to a mixture of biphenyls *(21)* and *(25)* are readily discernible in Scheme 2. The stages *(19)* → *(21)* represent the well-known rearrangement and homolytic substitution as revealed by the elegant work of *Hey*, *Huisgen*, and their collaborators [14,15]. This reaction scheme must, however, be augmented by the additional steps *(22)* → *(25)* to include a concomitant heterolysis, which is inferred from fluorine-labeling experiments. By contrast, heterolysis of acylarylnitrosamines in a polar medium such as acetic acid or methanol has been postulated before [15,16] but was precluded for benzene solutions [15]. It is of interest that acylalkylnitrosamines have recently been shown to decompose by a polar mechanism even in non-polar solvents as a result of ^{18}O tracer studies carried out by *White* and *Aufdermarsh* [17]. For instance, *N*-(n-hexyl)-*N*-nitroso-2-naphthamide *(27)* disintegrates *via* formation of the diazonium salt *(29)* to give the ester *(30)* with completely equilibrated oxygens. This technique is obviously not applicable to the aromatic nitroso compounds since the acyloxy moiety does not recombine with the aryl group.



When the products from the above fluorine-labeling experiments were separated by fractional distillation of the reaction mixture under anhydrous conditions, and not by extraction with aqueous solvents, the acid fluoride RCOF derived from the acyl moiety of the starting nitroso compound F–ArN(NO)COR was obtained in high yield. For instance, the benzoylarylnitrosamine *(19)* gave benzoyl fluoride, and analogous acetyl or formyl compounds in the benzene or naphthalene series yielded acetyl or formyl fluoride respectively [12]. Blank experiments excluded the possibility that these products were formed purely incidentally to the main reaction, perhaps just by combination of the organic acid RCO_2H and hydrogen fluoride, both of which are present during the reaction (see Scheme 2).

We interpret the origin of the acyl fluoride RCOF in the following way because this explanation correlates with a number of independent observations: Both the parent nitroso compound ArN(NO)–COR *(19)* and its isomeric diazoester ArN=NOCOR *(20)* can dissociate into their respective ion pairs. These relatively stable pairs can interact and exchange partners to form the new ion pairs *(32)* and *(33)*. In the case of the decomposition of the 4-fluorophenylnitroso compound *(19)* an interchange of the cationic moieties between the intimate ion pairs *(31)* and *(23)* [for the formation of the ion pair *(23)* see Scheme 2] leads to the observed benzoyl fluoride *(35)* as shown in Scheme 3.



Scheme 3. Formation of benzoylfluoride in the decomposition of *N*-(4-fluorophenyl)-*N*-nitrosobenzamide.

The simultaneously formed diazoanhydride *(38)* is a highly unstable free-radical source [18] whose breakdown products are indistinguishable from those expected from the starting nitroso compound *(19)*. Intermediacy of diazoanhydrides has indeed been postulated again recently in a modified reaction scheme for the thermolysis of acylarylnitrosamines (see Scheme 4) [19].

[14] *W. S. M. Grieve* and *D. H. Hey*, J. chem. Soc. (London) *1934*, 1797; *E. C. Butterworth* and *D. H. Hey*, *ibid. 1938*, 116; *D. H. Hey*, *A. Nechvatal*, and *T. S. Robinson*, *ibid. 1951*, 2892.

[15] *R. Huisgen* and *G. Horeld*, Liebigs Ann. Chem. *562*, 137 (1949).

[16] *D. F. De Tar*, J. Amer. chem. Soc. *73*, 1446 (1951).

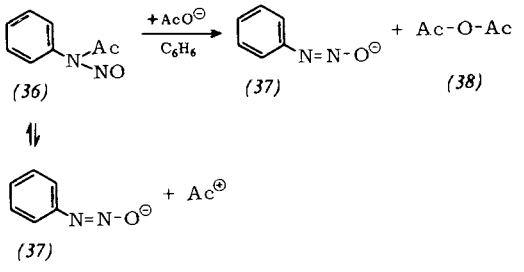
[17] *E. H. White* and *C. A. Aufdermarsh*, J. Amer. chem. Soc. *83*, 1174, 1179 (1961).

[18] *E. Bamberger*, Ber. dtsch. chem. Ges. *29*, 446 (1896); *53*, 2314 (1920); *Th. Kauffmann*, *H. O. Friestad*, and *H. Henkler*, Liebigs Ann. Chem. *634*, 64 (1960).

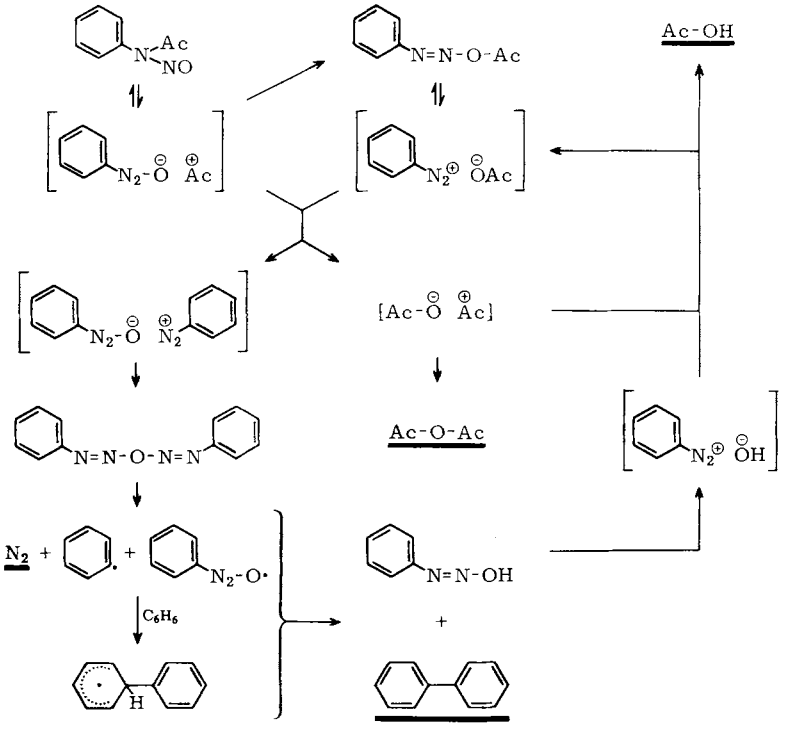
[19] *C. Rüchardt* and *B. Freudenberg*, Tetrahedron Letters *1964*, 3623; *C. Rüchardt*, *B. Freudenberg*, and *E. Merz*, Abstracts of Papers of the International Symposium on Organic Reaction Mechanism, Cork, Ireland 1964, p. 28; *C. Rüchardt*, Angew. Chem. *77*, 974 (1965); Angew. Chem. internat. Edit. *4*, 964 (1965).

Moreover, the participation of an acylium ion in the isomerization of nitroso compound to diazoester [$C_6H_5-CO^{\oplus}$ in Scheme 3, *(19)* → *(20)*] is in some agreement with the kinetic results obtained by *Hey* [20] and *Huisgen* [21] although these workers prefer a non-ionic interpretation of these data. Yet it appears that the rate of this rearrangement depends on the structure of the acyl group in the nitroso compound in a way expected for an S_N1 process, *i.e.* by a mechanism involving an acylium ion. Thus the isomerization velocity of ArN(NO)CO–R increases in the order $R = H < CH_3 < C_2H_5 <$ iso-C_3H_7 but is little affected by changes in the aryl moiety; this is feasible since the aromatic ring neither participates in the migration nor has it any conjugative influence on the moving acyl or receiving nitroso group.

Since our experiments were carried out, *Rüchardt* [19] has suggested a modified decomposition mechanism of acylarylnitrosamines, which embodies several features inferred above from fluorine-labeling experiments. This new reaction scheme overcomes an intrinsic weakness of the older one [22] which assumed intermediacy not only of aryl but also of acyloxy radicals ($RCO_2\cdot$) yet could not account for the failure of the latter to liberate carbon dioxide. This anomaly was explained away by a "cage mechanism" [15,23] which, however, became incompatible with later results [24]. While we fully agree with *Rüchardt*'s reaction scheme we consider it unnecessary to postulate that the initial diazotate anion *(37)* arises from the interaction of an acetate ion and the nitrosamine.



The spontaneous dissociation of the nitroso compound *(36)*, as evidenced by acyl fluoride formation in our labeling experiments (see Scheme 3), seems to us a more feasible source for this key intermediate. Consequently the appropriate acid anhydride, *e.g. (38)*, which has been observed in several reactions [19,25] is not formed as originally suggested from the nitroso compound *(36)*, but arises later in the reaction by a process analogous to that of acyl fluoride formation in Scheme 3. This process is shown in Scheme 4, which represents essentially the reaction scheme proposed by *Rüchardt* [19] except for the modifications mentioned above with some consequential alterations. Further support of this scheme comes from recent ESR measurements [25a] which confirmed the presence of aryldiazotate radicals ($ArN_2O\cdot$).



Scheme 4. Decomposition mechanism of acetylarylnitrosamine. Square brackets denote ion pairs and isolated reaction products are underlined.

[20] *D. H. Hey, J. Stuart-Webb*, and *G. H. Williams*, J. chem. Soc. (London) *1952*, 4657.

[21] *R. Huisgen* and *L. Krause*, Liebigs Ann. Chem. *574*, 157 (1951).

[22] *H. Zollinger*: Azo and Diazo Chemistry. Interscience, New York 1961, pp. 153–159.

[23] *E. L. Eliel, M. Eberhardt, O. Simamura*, and *S. Meyerson*, Tetrahedron Letters *1962*, 749.

[24] *E. L. Eliel* and *J. G. Saha*, J. Amer. chem. Soc. *86*, 3581 (1964); *D. B. Denney, N. E. Gershman*, and *A. Appelbaum*, *ibid.* *86*, 3180 (1964).

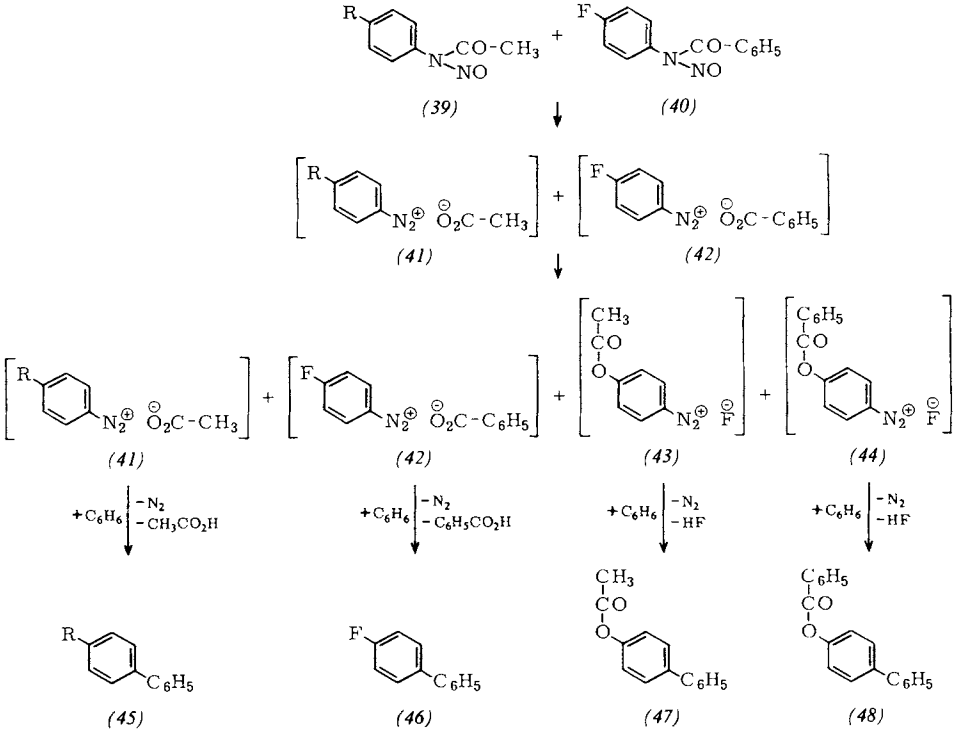
[25] The reaction mixture from the decomposition of $C_6H_5-N(NO)-CO-C_6H_5$ in benzene showed two sharp bands at 1790 and 1725 cm^{-1} characteristic of benzoic anhydride in the infrared spectrum. *H. Suschitzky*, unpublished result.

[25a] *G. Binsch, E. Merz*, and *C. Rüchardt*, Chem. Ber. *100*, 247 (1967).

So far it has been tacitly assumed that the decomposition mechanism deduced for fluorine-substituted acylarylnitrosamines is applicable to the whole class of these compounds regardless of aromatic substituent. Fluorine is probably unique in providing mechanistic evidence in this reaction since the numerous observations of decomposition of non-fluorinated nitrosamines reported over the last twenty-five years do not contain a single observation of anionic displacement affecting another substituent. The specificity of fluorine was confirmed when chlorine replacement could not be detected by even a most careful product analysis of the reaction mixture obtained from *N*-nitroso-*p*-chlorophenylacetamide. Yet it is unlikely that only fluorine substituted nitrosamines have the prerogative of undergoing heterolysis. In order to find out whether other nitrosamines form ion pairs besides free radicals, regardless of the nature of their ring-substituent, we carried out several mixed decompositions[12]. Thus various acetylarylnitrosamines with substituents of different electronic properties [*(39)*, R = Cl, CH_3, NO_2, H in the *para* position as well as CH_3 in the *meta* position] were made to decompose (each separately) in dry benzene containing some *N*-nitroso-*p*-fluorophenylbenzamide *(40)*. If the two nitrosoamines *(39)* and *(40)* disintegrated at a similar rate and both heterolysed to give diazonium ions, two sets of ion pairs, namely *(41)* and *(42)*, would be present in the reaction mixture. As a consequence, two species of anions, namely benzoate and acetate, would be competing for displacement of aromatic fluorine in *(42)* and four different biphenyls *(45)–(48)* would be produced by subsequent events as shown in Scheme 5. Formation of the 4-acetoxybiphenyl *(47)* would be clearly indicative of the fact that the breakdown of the acetylnitrosamine *(39)* under test is not purely homolytic but has also included the ionic intermediate *(41)*. This was confirmed by product analysis using gas-liquid and column chromatography since the diagnostic 4-acetoxybiphenyl *(47)* was present (up to 17%) in each of the mixed decompositions in addition to the expected three biphenyls *(45)*, *(46)*, and *(48)*. The possibility that the crossed product *(47)* is due to substitution of the diazonium compound *(42)* by acetic acid rather than by the anion from the ion pair *(41)* was discounted by control experiments. It is thus shown conclusively that acylarylnitrosamines of all types decompose *via* a route involving homolytic and heterolytic steps.

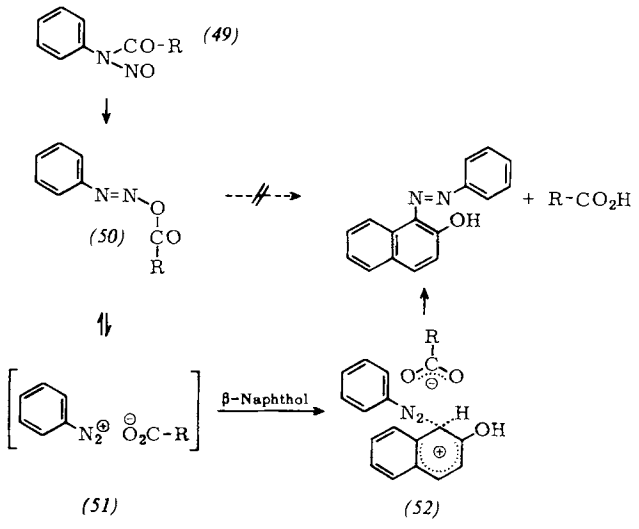
IV. Coupling Mechanism of Acylarylnitrosamines in Non-Aqueous Media

The information gathered from fluorine labeling on the behavior of acylarylnitrosamines allows us to make some relevant observations on the mechanism of azo coupling in non-aqueous solvents. *Huisgen*[15,21,26] was able to determine the isomerization rate of acylarylnitrosamines *(49)* into diazoesters *(50)* simply by measuring colorimetrically their azo-dye production with added β-naphthol since the latter process is a much faster reaction than the former. Dye formation proceeded more rapidly in benzene than in acetic acid and as the non-polar solvent was presumed to contain only the diazoester *(50)* coupling was ascribed to this species rather than to its "dissociated" form, the diazonium ion *(51)*. This postulate is, however, at



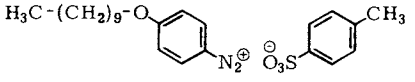
Scheme 5. Decomposition of an acetyl and benzoylnitrosamine in admixture.

[26] *R. Huisgen*, Liebigs Ann. Chem. *573*, 163 (1951); *574*, 184 (1951).

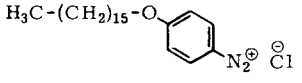


Scheme 6. Coupling of acylarylnitrosamine with β-naphthol in benzene.

variance with *Bradley* and *Thompson*'s observation [27] on diazonium salts such as *p*-(n-decyloxy)benzenediazonium-*p*-toluenesulfonate *(52a)* or the *p*-(n-hexadecyloxy)benzene diazonium chloride *(52b)* which in



(52a)



(52b)

spite of their moderate solubility in benzene nevertheless couple readily with β-naphthol in this medium to give azo dyes. These discrepancies can, however, be resolved on the basis that diazonium ions (as borne out by fluorine-labeling experiments) exist in the non-polar media and, like carbonium ions, are prone to form intimate ion pairs as the polarity of the solvent decreases. In a solvent such as benzene it is most probably the diazo ion pair rather than the covalent ester that undergoes azo coupling (see Scheme 6). The increased azo-coupling rate in benzene is possibly due to the favorable geometrical position as well as the polarity of the anionic partner, factors which ensure a rapid proton loss from the transition state *(52)*.

V. Fluorine Labeling of Various Aryl Radical Generators

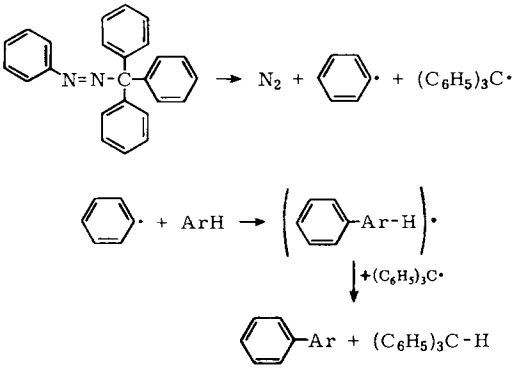
It was thought that "fluorine tagging" of other aromatic radical sources, particularly those which operate by homolytic cleavage of an aryl-nitrogen bond, would be a simple way to discover any inherent but hidden tendency to heterolytic fission. The results of this work in relation to currently accepted mechanisms are briefly summarized in the following sections [28].

[27] *W. Bradley* and *J. D. Thompson*, Nature (London) *178*, 1069 (1956).

[28] *P. Miles* and *H. Suschitzky*, Tetrahedron *19*, 385 (1963).

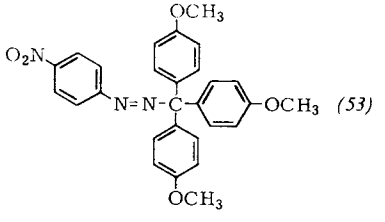
a) Phenylazotriphenylmethane

The decomposition of phenylazotriphenylmethane in hot benzene was first studied in 1934 by *Hey* [29a]. Subsequently a number of workers, *Hey*, *Wieland*, *Huisgen*, and their respective collaborators [29b–29g], have shown that the reaction involves free-radical intermediates while other workers have put forward a cage process in which free radicals are not involved [23]. The accepted mechanism for the homolytic decomposition of phenylazotriphenylmethane in an aromatic solvent ArH is outlined in Scheme 7.



Scheme 7. Homolytic decomposition of phenylazotriphenylmethane.

An unsuccessful attempt has been made to induce heterolysis by introducing electronically different substituents into the azo compound, *e.g. (53)*, and by the use of various solvents [30].



(53)

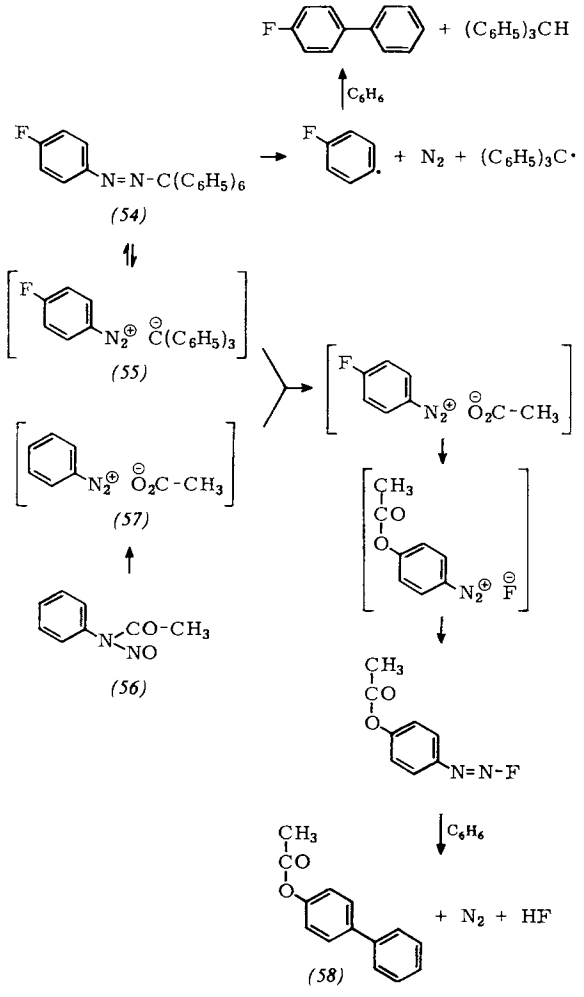
Only products indicative of a free-radical breakdown were obtained.

We studied the same problem by causing *p*-fluorophenylazotriphenylmethane *(54)* to decompose in hot benzene. Heterolysis of the former to give the diazonium ion pair *(55)* could possibly lead to fluorine replacement by the triphenylmethyl anion of *(55)*. However, no ionic fluorine was detected; this could be attributed to the unreactivity of this bulky, resonance-stabilized triphenylmethyl anion. In order to provide a more nucleophilic agent the reaction was carried out in the presence of *N*-nitrosoacetanilide *(56)*, which we know

[29a] *D. H. Hey*, J. chem. Soc. (London) *1934*, 1966. [b] *D. H. Hey*, *C. J. M. Stirling*, and *G. H. Williams*, J. chem. Soc. (London) *1955*, 3963. [c] *G. L. Davies*, *D. H. Hey*, and *G. H. Williams*, *ibid. 1956*, 4397. [d] *D. H. Hey*, *M. J. Perkins*, and *G. H. Williams*, Tetrahedron Letters *1963*, 445. [e] *D. H. Hey*, *M. J. Perkins*, and *G. H. Williams*, J. chem. Soc. (London) *1965*, 110. [f] *H. Wieland*, *K. Heyman*, *T. Tsatsas*, *D. Juchum*, *G. Varvoglis*, *G. Labriola*, *G. Dobbelstein*, and *H. S. Boyd-Barrett*, Liebigs Ann. Chem. *514*, 145 (1935). [g] *R. Huisgen* and *H. Nakatan*, *ibid. 586*, 70 (1954). [h] *R. Huisgen* and *R. Grashey*, *ibid. 607*, 46 (1957).

[30] *M. D. Cohen*, *J. E. Leffler*, and *L. M. Barbato*, J. Amer. chem. Soc. *76*, 4149 (1954).

from previous work (see Scheme 4) to release the reactive acetate ion under these conditions. Fluoride ions and the diagnostic 4-acetoxybiphenyl *(58)* were



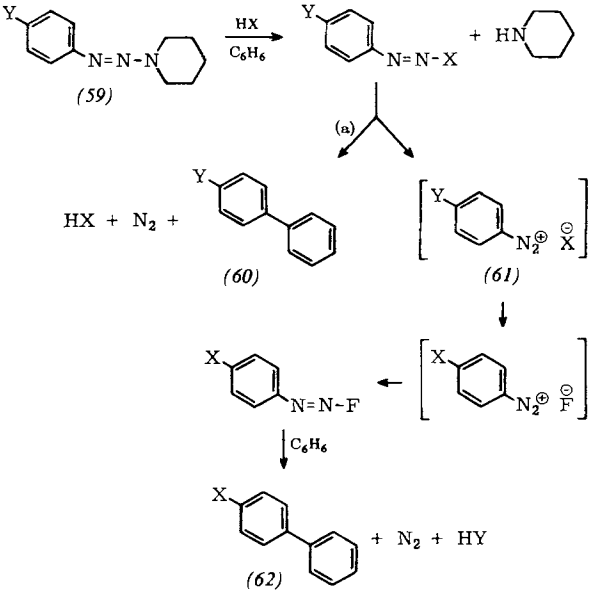
Scheme 8. Mixed decomposition of *p*-fluorophenylazotriphenylmethane and *N*-nitrosoacetanilide.

in fact detected, a result which is best accounted for by interaction of the two ion pairs *(55)* and *(57)*. As is shown in Scheme 8, the ion pair *(55)* is a heterolytic product of the azo compound *(54)*.

The other reaction products were triphenylmethane, triphenylmethanol, triphenylmethylperoxide, and 4-fluorobiphenyl which are normally expected from the homolysis of *(54)*. The results of recent experiments [29e] in which two different azo compounds were made to decompose together in benzene for a limited time and in which the undecomposed azo compounds were found to have exchanged their trityl groups, albeit to a small extent, could also be explained on our ion-pair hypothesis. This evidence is, however, not fully conclusive as considerable experimental difficulties in assessing the products were reported.

b) *N*-(*p*-Fluorophenyldiazo)piperidine

Thermolysis of triazenes [31], for instance of the piperidene derivative *(59)*, Y = H, in benzene solution (containing acids), produces, *via* the intermediate formation of free radicals, nitrogen, a biphenyl, and an amine (see Scheme 9: Route a). When the fluorine-labeled triazene *(59)*, Y = F, was made to decompose in a boiling mixture of benzene (10 parts) and acetic acid (1 part), 4-acetoxybiphenyl *(62)*, X = AcO, and fluoride ions in addition to the products expected from the homolysis *(60)*, X = AcO, were formed. An analogous result was observed when hydrochloric acid was used instead of acetic acid; the diagnostic product 4-chlorobiphenyl *(62)*, X = Cl, was formed.



Scheme 9. Thermolysis of *p*-fluorophenyldiazopiperidine.

Again the presence of the two biphenyls *(60)* and *(62)*, X = AcO or Cl, is indicative of a dual mechanism in the pyrolysis of the triazene, as set out in Scheme 9. Fluorine replacement obviously occurs at the ion-pair stage *(61)*, X = $AcO^{\ominus}$ or $Cl^{\ominus}$, while the triazene itself does not dissociate into ions for piperidinobiphenyl is not a reaction product.

c) *p,p'*-Difluorodiazoaminobenzene

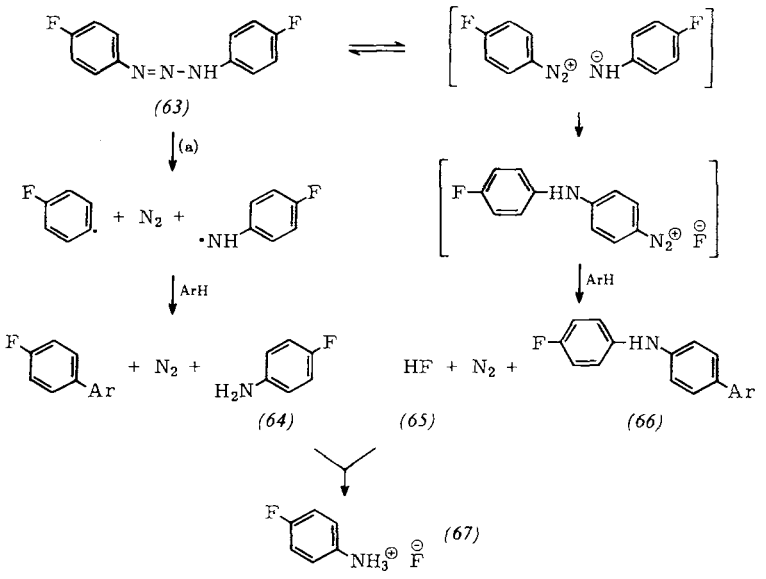
Diazoaminobenzenes have recently been reported by *Hardie* and *Thomson* [32] to be sources of free radicals when heated in a high-boiling solvent. Nitrogen, and anilino and aryl radicals are produced; combination of the latter with an aromatic solvent leads to biaryl formation as set out in Scheme 10 (cf. Route a).

Decomposition of the fluorine analogue *(63)* in boiling chlorobenzene gave *p*-fluoroaniline hydrofluoride *(67)* which deposited on the walls of the reflux condenser This substance is formed undoubtedly by interaction of the homolytically produced *p*-fluoroaniline *(64)* and heterolytically formed hydrogen fluoride *(65)*. The predicted diphenylamine *(66)* was not isolated from the tarry reaction mixture which, however, gave a strong diphenylamine test [33].

[31] *J. Elks* and *D. H. Hey*, J. chem. Soc. (London) *1934*, 441.

[32] *R. L. Hardie* and *R. H. Thomson*, J. chem. Soc. (London) *1958*, 1286.

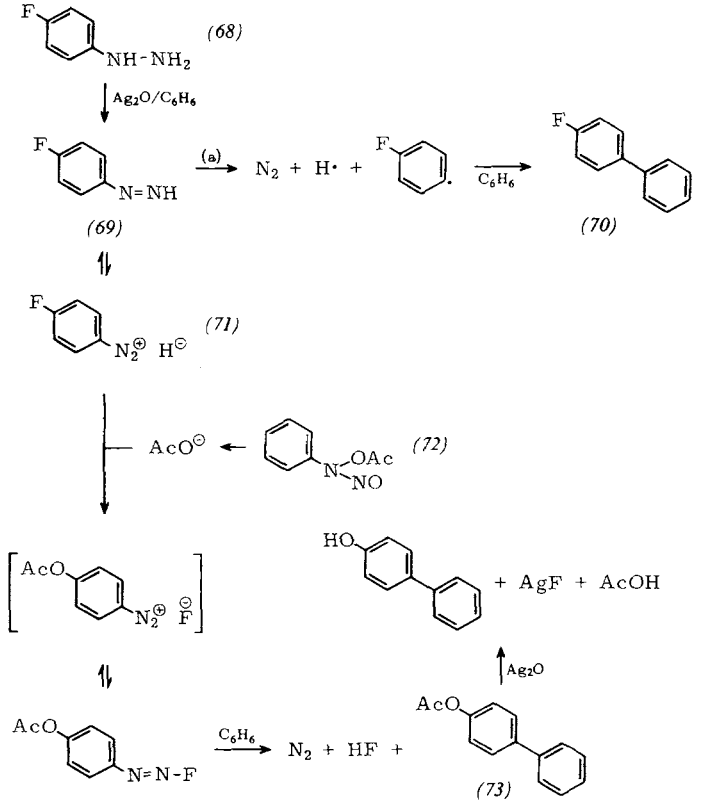
[33] Concentrated sulfuric acid and sodium nitrite produced an immediate blue color on addition of a trace of recation product *cf. F. Feigl*, Spot Tests. Elsevier, New York 1954, Vol. II, p. 126



Scheme 10. Thermolysis of *p,p'*-difluorodiazoaminobenzene in an aromatic solvent.

d) *p*-Fluorophenylhydrazine

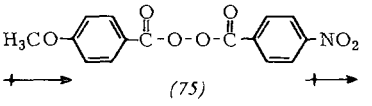
Oxidation of arylhydrazines in an aromatic solvent with silver oxide liberates aryl radicals, which attack the solvent to form biaryls [34]. This homolysis probably involves the covalent diazo compound *(69)*, which could feasibly be in equilibrium with the aryldiazonium hydride *(71)*. If so, replacement of a fluorine atom at the *para*-position by the hydride ion is possible; but this is improbable because the hydride ion will be too readily removed by the oxidizing agent. It was, therefore, not unexpected to find that treatment of *p*-fluorophenylhydrazine *(68)* with silver oxide in benzene gave *p*-fluorobiphenyl *(70)*, in accordance with Route (a) in Scheme 11, but no fluoride ions. In the presence of *N*-nitrosoacetanilide *(72)*, which provides a diazonium acetate and with it the much more effective acetate anion, the reaction products were 4-fluorobiphenyl and 4-hydroxybiphenyl [28]. Moreover, an aqueous extract of the silver residues gave a strongly positive test for ionic fluorine. The anticipated 4-acetoxybiphenyl *(73)* could not be isolated as it suffered hydrolysis *in situ* to its 4-hydroxy-derivative *(74)*. By analogy with the previous conclusions a rational scheme for phenylhydrazine oxidation can be advanced (see Scheme 11) which clearly illustrates operation of a dual mechanism.



Scheme 11. Oxidation of *p*-fluorophenylhydrazine with silver oxide in benzene.

e) *p*-Fluorobenzoyl peroxide

Thermal decomposition of diaroyl peroxides is judged to be the best method of providing aryl radicals because it usually gives the "cleanest" reaction products. Its mechanism has probably received more attention than that of any other aryl radical source [29a, 35]. Unsymmetrical peroxides such as *p*-methoxy-*p'*-nitrobenzoylperoxide *(75)* in which the substituents induce



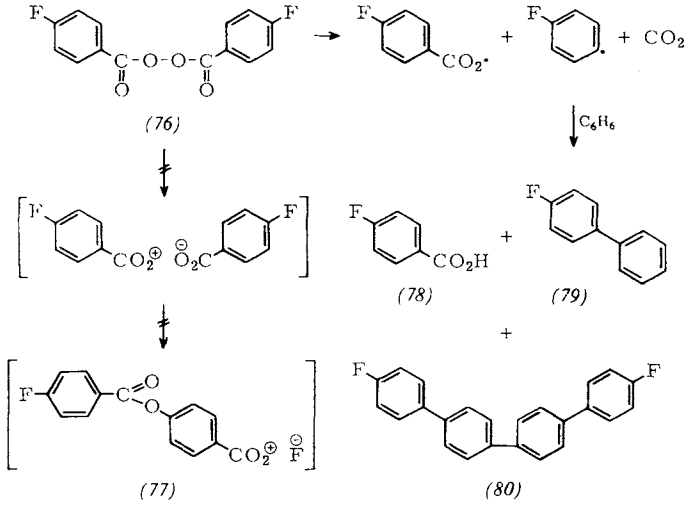
a unidirectional electron-flow and thereby distort the molecule electronically can, according to *Leffler* [36], heterolyse in nitrobenzene in presence of acetic acid or

[34] *R. L. Hardie* and *R. H. Thomson*, J. chem. Soc. (London) *1957*, 2512.

[35] *P. Gelisson* and *P. H. Hermans*, Ber. dtsch. chem. Ges. *58*, 285 (1925); *D. F. De Tar* and *R. A. J. Long*, J. Amer. chem. Soc. *80*, 4742 (1958); *E. L. Eliel*, *S. Meyerson*, *Z. Welvart*, and *S. H. Wilen*, *ibid. 82*, 2936 (1960); *M. Eberhardt* and *E. L. Eliel*, J. org. Chemistry *27*, 2289 (1962); *G. H. Williams*, Homolytic Aromatic Substitution. Pergamon Press, Oxford 1960, pp. 34–41.

[36] *J. E. Leffler*, J. Amer. chem. Soc. *72*, 67 (1950).

thionyl chloride, as inferred from product analysis. If the fluorine labeled peroxide *(76)* can dissociate into ions (Scheme 12) then fluoride ions *(77)* should be detectable in the reaction mixture. However, only compounds expected from a free radical process, namely *p*-fluorobenzoic acid *(78)*, 4-fluorobiphenyl *(79)*, and a little *p,p'*-difluoro-*p*-quaterphenyl *(80)* were obtained in benzene [28]. Pyrolysis in the presence of *N*-nitrosoacetanilide did not lead to fluorine replacement whatever solvent was employed.



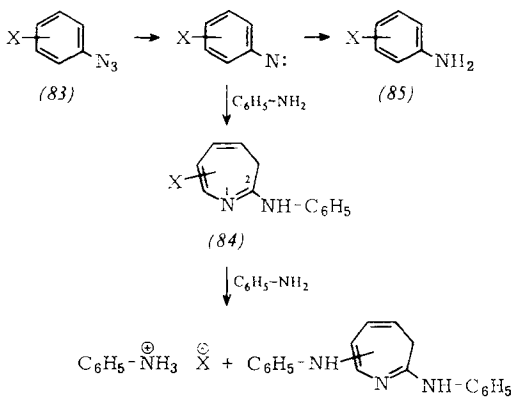
Scheme 12. Thermal decomposition of *p*-fluorobenzoyl peroxide in benzene.

VI. Thermolysis of Fluorophenyl Azides

The decomposition of aryl azides *(81)* in hot solvents leads to the loss of nitrogen and formation of a highly reactive, unstable intermediate *(82)* which, because of its isoelectronic nature with, and chemical resemblance to, carbene [38], is best called nitrene [37]. As nitrenes often behave as an electrophilic species (Ar–N:), we thought that the electron deficient nitrogen may render

$$\underset{(81)}{Ar\text{-}N_3} \xrightarrow[\text{in solution}]{\Delta} N_2 + \underset{(82)}{Ar\text{-}\ddot{N}:}$$

a *para*- or *ortho*-positioned fluorine labile towards nucleophilic attack in a manner analogous to an aromatic diazonium group $ArN_2^{\oplus}$. Indeed, thermolysis of *o*- or *p*-fluorophenyl azide in chlorobenzene [39] containing a little aniline as the nucleophile produced a sublimate in the reflux condenser which was essentially aniline hydrofluoride. When we found, however, that any halogen, even in the *meta* position, was eliminated with formation of the corresponding anilinium halide it became obvious that the loss of halogen was not due to a simple nucleophilic aromatic substitution. We are mentioning this experiment as a cautionary example. Had we been working only with compounds containing fluorine in the *o*- and *p*-positions, an erroneous conclusion could have easily been drawn. It is important to realize that mobility of a fluorine atom in the *ortho* or *para* position is diagnostic of an activating



Scheme 13. Thermal decomposition of halogenophenyl azides in aniline.

aromatic intermediate only if it has been demonstrated that this halogen is not replaceable in the *meta* position.

A full discussion and presentation of the reasons for this unusual halogen replacement are outside the scope of this article but can be found elsewhere [39]. However, to complete the picture it may be briefly stated that a phenyl azide with a halogen in the *ortho*, *meta*, or *para* position *(83)* decomposes in aniline to give a small quantity of the 6-, the 3- and the 5-, or the 4-halogenoazepine *(84)*, respectively. Halogen in any position of this heterocycle was found to be prone to nucleophilic attack and is thus readily replaceable by the added aniline or by the corresponding halogenoaniline *(85)*, which is a normal by-product formed by addition of hydrogen to the halogenonitrene as shown in Scheme 13.

VII. Aminolysis of 3-Aryl-4-bromosydnones and Acid Hydrolysis of 3-Arylsydnone Imines

We found [40] that the aminolysis of 3-aryl-4-bromosydnones *(86)* with a secondary amine, for example piperidine, yielded the anticipated amino acid amide *(87)* but primary amines, for instance cyclohexylamine, gave an unexpected result. Nitrogen was slowly liberated and the main product proved to be the Schiff base *(90)* containing two cyclohexyl moieties. Tentatively we interpreted this unforeseen cleavage of the hetero-

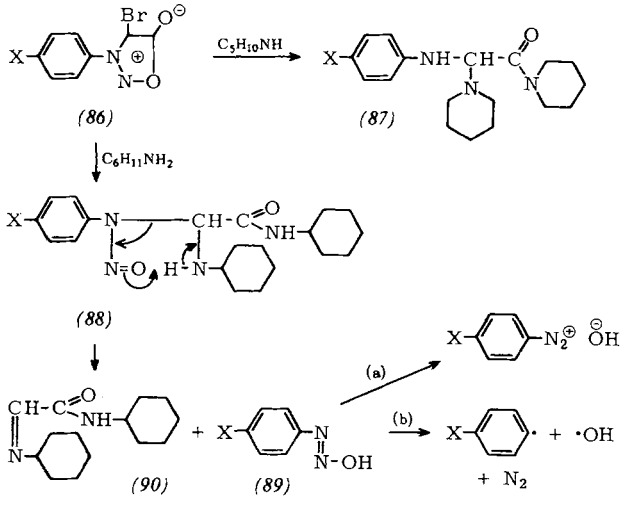
[37] Naming of this intermediate is unfortunately not uniform at present. The terms azene and imidogen are also used in the Anglo-Saxon literature while in German the intermediate is referred to as "Imen".

[38] *L. Horner* and *A. Christmann*, Angew. Chem. *75*, 707 (1962); *R. A. Abramovitch* and *B. A. Davies*, Chem. Rev. *64*, 149 (1964); *M. Apple* and *R. Huisgen*, Chem. Ber. *91*, 12 (1958); *92*, 2961 (1959); *W. von E. Doering* and *R. A. Odum*, Tetrahedron *22*, 81 (1966).

[39] *R. K. Smalley* and *H. Suschitzky*, J. chem. Soc. (London) [Suppl. 2] *1964*, 5922.

[40] *M. Bellas* and *H. Suschitzky*, Chem. Commun. (London) *7*, 136 (1965); *M. Bellas* and *H. Suschitzky*, J. chem. Soc. (London) *C 1966*, 189; *G. Puranik* and *H. Suschitzky*, J. chem. Soc. (London) *C 1967*, 1006.

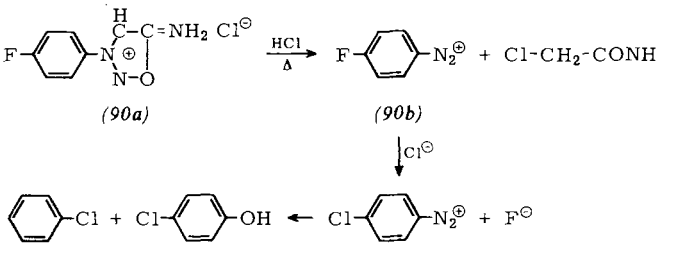
cycle as a two-step process the first stage producing the nitroso-compound *(88)*. A 1,6 interaction between the nitroso oxygen and the aminohydrogen could feasibly lead to the observed azomethine *(90)* and, of necessity, to the diazohydroxide *(89)*, a reaction scheme for which we had of course no evidence. However, this mechanism seemed capable of being tested by fluorine labeling. If the postulated diazohydroxide contained a fluorine atom in the *para* position *(89)*, X = F, then dissociation (*cf.* Route a) would render this atom sufficiently labile to promote its replacement in the nucleophilic environment. Accordingly we tested the *p*-fluorophenylsydnone *(86)*, X = *p*-F, with cyclohexylamine and found not only the expected Schiff base *(90)* but also ionic fluorine in the reaction mixture. In the case of *m*-fluorophenylsydnone *(96)*, X = *m*-F, no fluoride ions were produced thus establishing the nucleophilic nature of the replacement of the fluorine atom in the *para* position and thereby corroborating the proposed mechanism as given in Scheme 14.



Scheme 14. Aminolysis of 3-aryl-4-bromosydnones.

It is noteworthy that *p*-chlorophenylsydnone *(96)*, X = *p*-Cl, did not furnish chloride ions when treated with the amine, which again stresses the distinction of fluorine as a chemical label. One of the products from the ammonolysis of chlorosydnone was chlorobenzene, which is in keeping with the proclivity of the aryl radical $ClC_6H_4\bullet$ to abstract hydrogen. Homolysis of the intermediate diazohydroxide *(89)*, X = *p*-Cl, (Route b in Scheme 14) is responsible for the presence of this radical as well as for the observed evolution of nitrogen.

Russian workers[40a] have recently suggested that 3-phenylsydnone imine is hydrolysed on treatment with hot hydrochloric acid, a diazonium ion being formed as an intermediate. Since participation of an aryl diazonium cation can be diagnosed by using aromatic fluorine as a label we prepared the *p*-fluorophenylsydnone imine *(90a)*, and hydrolysed it with hydrochloric acid. At the postulated diazonium stage *(90b)*, the fluorine would be rendered labile towards nucleophilic attack by the chloride ions. Consequently chlorobenzene, *p*-chlorophenol, and fluoride ions should be present in the reaction mixture. On the other hand *m*-fluorophenylsydnone imine should not lose its fluorine atom. All these predictions were experimentally verified and the reaction path in (Scheme 15) for the acid hydrolysis of aryl sydnone imines is thus confirmed.

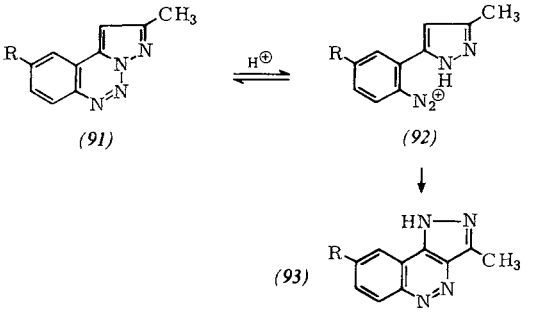


Scheme 15. Acid hydrolysis of 3-Arylsydnone imines.

VIII. Potential Scope of Aromatic Fluorine Labeling

It seems appropriate to conclude this brief review of a novel and little explored method by drawing attention to some mechanistic problems which could well be amenable to "fluorine tagging". Even a random perusal of the literature yields a crop of reactions of uncertain mechanism where a differential diagnosis between a free radical or a heterolytic pathway could be made. Certain rearrangements of nitrogen heterocyclic compounds are a potentially fruitful field in this respect, particularly if intermediacy of a diazonium structure is suspected.

For instance, the conversion of the triazine *(91)*, R = H, into the cinnoline *(93)*, R = H, by warm hydrochloric acid has tentatively been explained[41] by a

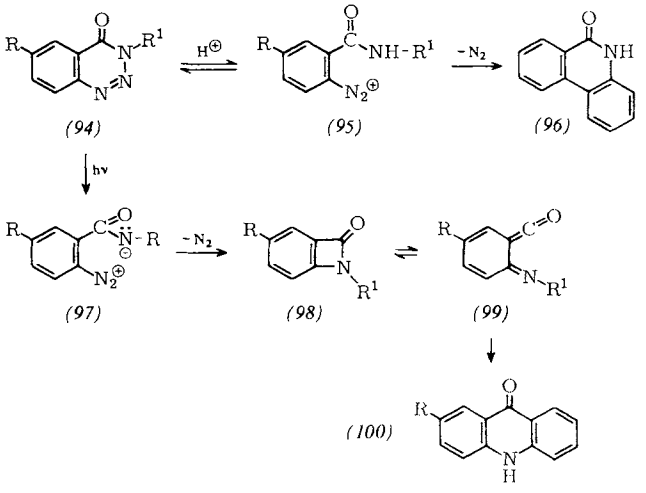


heterolytic cleavage involving the pyrazolylphenyldiazonium ion *(92)*, R = H, as an intermediate. Its rotation through 180 ° about the central bond is followed by cyclization yielding the product *(93)*. Under similar conditions the related ring system of benzotriazin-4-one *(94)*, $R^1 = C_6H_5$, yields a small quantity of the phenanthridone *(96)*. On the other hand thermal decomposition of *(94)*, $R^1 = C_6H_5$, at 280 °C

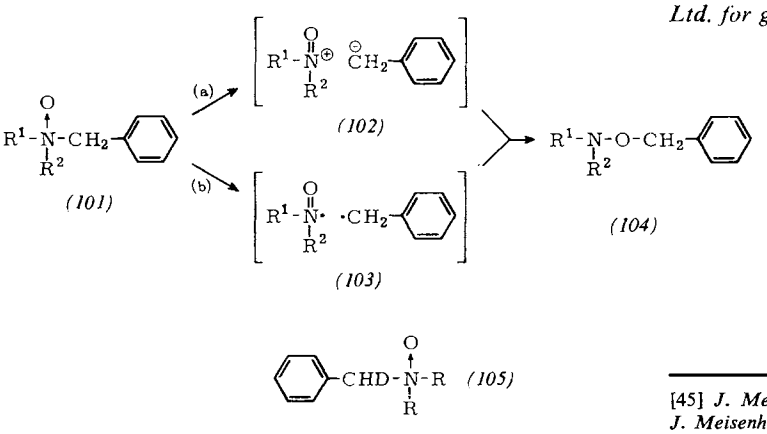
[40a] *L. E. Kholodov* and *V. G. Yashunskii*, Ž. obšč. Chim. *33*, 3336 (1963).

[41] *M. S. Gibson*, Chem. and Ind. *1962*, 698.

was reported [42] to give a mixture of the phenanthridone *(96)* and acridone *(100)* and these results were interpreted in terms of a radical mechanism. However,



the behavior of 3-aminotriazinone *(94)*, $R^1 = NH_2$, in acid was accounted for by intervention of the diazonium ion *(95)*, $R^1 = NH_2$ [43]. Results of recent studies on the photolysis [44] of this system, *e.g. (94)*, $R' = C_6H_5$, have again led to the assumption that it dissociates first to give a diazonium ion *(97)*. Loss of nitrogen leads to the formation of the cyclic amide *(98)* or its valence tautomer *(99)* either of which is responsible for all observed products such as acridone *(100)*. Direct chemical evidence for or against participation of the postulated diazonium ions *(92)*, *(95)*, or *(97)* in these reactions could feasibly be obtained by using the "fluorine-labeled" starting materials *(91)*, R = F, and *(94)*, R = F.



The scope of fluorine labeling is by no means limited to reactions with a potential diazo intermediate. For instance, another problem which would qualify for this labeling method is the well-known but little understood Meisenheimer rearrangement [45] of amine oxides to hydroxylamines *e.g., (101)* → *(104)*, which occurs on heating. Recent evidence based on the stereochemical outcome of this isomerization, namely substantial racemization of the optically active [α-D]-benzylamine-*N*-oxide *(105)* excludes an S_Ni type of rearrangement [46]. However, no clear-cut decision between the heterolytic pathway (a) and the homolytic process (b) can really be made, although the authors of these experiments are inclined to favor the latter [46]. Since we have shown that the *N*-oxide group activates aromatic fluorine more than any other halogen towards nucleophilic substitution [47] the rearrangement of a *p*-fluorophenylamine *N*-oxide, *e.g. (101)*, $R_1 = p\text{-}F\text{-}C_6H_4$, could throw considerable light on the mode of this reaction. If the ionic mechanism (a) were operative the nucleophilically active fluorine in the starting material *(101)*, $R_1 = p\text{-}F\text{-}C_6H_4$, or possibly in the cation *(102)*, $R_1 = p\text{-}F\text{-}C_6H_4$, would suffer replacement by attack of the benzyl anion *(102)*. If on the other hand the Meisenheimer rearrangement involved, as suggested [46], a homolytic process (b), ionic fluorine would not be found in the reaction mixture.

I am much indebted to my co-workers Dr. I. K. Barben, Dr P. Miles, Dr. M. Bellas, Dr. R. K. Smalley, Dr. G. Puranik, and D. Price for their enthusiastic support and to the Research Fund of the Chemical Society (London), the Geigy Co. Ltd., Smith, Kline and French (Pa. U.S.A.), and the S. R. C. (London) for generous financial help and to Dr. P. Koch of Koch-Light Laboratories Ltd. for gifts of fluorine compounds.

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German version: Angew. Chem. 79, 636 (1967)

[42] *D. H. Hey, C. W. Rees,* and *A. R. Todd,* Chem. and Ind. *1962*, 1332.

[43] *M. S. Gibson* and *M. Green,* Tetrahedron *21*, 2191 (1965).

[44] *G. Ege,* Angew. Chem. *77*, 723 (1965); Angew. Chem. internat. Edit. *4*, 699 (1965); *E. M. Burgess* and *G. Milne,* Tetrahedron Letters *1966*, 93.

[45] *J. Meisenheimer,* Ber. dtsch. chem. Ges. *52*, 1667 (1919); *J. Meisenheimer, H. Greeske,* and *A. Wilmersdorf,* ibid. *55*, 513 (1922).

[46] *U. Schöllkopf* and *H. Schäfer,* Liebigs Ann. Chem. *683*, 42 (1965); *U. Schöllkopf, M. Patsch,* and *H. Schäfer,* Tetrahedron Letters, 1964, 2515.

[47] *M. Bellas* and *H. Suschitzky,* J. chem. Soc. (London) *1963*, 4007; *1964*, 4561; *1965*, 2096; Chem. Commun. (London) *15*, 367 (1965); *D. Price* and *H. Suschitzky,* unpublished.

Electrophilic Substitution of Heteroaromatic Compounds with Six-Membered Rings[**]

BY A. R. KATRITZKY AND C. D. JOHNSON[*]

IN COLLABORATION WITH

G. P. BEAN, P. BELLINGHAM, P. J. BRIGNELL, B. J. RIDGEWELL, N. SHAKIR, O. TARHAN, M. VINEY, AND A. M. WHITE

The limited amount of quantitative data available on the electrophilic substitution of heterocycles is surveyed. Initial objectives are first to determine the species undergoing substitution and then to find out the amount by which the heterocyclic atom or group activates or deactivates the ring by comparison with the corresponding benzenoid compound. When sufficient data are available it is hoped to correlate this by means of a Hammett-type treatment or by MO methods.

The mechanism of electrophilic substitution in benzenoid compounds is now comparatively well understood and the subject has been comprehensively reviewed [1]. On the other hand our knowledge of the mechanism of heteroaromatic electrophilic substitution is meager and it was therefore considered important to study this mechanism both to rationalize the mass of qualitative information, and to aid the prediction of the feasibility of new reactions.

For example it is a familiar fact that the nitration of pyridines proceeds only under vigorous conditions and that product yields are poor. At present it is not known whether this is due to the low reactivity of the positively charged conjugate acid of pyridine toward the electrophile $NO_2^{\oplus}$, or whether the reaction took place on the very small amount of free base present under the strongly acidic conditions.

The present review summarizes the results obtained in our studies together with results obtained by other workers, notably *J. Ridd* at University College, London, and *K. Schofield* at the University of Exeter.

There are two major questions to be answered regarding the quantitative aspects of the substitution of heterocycles: 1) What species are involved; for example as above does the heterocyclic compound react in the form of free base or as the conjugate acid? 2) In what way does the annular heteroatom affect the rate of substitution at carbon atoms in the various ring positions?

Several criteria may be used to decide which species is reacting:

1a) The most direct is to compare the kinetic rate with that for model compounds in which the possibilities of ionisation or tautomerism are eliminated.

1b) The "rate profile" may be determined, *i.e.* the manner in which the rate depends on the acidity of the medium. Then, if the manner in which the ratio of the concentration of base to conjugate acid varies over the acidity range in question is known (*i.e.* the acidity function followed by the base), the theoretical change of rate for reaction *via* each of the possible reacting forms may be calculated and compared with that found.

1c) The entropy of activation, determined by Arrhenius plots, is expected to be considerably greater for reactions between two singly charged species of the same sign (*Frost* and *Pearson* predict [2] *ca.* −20 e.u.) than for reaction between a neutral species and one with a single charge.

1d) The encounter rate criterion can be applied in those cases where the concentration of a free base in a strongly acid solution is so low that, even if every molecular collision resulted in reaction, the calculated reaction rate would be lower than that measured. This limiting rate, the encounter rate, is given by:

$$k(\text{encounter}) = \frac{kT}{3\eta} \cdot \frac{(r_A + r_B)^2}{r_A r_B} \cdot \frac{N}{100} \qquad (1)$$

(where η is the viscosity of the medium, k is Boltzmann's constant, N is Avagadro's number, and r_A and r_B are the radii of the ions).

The rate constant (k') for reaction on the free base may be calculated from

$$n \log k' = n \log k + pK_a - H_0 \qquad (2)$$

(where n is unity for a Hammett base [*], and k is the observed rate constant).

[*] Prof. A. R. Katritzky and Dr. C. D. Johnson
School of Chemical Sciences, University Plain
University of East Anglia
Norwich, Norfolk (England)

[**] Based on lectures given at the Heterocyclic Conference for College Teachers, Bozeman, Montana; I. C. I. Petrochemical and Polymer Laboratory, Runcorn; University of California, Los Angeles; Groningen, Warsaw, Berlin, Rome, Exeter, and elsewhere, 1964–1967.

[1] *C. K. Ingold*: Structure and Mechanism in Organic Chemistry. Cornell University Press, New York 1953, Chapter VI.

[2] *A. A. Frost* and *R. G. Pearson*: Kinetics and Mechanism. Wiley, New York 1953, p. 132.

[*] Such Hammet bases are defined in [8]; reference base is *e.g.* *o*-nitroaniline.

When the nature of the reactive species in an electrophilic substitution has been elucidated, the question of the quantitative effect of the heteroatom can be considered. The rate of reaction for a heterocyclic compound is compared with that for the correspondingly substituted benzene at the same temperature (to do this, considerable extrapolation is often required). The effect of the heteroatom may be treated in two main ways:

2a) The Hammett equation approach[3] attempts to assign Hammett sigma constants σ_p and σ_m to each type of hetero group (*e.g.* $\rangle N$, $\rangle N^{\oplus}H$, $\rangle O^{\oplus}$, $\rangle N^{\oplus}-O^{\ominus}$, *etc.*) and a ρ value for each type of electrophilic substitution.

2b) The molecular orbital approach[4] assigns to each heteroatom X a Coulomb integral α_x and for bonds C–X a resonance integral β_x. These values are used to derive a variety of molecular orbital parameters with which the partial rate factors may be compared.

As yet there are insufficient data for the application of either of the above approaches. It is the aim of work being presently carried out to remedy this deficiency, and to enable a test of some of the diverse theoretical treatments which are possible.

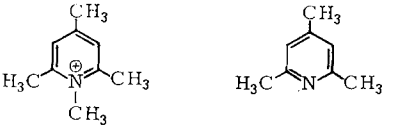
A. Pyridines

Extensive preparative work on the electrophilic substitution of pyridines has been reviewed by *Abramovitch*[5]. The strongly deactivating and *meta*-directing influence of the heteroatom is apparent; other substituents exert influences qualitatively similar to their behavior in benzenoid systems. A complicating factor is the catalysis caused by various metal salts which is thought to result from coordination of the metal with the pyridine nitrogen atom and possible back-donation of electrons to the ring.

1. Acid-Catalysed Hydrogen Exchange

Acid catalysed hydrogen exchange of pyridines was initially studied[6,10] by use of tritium as a tracer. Although pyridine and 4-picoline were found to be unreactive under the most vigorous conditions studied, exchange proceeded smoothly with 2,6-di- and 2,4,6-tri-methylpyridine. The reactions were investigated by heating aliquots of sulfuric acid, tritiated water, and the substituted pyridine at predetermined temperatures in sealed tubes for a known time. The base was isolated as the picrate, and the water produced on combustion of the picrate was monitored. The results obtained showed that the reaction was a first order reaction and that it occurred, as is suggested by the following criteria, on the conjugate acid:

a) 1,2,4,6-Tetramethylpyridinium ion *(1)* reacted slightly faster than the 2,4,6-trimethylpyridine *(2)*; an *N*-methylpyridinium cation would be expected to react faster than the corresponding protonated pyridinium cation, just as a methyl group causes a rate enhancement in benzenes.



(1) *(2)*

b) Plots (cf. Fig. 1) show that log *k* increased linearly with $-H_o$, slopes of 0.45 to 0.77 being found. Although these slopes are smaller than those found for benzenoid derivatives[7], the evidence indicates that the magnitudes of the slopes increase as the temperature is lowered, and rough extrapolations give reasonable room-temperature slopes. Further, the slopes for the bases and the *N*-methyl derivative *(1)* are similar. If reaction had been occurring on the free base, the variation of rate with acidity would have been much less, as the increasing activity of hydrogen ions (H^+ and T^+) would be counterbalanced by a decreasing amount of free base available for reaction.

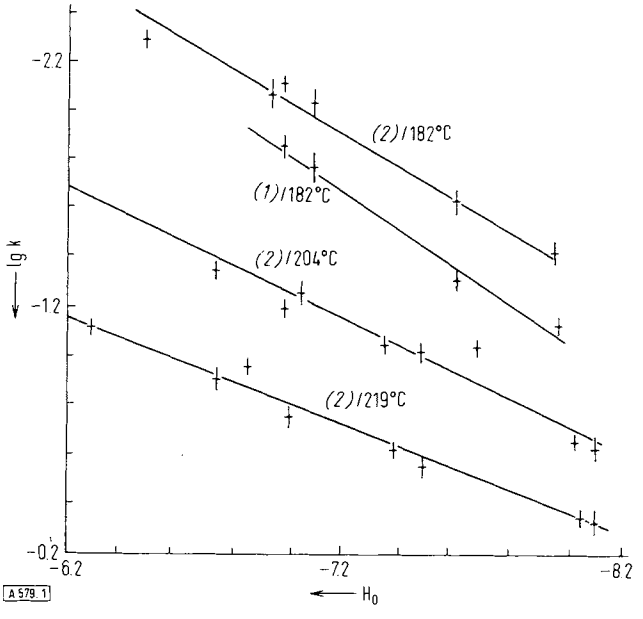


Fig. 1. Rate profiles for the acid-catalysed hydrogen exchange of 2,4,6-trimethylpyridine.

c) Calculated collision frequency factors, assuming reaction proceeds on the free base, are quite unreasonable, and exclude reaction *via* the free base (for details, examples, and discussion cf. [6]).

Rate comparisons with benzenoid compounds to obtain values for the deactivating effect of the $=\overset{\oplus}{N}H-$ group, as compared with $=CH-$, are as yet approximate because of lack of data, but indicate a deactivating factor of *ca.* 10^{-18} at the *meta* position.

[3] *H. H. Jaffe* and *H. Lloyd Jones* in *A. R. Katritzky*: Advances in Heterocyclic Chemistry. Academic Press, New York-London, 1964, Vol. 3, Chapter 2.

[4] *J. H. Ridd* in *A. R. Katritzky*: Physical Methods in Heterocyclic Chemistry. Academic Press, New York-London 1963, Vol. 1, p. 209.

[5] *R. A. Abramovitch* and *J. G. Saha* in *A. R. Katritzky*: Advances in Heterocyclic Chemistry. Academic Press, New York-London 1966, Vol. 6.

[6] *A. R. Katritzky* and *B. J. Ridgewell*, J. chem. Soc. (London) *1963*, 3743.

[7] *V. Gold et al.*, J. chem. Soc. (London) *1965*, 3609.

The acid-catalysed hydrogen exchange of aminopyridines is potentially more complicated. Here reaction could occur *via* free base, first conjugate acid, or second conjugate acid. For ideal behavior, where equilibrium and kinetic protonation both follow H_0, we should expect a rate profile as in Figure 2.

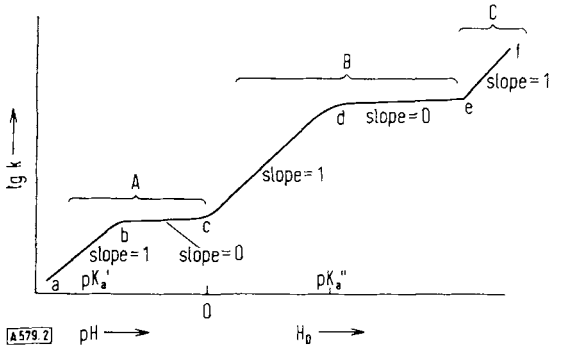


Fig. 2. Idealized rate profile for acid-catalysed hydrogen exchange of various highly protonated aromatic bases.
A: free base; B: first conjugate acid; C: second conjugate acid.

For other cases it can be shown[7a] that for exchange on a species, the concentration of which is not changing rapidly with acidity, $\delta \log k/\delta H_0 = \delta H_x/\delta H_0$ where H_x is the acidity function for kinetic C-protonation. For exchange of a species mainly present as its conjugate acid:

$$\delta \log k/\delta H_0 = \delta H_x/\delta H_0 - \delta H_y/\delta H_0$$

where H_y is the acidity function followed for equilibrium protonation of the species in question. The study of the hydrogen exchange of 4-amino-, 4-amino-2,6-dichloro-, and 2-amino-5-methyl-pyridine has shown rate profiles corresponding to the portions b-c, c-d, and d-e of Figure 2[7a].

The above treatment requires assumptions about the acidity functions followed by pyridines, and the variation of acidity functions with temperatures. Polyhalogeno-pyridines have been shown to be Hammett bases[8]. Available data on the effect of temperature on acidity functions is sparse and does not include observations for temperatures above 80 °C. There is an indication, however, that such effects are neither large nor discontinuous[9].

2. Nitration

1,2,4,6-Tetramethylpyridinium ion can be nitrated under the same reaction conditions as 2,4,6-trimethylpyridine, indicating that the latter compound reacts as the conjugate acid[11]. This is confirmed by the kinetic results; a rate profile for 2,4,6-trimethylpyridine at 101.3 °C is shown in Fig. 3. The general shape of the plot indicates conjugate acid nitration. This shape is characteristic[12] for a nitration in which the substrate concentration does not change significantly

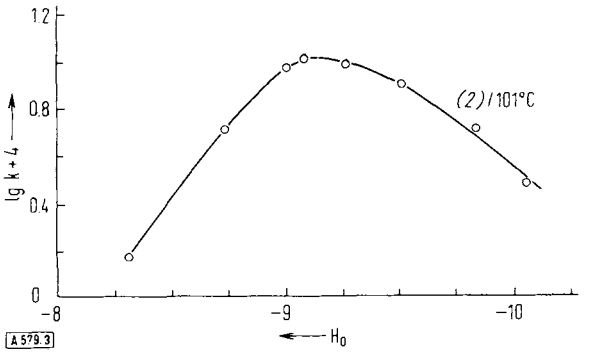


Fig. 3. Rate profile for the nitration of 2,4,6-trimethylpyridine at 101 °C.

with acidity. For nitration as free base a different shape is expected; the curve should be tilted in a clockwise direction because of the decreasing concentration of the substrate available for nitration as the acidity increases (cf. Fig. 4). In addition, calculated encounter rates show that there is insufficient free base present for its nitration to explain the results obtained. Again, rate comparisons with benzenoid compounds are complicated by lack of data, but a rough estimate gives a deactivating factor of *ca.* 10^{-12} for $=NH^{\oplus}$ at the *meta* position; however, derivation of this value necessitates assumptions regarding the constancy of the effect of methyl groups.

Nitration of a pyridine derivative *via* the free base might be expected (if the basicity of the pyridine nitrogen were low).

2,6-Dichloropyridine ($pK_a = -2.8$[8]) was found to undergo nitration in the 3-position smoothly at 100 °C, and a partial rate profile for nitration at this position,

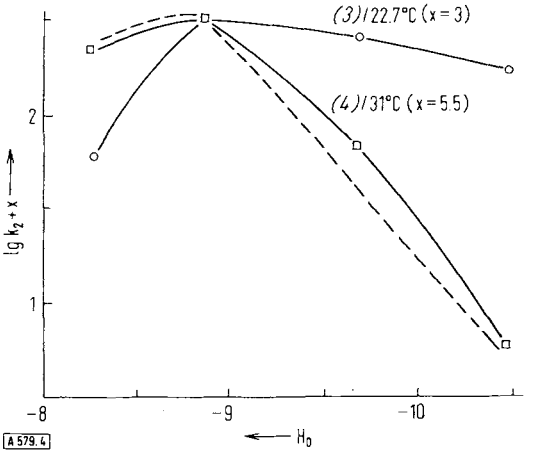


Fig. 4. Rate profiles for the first and second nitrations of 2,6-dimethoxypyridine (the broken curve was calculated for the free base).

together with a low entropy of activation (−10 e.u. in 98.3 % H_2SO_4), indicated reaction as the free base. 2,6-Dimethoxypyridine *(3)* could be nitrated to yield successively the 3-mono- *(4)* and 3,5-di-nitro derivative *(5)*[13]. The rate profiles (Fig. 4) show that the first of these nitrations occurs on the conjugate acid of 2,6-dimethoxypyridine, and that the introduction of the first nitro-group lowers the basicity such that

[7a] *G. P. Bean, C. D. Johnson, A. R. Katritzky, B. J. Ridgewell,* and *A. M. White,* J. chem. Soc. (London), in press.

[8] *C. D. Johnson, A. R. Katritzky, B. J. Ridgewell, N. Shakir,* and *A. M. White,* Tetrahedron *21,* 1055 (1965).

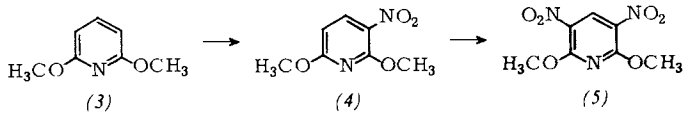
[9] *A. I. Gel'bshtein, G. G. Shcheglova,* and *M. I. Temkin,* Ž. neorg. Chim. *1,* 596 (1956).

[10] *C. Mantescu* and *A. T. Balaban,* Canad. J. Chem. *41,* 2120 (1963).

[11] *A. R. Katritzky* and *B. J. Ridgewell,* J. chem. Soc. (London) *1963,* 3882.

[12] *P. B. de la Mare* and *J. Ridd:* Aromatic Substitution. Butterworths, London 1959, p. 64.

[13] *C. D. Johnson, A. R. Katritzky,* and *M. Viney,* J. chem. Soc. (London), in press.



(3) (4) (5)

sufficient of the free base of *(4)* is present for it to compete successfully with the corresponding conjugate acid in the second nitration stage.

Fig. 4 also shows a "corrected" line which has been obtained from the conjugate acid curve by incorporating the concentration of free base, assuming that it is still a Hammett base at these acidities. This closely parallels the curve obtained for 3-nitro-2,6-dimethoxypyridine, indicating that the latter undergoes further nitration *via* the free base, or conversely, we may consider it as an indication that pyridine compounds follow the Hammett acidity function in very strong sulfuric acid medium.

By measuring the rates of nitration of 1,3-dichloro- and 1,3-dimethoxy-benzene, the deactivation relative to benzene of the $\rangle N$ "substituent" may be calculated. These rates have been measured, giving values of

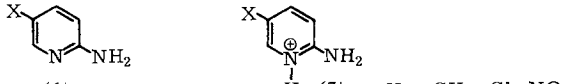
$$\log \frac{k_2\,(\text{dichlorobenzene})}{k_2\,(\text{dichloropyridine})} = 1.5 \text{ and } \log \frac{k_2\,(\text{dimethoxybenzene})}{k_2\,(\text{dimethoxypyridine})} = 2.3;$$

where k_2 is the bimolecular rate constant.

These values are far smaller than is expected, and suggest that the same substituent may exert a different mesomeric effect in the pyridine than in the benzene system.

3. Bromination [14]

5-Substituted 2-aminopyridines *(6)* are brominated smoothly at the 3-position in aqueous sulfuric acid and the rates may be conveniently measured by the decrease in the bromine/bromide potential. At acidities in the range +0.5 (pH) to −3.5 (H_0) straight line rate profiles with approximately unit slopes are found, indicating that bromination is occuring on the free base species *(6)*, and not on the conjugate acids *(7)*.



(6) (7) X = CH_3, Cl, NO_2

By comparison with corresponding *para*-substituted anilines, it is found that the $\rangle N$ "substituent" deactivates by a factor of *ca.* 0.54 for this particular reaction [15].

Numerous examples of other electrophilic substitution reactions are known to occur in pyridines, but no kinetic work has been carried out on them. The qualitative work reported has been well reviewed by *Abramovitch* [5] and includes sulfonation, mercuration, nitration and diazo coupling.

B. Pyridine *N*-Oxides

The discovery by *Ochiai* [16] that pyridine *N*-oxide is easily nitrated in the 4-position was one of the most important discoveries in pyridine chemistry, and led to further work on the electrophilic substitution reactions of pyridine *N*-oxides [5, 17].

The electrophilic substitutions [16] of pyridine *N*-oxide to yield the 4-nitro derivative on nitration, but the 3-sulfonic acid on sulfonation, has given rise to some speculation. Kinetic evidence is now available which



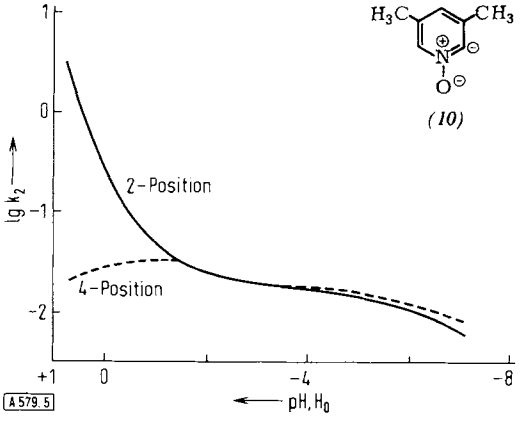
(8) (9)

proves that 4 substitution is a reaction of the free base *(8)*, and that 3 substitution occurs on the conjugate acid *(9)*. This evidence is detailed below.

1. Acid-Catalysed Hydrogen Exchange [19, 20]

Hydrogen exchange in 2,4,6 trimethylpyridine *N*-oxide was found to proceed smoothly in the 3- and 5-positions at 200 °C without decomposition. Plotting log k against H_0 gave a slope of 0.35 which, although less than the slopes for the pyridine series, nevertheless suggests that exchange proceeds through the conjugate acid. Entropies of activation are consistent with this conclusion. Attempts to measure the exchange on 1-methoxy-2,4,6-trimethylpyridinium ion failed due to decomposition of this substrate. 2,6-Dimethylpyridine *N*-oxide proved difficult to study because of concurrent decomposition; however, exchange was shown to occur in the 3-position at an H_0 of −8.15. There is some indication from the NMR spectrum that at sufficiently low acidities there is a change in mechanism leading to exchange in the 4-position.

3,5-Dimethylpyridine *N*-oxide was found to undergo ready exchange of the 2- and 4-position protons.



(10)

Fig. 5. Rate profile for the acid-catalysed hydrogen exchange of 3,5-dimethylpyridine *N*-oxide.

[14] *P. J. Brignell, P. E. Jones,* and *A. R. Katritzky,* unpublished work.

[15] *R. P. Bell* and *E. N. Ramsden,* J. chem. Soc. (London) *1958,* 161; *R. P. Bell* and *T. Spencer, ibid. 1959,* 1156; *R. P. Bell* and *D. J. Rawlinson, ibid. 1961,* 63.

[16] *E. Ochiai,* J. org. Chemistry *18,* 534 (1953); *A. R. Katritzky,* Quart. Rev. (Chem. Soc., London) *10,* 395 (1956).

[17] *A. R. Katritzky* and *J. M. Lagowski*: *N*-Oxides. Methuen, London, in press.

[18] *T. Okamoto* and *T. Kawazoe,* Bull. chem. Soc. Japan *1964,* 1384.

[19] *C. D. Johnson, A. R. Katritzky,* and *A. White,* J. chem. Soc. (London), in press.

[20] *A. R. Katritzky, B. J. Ridgewell,* and *A. M. White,* Chem. and Ind. *1964,* 1576.

Exchange rates for these positions vary little with acidity (Fig. 5); the rate profiles rescemble that for 4-pyridone (Fig. 7), which is known to exchange as the free base (see section C 1). At low acidities the exchange rate at the 2-position increases rapidly, probably due to the formation of increasing amounts of zwitterions of type X; similar zwitterions are formed by deprotonation of pyridine *N*-oxide itself [18].

Comparison of rates of exchange of 2,4,6-trimethylpyridine and 2,4,6-trimethylpyridine *N*-oxide indicates that $\diagdown N^{\oplus}-OH$ is slightly more deactivating than $\diagdown N^{+}H$; this is probably due to the electron-attracting effect of the hydroxyl group [20].

Preliminary studies have also been made on 3-hydroxypyridine, for which the rate profile shows that reaction proceeds *via* the free base. It is not yet certain, however, whether the 2- or 6-hydrogen is exchanging [19]. 3,5-Dimethoxypyridine *N*-oxide exchanges in the 2-position; below about H_0 −3.5, the reaction proceeds *via* the free base, and at higher acidities on the conjugate acid [19].

2. Nitration

Schofield has shown that the *N*-methoxypyridinium cation does not undergo nitration under the conditions which allow easy reaction of pyridine *N*-oxide and concluded that the latter is nitrated as the free base [21].

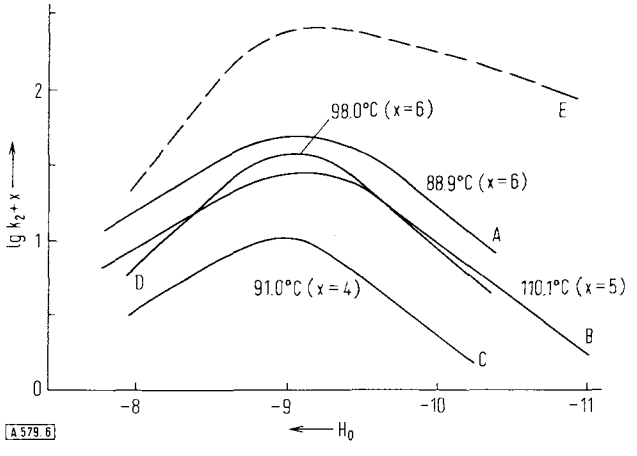
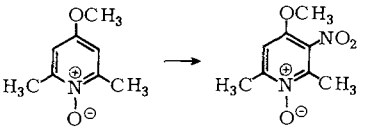


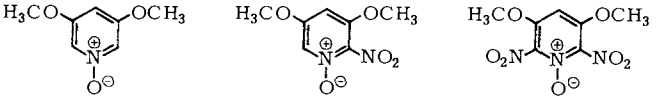
Fig. 6. Rate profile for the nitration of pyridine *N*-oxides [A: 2,6-dichloropyridine *N*-oxide; B: pyridine *N*-oxide; C: 3,5-dimethylpyridine *N*-oxide; D: 3,5-dichloropyridine *N*-oxide]. The broken curve represents the corrected rate profile (H_A function) for 2,6-dichloropyridine *N*-oxide.

The rate profiles have been measured (Fig. 5) [22] for the nitration of 2,6-dichloro-, 3,5-dichloro-, and 3,5-dimethylpyridine *N*-oxide together with that for the parent compound. A recent paper [8] indicates that pyridine *N*-oxides are Hammett bases; a reappraisal of this work involving pyridine *N*-oxides of much lower basicity than those originally reported modified this conclusion and showed that the pyridine *N*-oxides follow approximately the H_A function [25]. Adjustment of the rate profiles (Fig. 6), using this information to correct for the variation in concentration of free base, gives a curve which is similar in shape to that obtained for the concentration of nitronium ion, confirming reaction *via* the free base.



(11) *(12)*

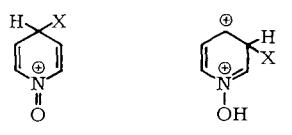
Nitration of a pyridine *N*-oxide in the 3-position was achieved in the case of the 2,6-dimethyl-4-methoxy derivative *(11)* → *(12)*; here the rate profiles indicate [13] nitration on the conjugate acid. The partial rate factor for nitration at the 4-position in pyridine-*N*-oxide is estimated as 10^{-4} [21]. Nitration in the 2-position has also been achieved [21a,22] in the case of 3,5-dimethoxypyridine *N*-oxide *(13)*. The 3,5-dimethoxy-2-nitropyridine *N*-oxide *(14)* then undergoes 6- rather than 4-nitration to yield the 2,6-dinitro compound *(15)*. Rate profile data indicate that reaction in both cases is *via* the conjugate acid.



(13) *(14)* *(15)*

3. Substitution Orientation

The nitration of pyridine *N*-oxides occurs preferentially in the 4-position while the slower, and therefore usually more selective, reaction of electrophilic hydrogen exchange attacks the more abundant but less reactive conjugate acid molecule in the 3-position. A possible explanation for this difference in substitution orientation is that the electron withdrawing effect of the nitro group in the Wheland intermediate *(16)* for 4-substitution is acceptable, whereas this inductive effect causes a large decrease in stability for the doubly-charged Wheland intermediate *(17)* for 3 substitution.



(16) *(17)*

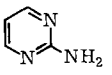
In these reactions, the transition state is probably close to the Wheland intermediate, and it could be that the inductive effects mentioned cause nitration to proceed *via (16)* whereas acid-catalysed hydrogen exchange can occur *via (17)*.

[21] *R. B. Moodie, K. Schofield,* and *M. J. Williamson,* Chem. and Ind., *1964,* 1577.

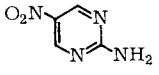
[21a] *H. J. den Hertog, M. van Ammers,* and *S. Schukking,* Recueil Trav. chim. Pays Bas *74,* 1171 (1955).

[22] *C. D. Johnson, A. R. Katritzky,* and *N. Shakir,* J. chem. Soc. (London), in press.

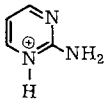
As a test of this hypothesis we[23] measured the first and second pK_a values of the pyrimidines *(18)* and *(19)*. The structure of the mono- and di-cations are of types *(20)* and *(21)*[23a]; a larger effect of the nitro group on the second pK_a than on the first pK_a would be expected if the above hypothesis were valid. The effect on the second pK_a due to the nitro group is 1.0 pK unit greater than its effect on the first pK_a, which is in the right direction, but smaller than expected.



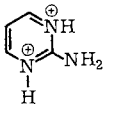
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(19)



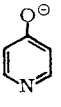
(20)



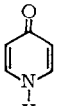
(21)

C. Pyridones and Pyrones[24,26]

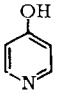
The mechanism of substitution of the pyridones is of particular interest both because of the ease with which such compounds are attacked by electrophiles and because of the large number of forms which could undergo reaction. For 4-pyridone these include the anion *(22)*, the oxo form *(23)*, the hydroxy form *(24)* and the cation *(25)*.



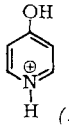
(22)



(23)



(24)



(25)

1. Acid-Catalysed Hydrogen Exchange

Rate profiles for the deuteration of 4-pyridone at two temperatures (Fig. 7) show that the rate varies by less than a factor of 4 over 14 logarithm units of acidity (pH=4 to H_0 =−10). This indicates that the reaction proceeds *via* a neutral form of pyridone; a conclusion which is supported by the low entropy of activation (*ca.* −8. e.u.).

The rate profile of 1-methyl-4-pyridone (Fig. 7) is similar to that of 4-pyridone, whereas 4-methoxypyridine does not react under these conditions: these

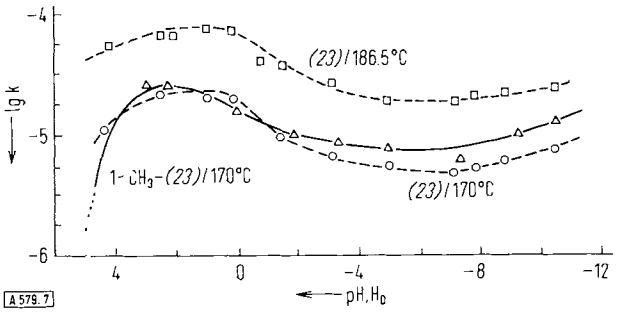
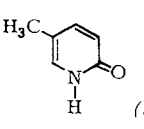


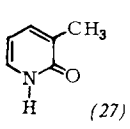
Fig. 7. Rate profile for the acid-catalysed hydrogen exchange of 4-pyridone *(23)* and for 1-methyl-4-pyridone (continuous line).

facts show that 4-pyridone undergoes reaction on the oxo form *(22)*. The hydroxy form is further excluded by encounter rate calculations, which were made assuming that *N*-protonation of the hydroxy form *(24)* would follow the Hammett acidity function and that *O*-protonation of the oxo form *(19)* would follow the amide acidity function (H_A)[25].

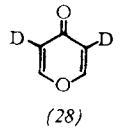
Consideration of the rate of exchange of the phenoxide anion shows that the introduction of $NH^{\oplus}$ for CH in this ion *meta* to the reacting site lowers the rate by a factor of about 10^7.



(26)



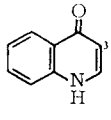
(27)



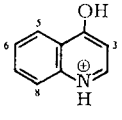
(28)

Preliminary studies of deuterium exchange in the 3-position of 5-methyl-2-pyridone *(26)* and in the 5-position of 3-methyl-2-pyridone *(27)* indicate that in both these cases also the reaction proceeds *via* the neutral oxo form shown.

It has also been shown that 4-quinolone at low acidities (H_0 <−7) exchanges as the neutral species *(29)* at the 3-position. On increasing the acidity, reaction *via* the conjugate acid occurs successively in the 3-, 6-, 8-, and 5-positions *(30)*.



(29)



(30)

For 2,6-dimethyl-4-pyridone there is a changeover from conjugate acid to free base reaction on lowering the acidity to H_0 = −3 which indicates a deactivation of *ca.* 10^7 on protonation.

Investigation of the hydrogen-exchange reactions of pyrones and thiopyrones is also being carried out[26].

4-Pyrone is converted to the 3,5-dideuterio-derivative *(28)* in neutral or weakly acidic solution; however, this reaction is not a simple electrophilic substitution[27], but proceeds *via* a base-catalysed mechanism.

[23] *P. J. Brignell, A. R. Katritzky,* and *O. Tarhan,* unpublished work.

[23a] *A. R. Katritzky* and *J. M. Lagowski* in *A. R. Katritzky*: Advances in Heterocyclic Chemistry. Academic Press, New York-London 1963, Vol. 1, p. 339.

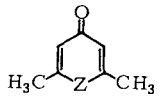
[24] *P. Bellingham, C. D. Johnson,* and *A. R. Katritzky,* Chem. and Ind., 1384 (1965).

[25] *A. R. Katritzky, A. J. Waring,* and *K. Yates,* Tetrahedron *19*, 465 (1963).

[26] *P. Bellingham, C. D. Johnson,* and *A. R. Katritzky,* J. chem. Soc. (London), in press.

[27] *P. Beak* and *G. A. Carls,* J. org. Chemistry *29*, 2678 (1964); *D. W. Mayo, P. J. Sapienza, R. C. Lord,* and *W. D. Phillips, ibid. 29*, 2682 (1964).

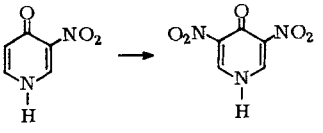
Preliminary results indicate that compounds *(31a)* and *(31b)* exchange as the conjugate acids.



(31a), Z = O
(31b), Z = S

2. Nitration [23]

4-Pyridone can be nitrated in mixed acids to yield successively 3-nitro- *(32)* and then 3,5-dinitro-4-pyridone. A spectrophotometric study of the first nitration gave a rate profile (Fig. 8) indicating reaction



(32) *(33)*

on a species whose concentration was not altering significantly in the range $H_0 = -8.2$ to -10.5. This can only be the conjugate acid *(25)*; a conclusion supported by the large negative entropy of activation (−20.3 e.u.) found from an Arrhenius plot at $H_0 = -9.33$. The nitration rate was found to be comparable with that for the nitration of 4-methoxypyridine, and that for 1-methyl-4-pyridone.

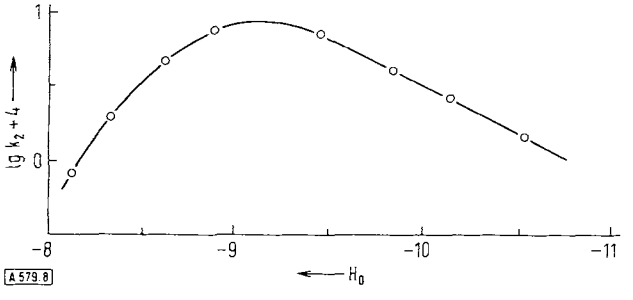


Fig. 8. Rate profile for the nitration of 4-pyridone *(23)* at 86 °C.

It is of interest that 4-pyridone is nitrated as the conjugate acid within an acidity range in which it undergoes acid-catalysed hydrogen exchange as the free base. This must be due to the greater selectivity of the hydrogen-exchange reaction compared to the nitration which involves the more reactive $NO_2^{\oplus}$ ion. This behavior serves to emphasize the abnormality of the reverse sequence already described for the pyridine *N*-oxides.

D. Polycyclic Heteroaromatic Compounds with Six-Membered Rings

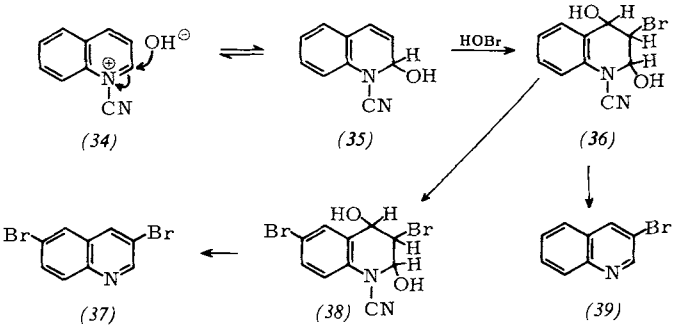
Much work has been done in determining the position of substitution in polycyclic heteroaromatics, and in some cases accurate ratios of the various isomers formed have been determined. The positions of substitution within individual compounds have been correlated with considerable success by *Dewar* and *Maitlis* [28] using MO methods, but this work is outside the scope of the present review. Data enabling the determination of the nature of the species reacting, and absolute partial rate factors are very much more sparse. In addition, as discussed in detail by *Ridd* [4], only very limited success has attended attempts to correlate available rate data with MO parameters.

Austin and *Ridd* [29] have examined the kinetics of nitration of quinoline, which yields 5- and 8-nitroquinoline in approximately equal amounts. The slope of the rate profile, encounter-rate calculations, and the entropy of activation (−19.3 e.u.) in reactions with 85–98% sulfuric acid, all indicate that the reaction proceeds *via* the conjugate acid. Stepwise comparisons led to partial rate factors of *ca.* 10^{-7}. Independent work by *Schofield et al.* confirmed these conclusions by investigations in the lower acidity region (71–84% sulfuric acid); they also reported results for *N*-methyl quinolinium ions [21]. Similar work [21,30] with isoquinoline and the *N*-methylisoquinolinium cation again indicated reaction *via* the conjugate acid.

Schofield has also examined the nitration in the 5- and 8-positions of isoquinoline *N*-oxide in the acidity range 76.4–83.1% sulfuric acid. This compound has a rate profile which indicates reaction *via* the *N*-hydroxyisoquinolinium cation; this is borne out by the similar kinetics found for *N*-methoxyisoquinolinium perchlorate [21].

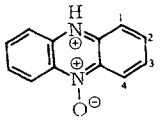
Johnson and *Ridd* [31] have clarified the mechanism whereby *N*-cyanoquinolinium ion *(34)* with aqueous solutions of bromine gives 3-bromoquinoline *(39)*. The reaction involves intermediate formation of the pseudo-base 1-cyano-1,2-dihydro-2-hydroxyquinoline *(35)*, which then undergoes bromination *via* an addition elimination (*(35)* → *(36)*) rather than a substitution mechanism, although straightforward electrophilic substitution may occur with excess bromine in the benzene ring, finally yielding 3,6-dibromoquinoline *(37)*.

J. Ridd et al. have demonstrated a 100-fold enhancement of the rate of nitration of *o*-phenanthroline [32] at



[28] *M. J. S. Dewar* and *P. M. Maitlis*, J. chem. Soc. (London) *1957*, 2521.
[29] *M. W. Austin* and *J. H. Ridd*, J. chem. Soc. (London), 4204 (1963).
[30] *R. B. Moodie*, *K. Schofield*, and *M. J. Williamson*, Tetrahedron *20*, Suppl. *1*, 89 (1964).
[31] *M. D. Johnson* and *J. H. Ridd*, J. chem. Soc. (London) *1962*, 283, 291.
[32] *A. F. Richards*, *J. H. Ridd*, and *M. L. Tobe*, Chem. and Ind. *1963*, 1727.

the 5-position over that of the parent compound by coordination with cobalt(III) cations. Studies are in progress to determine whether the difference in reactivity derives from reduction of the effective charge on the nitrogen or whether there is also an important degree of π-electron donation to the ring from the filled Co d_e orbitals.



(40)

Phenazine 5-oxide undergoes nitration at the 3-(and to a minor extent the 1-) position; kinetic criteria show that the monocation *(40)* is the reactive species [33].

[33] *A. R. Katritzky* and *B. Swedlund*, unpublished.

E. Conclusion

Very much remains to be accomplished. On the experimental side it is necessary to gain quantitative data as to the effect on rate of substitution (by a wide variety of electrophiles) of the replacement of a CH-group by an uncharged nitrogen atom, by various types of group incorporating a partially charged nitrogen ($N^{\oplus}H$, $N^{\oplus}-O^{\ominus}$, $N^{\oplus}-R$, $N^{\oplus}-OH$, *etc.*), and by charged $=S^{\oplus}-$ or $=O^{\oplus}-$. Only when more is known of the effects of these replacements towards the *ortho*, *meta*, and *para* positions, as well as effects relayed from one ring to another, will it be possible to develop and test the theoretical treatments, and, hopefully, to gain a real understanding of the field.

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German version: Angew. Chem. 79, 629 (1967)

Acetylcholinesterase[**]

BY N. ENGELHARD, K. PRCHAL, AND M. NENNER [*]

Acetylcholinesterase plays a vital part in the functioning of nerves, and serious physiological damage arises from its blockage by esters of phosphonic and phosphoric acid used e.g. in pesticides. The properties and the mechanism of action of acetylcholinesterase, which show many similarities to those of other hydrolases, are described. Therapeutic agents (reactivators) for the toxic phosphorus compounds specified are also discussed.

A. Introduction

The mechanism by which impulses are conducted along nerves and transferred from one nerve to another or to an end organ entails a complex interplay of electrical and chemical processes [1–3].

A nerve cell or neuron ordinarily consists of a nucleated cytoplast, short and extensively branched fibers (dendrites) projecting from it together with a filament (axon or neurite), up to 1 m long and generally branched at its end, and finally a membrane enveloping all these. During the conduction of an exciting impulse, an electric potential (action potential) travels along the neuron. This potential is produced by selective diffusion of Na^+ and K^+ through the membrane, as a result of which the concentration of these ions is changed on either side of the membrane. The transfer of an impulse to other excitable elements (neurons, muscles, or glands) occurs at meeting places (synapses) between the axons of one nerve

[*] Dr. N. Engelhard
Physiologisch-chemisches Institut der Universität Göttingen, Strahlenbiochemisches Laboratorium
Present address:
Merle Allee 45
5301 Röttgen (Germany)
Dipl.-Chem. K. Prchal
Breddestr. 17
43 Essen (Germany)
Dipl.-Chem. M. Nenner
Physiologisch-chemisches Institut der Universität Göttingen, Strahlenbiochemisches Laboratorium
Humboldtallee 7
34 Göttingen (Germany)

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[1] For reviews of neuro-physiology and -chemistry, see: a) *J. P. Schadé* and *D. H. Ford*: Basic neurology, an introduction to the structure and function of the nervous system. Elsevier, Amsterdam-London-New York 1965; b) *W. Blasius* in *Landois-Rosemann*: Lehrbuch der Physiologie des Menschen, 28th Edit., Urban u. Schwarzenberg, München-Berlin 1962, Vol. 2, p. 629; c) *H.-D. Henatsch* in [1b], Vol. 2, p. 547; d) *A. v. Muralt*: Die Signalübermittlung im Nerven. Birkhäuser, Basel 1946; e) Neue Ergebnisse der Nervenphysiologie. Springer, Berlin-Göttingen-Heidelberg 1958; f) *J. C. Eccles*, Ergebn. Physiol., biol. Chem. exp. Pharmakol. *51*, 299 (1961); g) The physiology of synapses. Springer, Berlin-Göttingen-Heidelberg 1964; h) *A. L. Hodgkin*, Angew. Chem. *76*, 661 (1964); i) *A. F. Huxley*, *ibid.* *76*, 668 (1964); k) *J. C. Eccles*, *ibid.* *76*, 674 (1964); l) *J. del Castillo* and *B. Katz*, Progr. Biophysics biophysic. Chem. *6*, 122 (1956), cf. p. 126; m) *C. G. Schmidt* in *B. Flaschenträger* and *E. Lehnartz*: Physiologische Chemie. Springer, Berlin-Göttingen-Heidelberg 1956, Vol. II/2a, p. 613; n) *H. McIlwain*, Annu. Rep. Progr. Chem. 1960, *57*, 367 (1961); o) *R. Whittam*, *ibid.* *57*, 379 (1961); p) Lectures delivered at "Symposium on the function of acetylcholine as a synaptic transmitter". Vancouver 1962, Canad. J. Biochem. Physiol. *41*, 2553–2653 (1963).

[2] a) *D. Nachmansohn*, Ergebn. Physiol., biol. Chem. exp. Pharmakol. *48*, 575 (1955); b) Chemical and molecular basis of nerve activity. Academic Press, New York-London 1959; c) Bull. Soc. Chim. biol. *45*, 29 (1963); d) in *M. Sela*: New perspectives in biology. Elsevier, Amsterdam-London-New York 1964, p. 176.

[3] *G. B. Koelle* in *Heffter-Heubners* Handbuch der experimentellen Pharmakologie. Springer, Berlin-Göttingen-Heidelberg 1963, Supplement, Vol. 15.

cell and appropriate receptors (*e.g.* dendrites) of another. The presynaptic membrane of the ramified axon accommodates minute vesicles, and it is probable that these vesicles, actuated by the action potential, release a chemical into the 100–200 Å wide synaptic gap between the presynaptic and the postsynaptic membrane (this chemical has been variously named action substance, transmitter substance, neurohumoral transmitter, *etc*). This substance thus reaches the receptor organ of the other excitable element and causes – *via* still unknown specific receptors – a very fast change in the ion-permeability of the membrane, which in turn produces an electric potential.

The first action substance was found by *Loewi* in 1921 during experiments on the *Nervus vagosympathicus* of excised frog's heart [4]. It was named 'vagus substance' and later identified [6, 7] as *O*-acetylcholine *(1)*, whose action on blood

$$(CH_3)_3\overset{\oplus}{N}-CH_2-CH_2-O-CO-CH_3\overset{\ominus}{O}H \qquad (1)$$

pressure, heart, and nerves had been known since 1914 [5]. Acetylcholine was subsequently shown to be the essential action substance of the parasympathetic and motor nerves, as well as of the sympathetic nerve fibers from the brain and spinal cord to the nerve ganglia. This group of nerves is therefore described as cholinergic. The other (postganglionic) nerves of the sympathetic nervous system are described as adrenergic, because their action substances are adrenalin and noradrenalin (sympathin I and E).

Not much is yet known of the manner in which acetylcholine affects the permeability of the membrane. According to *Nachmansohn*'s theory [2, 8], acetylcholine is responsible both for the transfer of impulses across the synaptic junction, and for their conduction along the neuron membrane. However, this second function has been questioned, and the theory of *Dale et al.* [11], according to which acetylcholine is involved only in the transfer of impulses across the synaptic junction, is now preferred.

According to an interesting theory proposed by *Koelle* [9], the action potential actuates the release of only a small amount of acetylcholine on the presynaptic membranes of nerves, probably including non-cholinergic ones, and this small amount then triggers off the liberation of a larger amount of acetylcholine in cholinergic nerves, or the liberation of some other action substance in non-cholinergic ones, the excitation being only then transferred to the postsynaptic membrane *via* the synaptic gap.

Before a second impulse can be transmitted the original state of the membranes must be re-established, and for this purpose the acetylcholine must be rapidly eliminated in a refractory phase. This is achieved by a highly active enzyme acetylcholinesterase (acetylcholine acetylhydrolase [3.1.1.7]) which hydrolyses acetylcholine within a few microseconds to acetic acid and choline having hardly any physiological action. In the presence of ATP and CoA, acetylcholine is resynthesized by the enzyme acetyl-CoA:choline-*O*-acetyltransferase [2.3.1.6], also called choline acetylase, discovered in 1943 by *Nachmansohn* and *Machado* [10]. Acetylcholine is finally stored in an inactive form and made ready for being triggered off a second time by a new action potential [2, 8, 10, 11] (see Fig. 1).

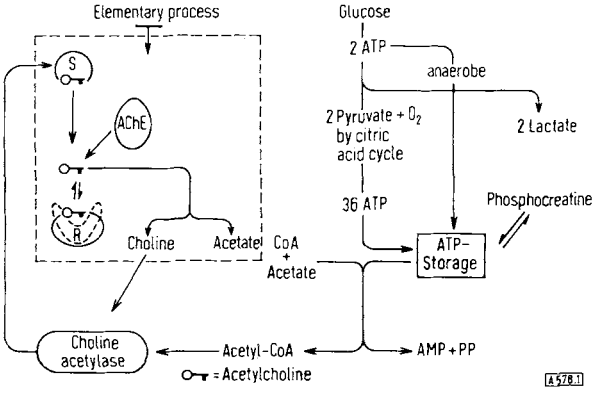
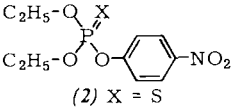
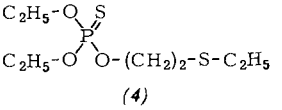


Fig. 1. Action of acetylcholine and its esterase in correlation with the metabolism (after *Nachmansohn* [2b]; cf. also [1a], p. 207). AChE = acetylcholinesterase; R = receptor protein; S = storage protein; The dotted boomerang in R indicates how this protein changes its shape, as a result of which the ion-permeability of the membrane is altered.

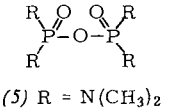
When the action of acetylcholinesterase is blocked, acetylcholine accumulates, and the original state of the membrane cannot be re-established. This leads to severe and often fatal endogenous poisoning involving *e.g.* irritation and paralysis. Death is generally caused by respiratory paralysis [3, 12, 13].



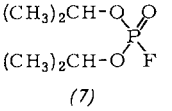
(2) X = S
(3) X = O



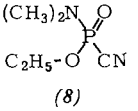
(4)



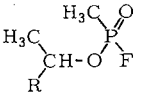
(5) R = $N(CH_3)_2$
(6) R = $O-C_2H_5$



(7)



(8)



(9) R = CH_3
(10) R = $C(CH_3)_3$

[4] *O. Loewi*, Pflügers Arch. ges. Physiol. Menschen Tiere *189*, 239 (1921).

[5] a) *H. H. Dale*, J. Physiology *48*, Proc. III (1914); b) *R. Hunt*, Amer. J. Physiol. *45*, 197, 231 (1918).

[6] a) *W. R. Witanowski*, Pflügers Arch. ges. Physiol. Menschen Tiere *208*, 694 (1925); b) *O. Loewi* and *E. Navratil*, *ibid. 214*, 678, 689 (1926).

[7] *E. Engelhart* and *O. Loewi*, Naunyn-Schmiedebergs Arch. exp. Pathol. Pharmakol. *150*, 1 (1930).

[8] *D. Nachmansohn* in [3], p. 701.

[9] a) *G. B. Koelle*, J. Pharmacy Pharmacol. *14*, 65 (1962); b) *D. N. McKinstry*, *E. Koenig*, *W. A. Koelle*, and *G. B. Koelle*, Canad. J. Biochem. Physiol. *41*, 2599 (1963).

[10] a) *D. Nachmansohn* and *A. L. Machado*, J. Neurophysiology *6*, 397 (1943); b) *D. Nachmansohn* in [3], p. 40.

[11] *C. Hebb* in [3], p. 55.

[12] a) *B. C. Saunders*: Some aspects of the chemistry and toxic action of organic compounds containing phosphorus and fluorine. University Press, Cambridge 1957; b) *R. D. O'Brien*: Toxic phosphorus esters. Academic Press, New York-London 1960; c) *R. D. O'Brien* in *R. M. Hochster*, and *J. H. Quastel*: Metabolic inhibitors. Academic Press, New York-London 1963, Vol. 2, p. 205; d) *D. F. Heath*: Organophosphorus poisons, anticholinesterases and related compounds. Pergamon Press, Oxford-London-New York-Paris 1961.

[13] *W. D. Erdmann* and *L. Lendle*, Ergebn. inneren Med. Kinderheilkunde (N.F.) *10*, 104 (1958).

The most dangerous inhibitors of acetylcholinesterase are "alkyl phosphates", which are mixed anhydrides of phosphonic (or phosphoric) acid esters formed with organic or inorganic acids[12,14]. These compounds include pesticides such as Parathion (E 605®) *(2)*, Systox® *(4)*, OMPA (Schradan) *(5)*, TEPP *(6)*, as well as the highly active chemical warfare agents (nerve gases) DFP *(7)*, Tabun *(8)*, Sarin *(9)*, and Soman *(10)*. Some alkyl phosphates have been introduced in therapy; thus, Paraoxon (E 600, Mintacol®) *(3)* is used as a miotic (pupillary contractant) in ophthalmology.

Acetylcholinesterase has been the subject of intensive research, promoted partly by the investigation of its physiological importance and partly by the need for an efficient therapeutic method against cases of poisoning by alkyl phosphates[13]. The main results of this work will be summarized below.

B. General Properties of Acetylcholinesterase [2,3,15–17]

I. Discovery and Characterization

Loewi[7] suggested as early as 1926 that acetylcholine is rapidly hydrolysed by an esterase in the blood, thus making its identification difficult. This was subsequently confirmed, and the enzymes responsible for this hydrolysis were detected in blood and in practically all animal tissues and organs[18]. In 1932, *Stedman, Stedman*, and *Easson*[19] succeeded in concentrating by a factor of about seven an esterase present in horse serum, which rapidly hydrolysed choline esters and was regarded as the enzyme responsible for the hydrolysis of acetylcholine. However, *Alles* and *Hawes*[20] later (1940/1941) found that the real enzyme, specific for acetylcholine, is another esterase present also in erythrocytes, one that is identical with neural acetylcholinesterase but different from the acetylcholinesterase in the serum.

As a result of much subsequent investigation, we now describe as cholinesterase in the broader sense all hydrolases that cleave choline esters and are inhibited by physostigmine (eserine) in a concentration of 10^{-5} M. Cholinesterases are subdivided into the following two types[15b,15d,21]:

a) Acetylcholine acetylhydrolase [3.1.1.7][22], acetylcholinesterase which is the acetylcholine-cleaving enzyme, and has variously been called in earlier literature erythrocyte-cholinesterase (e-type cholinesterase), cholinesterase I, and true or specific cholinesterase; this enzyme will be denoted by AChE.

b) Acetylcholine acylhydrolase [3.1.1.8][22], which has also been called cholinesterase (ChE), pseudocholinesterase, serumcholinesterase (s-type cholinesterase), non-specific cholinesterase, cholinesterase II, X-cholinesterase, and by names such as propionylcholinesterase and butyrylcholinesterase; this enzyme will be denoted by ChE.

It is often difficult to decide which type of cholinesterase one is dealing with, because the enzyme preparations are frequently mixtures of both types.

The above two types differ in the following respects[15d,21,24–26]:

1. The activity of AChE on homologous *O*-acylcholines decreases in the series acetyl $\geqslant$ propionyl $>$ butyryl, whilst the activity of ChE increases along the same series.

2. Acetylcholine concentrations exceeding about 3×10^{-3} M inhibit AChE, whereas ChE is not inhibited even by much higher concentrations (10^{-1} M).

3. AChE and ChE differ in their susceptibility to inhibition by selective inhibitors – a particularly important distinction.

Only AChE seems to be responsible for the hydrolysis of acetylcholine in the body, and the physiological function of ChE is still unknown. Nor is it yet certain whether the same acetylcholinesterase is present in various organs and organisms, and the origin of extracts must always be known for accurate characterization.

1. Occurrence of Acetylcholinesterase[2,15,27]

Acetylcholinesterase is one of the most widely distributed enzymes in the animal kingdom, but it has not been found in plants, and its occurrence in unicellular organisms is questionable.

Acetylcholinesterase occurs in tissues particularly at those sites which need it for their biological function, though it has also been found in other places, where its physiological function and identity with neural acetylcholinesterase are uncertain. In man and most other mammals, such acetylcholinesterase is localized almost entirely in the erythrocytes, whilst the serum (except bovine serum) is rich in cholinesterase. In fishes and birds, on the other hand, the erythrocytes are generally poor whilst the serum is rich in acetylcholinesterase. Hydrolases of the AChE type are also found in the blood of

[14] *G. Schrader*: Die Entwicklung neuer insektizider Phosphorsäure-Ester. 3rd. Edit., Verlag Chemie, Weinheim/Bergstr. 1963.

[15] a) *K.-B.* Augustinsson, Acta physiol. scand. *15*, Suppl. *52*, 1 (1948); b) in *J. B. Sumner* and *K. Myrbäck*: The enzymes. Academic Press, New York 1950, Vol. I/1, p. 443; c) *I. B. Wilson* in *P. D. Boyer, H. Lardy*, and *K. Myrbäck*: The enzymes. 2nd. Edit., Academic Press, New York-London 1960, Vol. 4/A, p. 501; d) *K.-B. Augustinsson* in [15c], Vol. 4/A, p. 521; e) *D. Nachmansohn* in *G. Pincus* and *K. V. Thimann*: The hormones. Academic Press, New York 1950, Vol. 2, p. 515; f) *R. Ammon* in *R. Ammon*, and *W. Dirscherl*: Fermente, Hormone, Vitamine. G. Thieme, Stuttgart 1959, Vol. 1, p. 128.

[16] *D. Nachmansohn* and *I. B. Wilson*, Advances in Enzymol. *12*, 259 (1951).

[17] *R. M. Krupka*, Canad. J. Biochem. *42*, 677 (1964).

[18] a) *E. Abderhalden* and *H. Paffrath*, Fermentforschg. *8*, 299 (1926); b) *F. Plattner et al.*, Arbeiten in Pflügers Arch. ges. Physol. Menschen Tiere *214*, 112 (1926) to *236*, 175 (1935); c) *K. Matthes*, J. Physiology *70*, 338 (1930).

[19] *Edgar Stedman, Ellen Stedman*, and *L. H. Easson*, Biochem. J. *26*, 2056 (1932).

[20] a) *G. A. Alles* and *R. C. Hawes*, J. biol. Chemistry *133*, 375 (1940); b) *R. C. Hawes* and *G. A. Alles*, J. Lab. clin. Med. *26*, 845 (1941); c) Cf. also *D. Richter* and *P. G. Croft*, Biochem. J. *36*, 746 (1942).

[21] *K.-B. Augustinsson* in [3], p. 93.

[22] Systematic name [23].

[23] Enzyme nomenclature, recommendations (1964) of the International Union of Biochemistry on the nomenclature and classification of enzymes, together with their units and the symbols of enzyme kinetics, in *M. Florkin* and *E. H. Stotz*: Comprehensive biochemistry. 2nd. Edit., Elsevier, Amsterdam-London-New York 1965, Vol. 13.

[24] *D. Nachmansohn* and *M. A. Rothenberg*, J. biol. Chemistry *158*, 653 (1945).

[25] *K.-B. Augustinsson*, Arch. Biochemistry *23*, 111 (1949).

[26] *K.-B. Augustinsson* in *D. Glick*: Methods of biochemical analysis. Interscience, New York-London 1957, Vol. 5, p. 1.

[27] *G. B. Koelle* in [3], p. 187.

the edible snail [27a] and in the venom of some snakes such as the cobra.

Particularly significant is the AChE content of the electric organ of the electric eel *(Electrophorus electricus)* [28,29] (this organ is therefore the preferred starting material in the preparation of concentrates) and of varieties of torpedo fish *(Torpedo marmorata, T. oscellata,* and *T. occidentalis)*. This enzyme has also been detected in the cranial ganglia of cuttlefish *(Loligo pealii* and *Sepia officinalis)*.

2. Analytical Determination [21,26]

Kinetic studies and the determination of the acetylcholinesterase activity in biological fluids, homogenates, extracts, and enzyme preparations are based on determining the amount of the substrate that remains unchanged after incubation with the enzyme for a specified time, or else on determining the amount of the products formed by the enzymatic reaction (*e.g.* the amount of acetic acid formed when the substrate is acetylcholine which is preferred in this capacity, though other substrates can also be used). Owing to their inaccuracy, the biological methods often used earlier for the determination of unchanged acetylcholine have been abandoned.

Hestrin's [30] chemical microanalytical method is generally used, in which the unchanged acetylcholine reacts with an alkaline solution of hydroxylamine to give acetylhydroxamic acid, whose ferric iron complex is then determined photometrically. Amongst the many modifications of this method, those devised by *Pilz* [31] and by *Bockendahl* and *Ammon* [32] seem to be suitable for routine clinical tests.

Hestrin's method enables one to vary the conditions of incubation – which of course is essential for kinetic studies – but it is said to give values 15–20% low for the initial rate of the enzymatic reaction [33], and is therefore better reserved for rapid routine tests.

In a sensitive micro-scale method for the direct photometric determination of the reaction product [34,35], *S*-acetylthiocholine is used as a substrate and the resulting thiocholine is determined with the aid of 5,5′-dithiodi-(2-nitrobenzoic acid). This method is particularly suitable for continuous monitoring of the hydrolysis with acetylcholinesterase [35].

Ammon's much-used determination of acetylcholinesterase depends on manometric measurements, in a Warburg apparatus, of the carbon dioxide liberated from $NaHCO_3$ by acetic acid formed in the enzymatic reaction [32,36,37]. This method enables one to follow the course of the reaction on a single charge, and it can therefore be used for kinetic studies. For routine work, however, this technique is too time-consuming. In kinetic investigations, furthermore, it suffers from the disadvantage that the pH of the reaction mixture can hardly be varied.

Further methods are based on the colorimetric [38] or the electrometric [39] determination of the slight pH change caused by the liberated acetic acid in a buffered medium. The activity of the enzyme is then calculated from the pH change in unit time. Alternatively, the pH is kept constant by continuously neutralizing the acetic acid with NaOH solution from a burette [40], the titer being directly proportional to the amount of acetylcholine that is hydrolysed by the enzyme. An accurate and fast method based on the use of an automatic titrating and recording device (pH-stat) [41,42] enables a number of parameters, such as the pH, the temperature, and the type and the concentration of salts, substrates, and inhibitors, to be varied within wide limits in kinetic work. Methods suitable for cytological investigations have been summarized by *Koelle* [27].

3. Preparation of Acetylcholinesterase Concentrates [15a,15b,16,21,43]

Mammalian erythrocytes and the electric organs of certain fishes are generally used as the source for this purpose.

A difficulty encountered in the isolation from erythrocytes is that the enzyme probably adheres to the cell membrane [15a, 44]. To effect the necessary separation, *Augustinsson* [15a] used lysolecithin, *Cohen* and *Warringa* [45] a pancreas extract, and *Zittle et al.* [46] a surfactant, polyoxyethylene-sorbitan laurate (Tween 20). However, the best concentrates so far prepared from erythrocytes showed a specific activity [47] of only 42 [45], and the yields were low.

Much more highly concentrated samples have been prepared from the electric organ of the electric eel, in

[27a] *H. Bockendahl* and *Th.-M. Müller*, Hoppe-Seylers Z. physiol. Chem. *341*, 185 (1965).

[28] *H. Grundfest*, Progr. Biophysics biophysic. Chem. 7, 1 (1957).

[29] *C. Chagas* and *A. P. de Carvalho*: Bioelectrogenesis, a comparative survey of its mechanisms with particular emphasis on electric fishes. Elsevier, Amsterdam-London-New York-Princeton 1961.

[30] *S. Hestrin*, J. biol. Chemistry *180*, 249 (1949).

[31] *W. Pilz* in *H.-U. Bergmeyer*: Methoden der enzymatischen Analyse. Verlag Chemie, Weinheim/Bergstr. 1962, p. 765.

[32] *H. Bockendahl* and *R. Ammon* in [31], p. 771.

[33] *L. T. Kremzner* and *I. B. Wilson*, J. biol. Chemistry *238*, 1714 (1963).

[34] *P. J. Garry* and *J. I. Routh*, Clin. Chem. (New York) *11*, 91 (1965).

[35] *G. L. Ellman, K. D. Courtney, V. Andres jr.*, and *R. M. Featherstone*, Biochem. Pharmacol. 7, 88 (1961).

[36] *R. Ammon*, Pflügers Arch. ges. Physiol. Menschen Tiere *233*, 486 (1934).

[37] *R. F. Witter*, Toxicol. appl. Pharmacol. *4*, 313 (1962).

[38] *H. Croxatto, R. Croxatto*, and *F. Huidobro*, An. Acad. biol., Univ. Chile *3*, 55 (1939); Chem. Abstr. *38*, 5516 (1944).

[39] *H. O. Michel*, J. Lab. clin. Med. *34*, 1564 (1949).

[40] a) *D. Glick*, Biochem. J. *31*, 521 (1937); b) C. R. Trav. Lab. Carlsberg, Sér. chim. *21*, 225, 263 (1938).

[41] a) *C. F. Jacobsen* and *J. Léonis*, C. R. Trav. Lab. Carlsberg, Sér. chim. *27*, 333 (1951); b) *I. B. Wilson* and *E. Cabib*, J. Amer. chem. Soc. *76*, 5154 (1954); c) *J. B. Neilands* and *M. D. Cannon*, Analytic. Chem. *27*, 29 (1955); d) *L. Larsson* and *B. Hansen*, Svensk kem. Tidskr. *68*, 521 (1956); e) *L. W. Cunningham* in *K. Lang* and *E. Lehnartz*: Hoppe-Seyler/Thierfelder, Handbuch der physiologisch- und pathologisch-chemischen Analyse. 10th Edit., Springer, Berlin-Göttingen-Heidelberg-New York 1964, Vol. 6/A, p. 279.

[42] The theory of the pH-stat is discussed by *e.g. C. F. Jacobsen, J. Léonis, K. Linderstrøm-Lang*, and *M. Ottesen* in [26], Vol. 4, p. 171.

[43] *D. Nachmansohn* and *I. B. Wilson* in *S. P. Colowick* and *N. O. Kaplan*: Methods in enzymology. Academic Press, New York 1955, Vol. 1, p. 642.

[44] *S. Paléus*, Arch. Biochemistry *12*, 153 (1947).

[45] a) *J. A. Cohen* and *M. G. P. J. Warringa*, Biochim. biophysica Acta *10*, 195 (1953); b) *M. G. P. J. Warringa* and *J. A. Cohen, ibid. 16*, 300 (1955).

[46] a) *C. A. Zittle, E. S. Della Monica*, and *J. H. Custer*, Arch. Biochem. Biophysics *48*, 43 (1954); b) *C. A. Zittle, E. S. Della Monica, J. H. Custer*, and *R. Krikorian, ibid. 56*, 469 (1955).

[47] Definitions by [23]: Specific activity = number of enzyme units per mg of protein; Enzyme unit = amount of enzyme that converts in 1 min 1 μmole of substrate (here acetylcholine) under specified conditions (here generally at pH 7–7.5 and 37–38 °C).

which the specific activity is initially much higher. Thus, *Rothenberg* and *Nachmansohn* [43,48] obtained concentrates with specific activities of up to 7700. The value of 11000 (pH 7.0, 25 °C) subsequently reached by *Kremzner* and *Wilson* [33] corresponds to almost maximum purity. This was achieved by eluting the prepurified extracts [48] on the following columns in succession: benzyl-DEAE-cellulose, Sephadex G-200, Cellex P, and DEAE-cellulose (twice).

4. Physical and Kinetic Characteristics of Acetylcholinesterase

The values reported for the molecular weight of acetylcholinesterase vary between 70000 and 31 million. Even the extreme values appeared plausible, since they were obtained for samples which had been proved uniform by electrophoretic, chromatographic, and centrifugal analysis. However, the wide variations in the molecular weight cannot be explained even if one assumes that the samples were not pure and that there were variations according to the source of the enzyme. It might be proposed that the enzyme forms variously large associated or polymeric molecules, depending on the experimental conditions [46,48–51].

It has been shown [52] that samples with specific activities between 5000 and 11000 behave alike on sedimentation, although the less active ones of these can be separated chromatographically into several components. One may regard as the most reliable the values obtained by *Kremzner* and *Wilson* with a sample extracted from electric eels [33] and having a specific activity of 11000 (25 °C, pH 7) [52] (see Table 1).

The equivalent weight per site points to four sedimenting subunits. However, it is not yet clear whether these can dissociate and exhibit independent activity.

Table 1. Physical and kinetic characteristics of acetylcholinesterase.

Sedimentation constant $s_{20\,°C,\,w}$	10.8 S	[52]
Diffusion coefficient $D_{4\,°C}$	2.6×10^{-7} cm²sec⁻¹	[52]
Friction ratio f/f_0	≈ 1.25	[52]
Molecular weight		
by sedimentation and diffusion	≈ 230000	[52]
by gel filtration	≈ 250000	[52]
by activity per site [50]	> 240000	[52]
Equivalent weight per site	≈ 54000	[52]
UV Absorption spectrum	λ_{max} = 280 mμ (2.29) λ_{min} = 250 mμ (1.37) shoulders at 290, 278, and 258 mμ	[53]
Optimum pH	8.25 (8.0–8.5)	[54]
Michaelis constant K_m (automatic titrator, 15–35 °C)	1×10^{-4}	[55]
Activity per site [56]	6.1×10^5 mole/min [also 52, 57, 50]	

[48] *M. A. Rothenberg* and *D. Nachmansohn*, J. biol. Chemistry *168*, 223 (1947).

[49] *H. C. Lawler*, J. biol. Chem. *234*, 799 (1959); *238*, 132 (1963).

[50] *H. C. Lawler*, J. biol. Chemistry *236*, 2296 (1961).

[51] a) *A. B. Hargreaves* in [29], p. 397; b) *A. B. Hargreaves*, *A. G. Wanderley*, *F. Hargreaves*, and *H. S. Gonçalves*, Biochim. biophysica Acta *67*, 641 (1963).

[52] *L. T. Kremzner* and *I. B. Wilson*, Biochemistry *3*, 1902 (1964).

[53] Figures in brackets are special extinction coefficients (cm² mg⁻¹).

[54] *J. A. Cohen* and *R. A. Oosterbaan* in [3], p. 299.

The kinetic characteristics of this enzyme have been the subject of many investigations under widely varying conditions [2b,3,15,54] (see also Table 1). The number of active sites has been determined *e.g.* from the inhibitory action of diethoxyphosphorylthiocholine or tetraethyl pyrophosphate [TEPP, *(6)*] labeled with ^{32}P [50]. *Wilson* and *Harrison* [57] carried out the determination by titration with *N,N*-dimethylcarbamoyl fluoride, whilst *Bender* and *Stoops* [61] have described a method in which *o*-nitrophenyl *N,N*-dimethylcarbamate is used. It has been deduced from the activity per site in 1 mole that the local concentration of acetylcholinesterase *in vivo* must be about 5×10^{-6} to 5×10^{-5} N in order to decompose acetylcholine at a sufficiently high rate [57].

The activity of the enzyme is affected by inorganic ions [54]. Thus, it is increased or decreased in the presence of NaCl according to whether the acetylcholine concentration is above or below about 10^{-3} M. *Myers* [58] has attributed this to an effect of the ionic strength on the equilibrium constants of the Michaelis complex ES and a substrate-inhibited complex ES_2. Divalent ions (*e.g.* Mg^{2+}) enhance the enzymatic activity much more than monovalent ions. The reason for this is not clear, but acetylcholinesterase is probably not a "metal-enzyme" [59]. To eliminate fortuitous ionic effects, it is advisable [54] to use *ca.* 0.15 M NaCl and 0.01–0.04 M $MgCl_2$ solutions, which has in fact been done in all the kinetic investigations discussed below. A protein such as gelatine is also often added to stabilize the enzyme solution [60].

C. Active Center and Reaction Mechanism [2b,15,17,54,62–64]

Most of the following discussion applies not only to acetylcholinesterase but also to related hydrolases, and conversely, many results obtained with the latter (*e.g.*

[55] *I. B. Wilson* and *E. Cabib*, J. Amer. chem. Soc. *78*, 202 (1956).

[56] The term "turnover number" should no longer be used [23].

[57] *I. B. Wilson* and *M. A. Harrison*, J. biol. Chemistry *236*, 2292 (1961).

[58] *D. K. Myers*, Arch. Biochem. Biophysics *37*, 469 (1952).

[59] Cf., *e.g.*, [41b] and *S. L. Friess*, *I. B. Wilson*, and *E. Cabib*, J. Amer. chem. Soc. *76*, 5156 (1954).

[60] Commercial preparations of acetylcholinesterase generally already contain these substances; thus, according to the manufacturer's data, erythrocyte acetylcholinesterase (*ex* Mann Research Laboratories, New York) was characterized by *ca.* 20 mg of AChE, 100 mg of gelatine, dissolved in 5 ml of 1 M sodium phosphate, pH 7.6, and 30.7 mg of NaCl.

[61] *M. L. Bender* and *J. K. Stoops*, J. Amer. chem. Soc. *87*, 1622 (1965).

[62] *I. B. Wilson* in *W. D. McElroy* and *B. Glass*: A symposium on the mechanism of enzyme action. Johns Hopkins Press, Baltimore 1954, p. 642.

[63] *F. Bergmann*, Advances Catalysis related Subjects *10*, 130 (1958).

[64] Various lectures on this topic are to be found in: a) Discuss. Faraday Soc. *20* (1955); b) *P. A. E. Desnuelle*: Molecular basis of enzyme action and inhibition (Proc. 5th International Congress of Biochemistry, Moscow 1961, Vol. 4), Internat. Union Biochemistry, Symposium Series. Pergamon Press, Oxford 1963, Vol. 24.

cholinesterase [65] and especially α-chymotrypsin [66]) are valid for acetylcholinesterase.

The catalytic action of acetylcholinesterase is due not to a coenzyme but to the structure of the enzyme protein itself. As the protein molecule folds, certain amino acid residues at distant sites of the chain are brought close to one another, forming an active center. The latter comprises two active sites: one fixes the substrate and is chiefly responsible for the specificity (anionic site), and the other effects the cleavage of the substrate (esteratic site).

I. Fixation of the Substrate, and Specificity (Anionic Site)

Acetylcholinesterase cleaves preferentially esters containing a cationic group (alkylammonium group). The best substrate is acetylcholine, whilst esters in which the cationic group is separated from the alcoholic oxygen by more than or fewer than two CH_2 groups are less suitable. Nevertheless, such esters are often efficiently hydrolysed by other cholinesterases. Chain branching and steric factors also play a part. Neutral esters such as ethyl acetate are cleaved much more slowly.

The preference for substrates containing a cationic group suggests the presence of an anionic site in the active center [67–71], *i.e.* a site which holds the substrate by electrostatic forces and which is accompanied by an adjacent esteratic site to catalyse the hydrolysis. The assumption that the enzyme contains two anionic sites [63, 72, 73] is probably incorrect [15c, 74].

Further evidence for an anionic site has emerged from experiments with reversibly cleavable inhibitors. The most active of the latter also possess a positively charged nitrogen atom; their inhibitory action is reduced when the cationic group is converted into a neutral one [68]. Finally, the salt effect of inorganic ions exerted on the inhibitory process also indicates an interaction of charged groups during fixation [70].

Other forces participating in the fixation of the substrate besides Coulombic ones are van der Waals forces involving the methyl groups of choline and uncharged substrates [71, 74, 75], and weak covalent bonding forces between the carbonyl carbon of the ester and the esteratic site [76–78]. Concerning the participation of hydrogen bonds see [71, 80b].

II. Cleavage of the Substrate (Esteratic Site)

According to *Wallenfels* and *Streffer*, enzymatic catalysis often relies on acid-base catalysis (cf. [86]). This necessitates the presence, in the esteratic site, of an "acidic" and a "basic" active group, whose function in the enzymatic reaction depends on the degree of protonation and thus on the pH of the medium. The existence of such active groups in acetylcholinesterase has been inferred by *Wilson* and *Bergmann* [68, 76] from the bell-shaped activity/pH curves (Fig. 2) which indicate a diminished activity above and below the optimum pH.

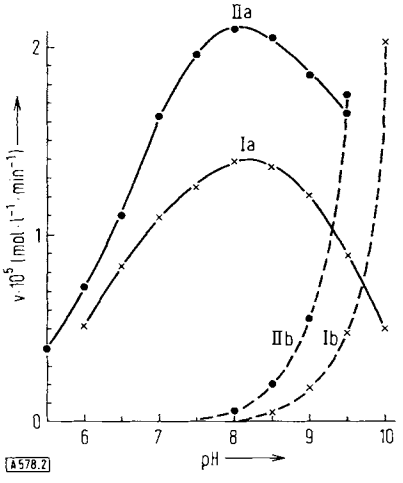


Fig. 2. Variation of the acetylcholinesterase activity with pH.
Curves Ia and IIa — rate of enzymatic cleavage of acetylcholine.
Curves Ib and IIb — rate of autohydrolysis of acetylcholine.
Acetylcholine concentration: × 2.06×10^{-4} mole/l, • 8.24×10^{-4} mole/l.
Enzyme concentration: 10 mg/l, bovine erythrocyte-AChE preparations (ex Mann Research Laboratories, New York; cf. [60]) in 0.1 M NaCl + 0.01 M $MgCl_2$ solution.
Titration with 0.02 N NaOH at 35 °C under nitrogen, with the aid of a pH-stat (Titrigraph, ex Radiometer Copenhagen).

The decrease in activity in acidic medium is due to inactivation of the basic active group by protonation. *Krupka* investigated the pH-dependence of the maximum cleavage rate of charged and uncharged substrates, and concluded that the basic group is composed of a first (B_1) and a second (B_2) group (pK 6.3 and 5.5, respectively) [80]. The activity drop in alkaline medium, on the other hand, is attributable to the inactivating deprotonation of the acidic group AH (pK

[65] *O. Svensmark* Aa,ct physiol. scand. *64*, Suppl. *245* (1965).
[66] For a review see, *e.g.*, *M. L. Bender* and *F. J. Kézdy*, J. Amer. chem. Soc. *86*, 3704 (1964).
[67] *E. A. Zeller* and *A. Bissegger*, Helv. chim. Acta *26*, 1619 (1943).
[68] *I. B. Wilson* and *F. Bergmann*, J. biol. Chemistry *185*, 479 (1950).
[69] *D. H. Adams* and *V. P. Whittaker*, Biochim. biophysica Acta *4*, 543 (1950).
[70] *D. K. Myers*, Arch. Biochemistry *27*, 341 (1950).
[71] *I. B. Wilson*, J. biol. Chemistry *197*, 215 (1952).
[72] *F. Bergmann, I. B. Wilson*, and *D. Nachmansohn*, Biochim. biophysica Acta *6*, 217 (1950).
[73] *F. Bergmann*, Discuss. Faraday Soc. *20*, 126 (1955).
[74] *S. A. Bernhard*, J. Amer. chem. Soc. *77*, 1966, 1973 (1955).
[75] *S. L. Fries, B. Witkop, R. C. Durant, L. J. Reber*, and *W. C. Thommesen*, Arch. Biochem. Biophysics *96*, 158 (1962).
[76] *I. B. Wilson* and *F. Bergmann*, J. biol. Chemistry *186*, 683 (1950).
[77] *F. Bergmann, I. B. Wilson*, and *D. Nachmansohn*, J. biol. Chemistry *186*, 693 (1950).
[78] *I. B. Wilson*, Biochim. biophysica Acta 7, 466 (1951).
[79] a) *K. J. Laidler*, Trans. Faraday Soc. *51*, 528 ,540, 550 (1955); b) *R. M. Krupka* and *K. J. Laidler*, *ibid. 56*, 1467, 1477 (1960).
[80] a) *R. M. Krupka*, Biochemistry *5*, 1983 (1966); b) *ibid. 5*, 1988 (1966).

9.2)[78,79]. Equations for the pH-dependence of the activity can be found in[76,79,81,82].

According to the simplest scheme for enzymatic reactions, an enzyme E and a substrate S combine to form a complex ES, which then decomposes into the reaction products. With acetylcholinesterase, these products are choline and an acetylated enzyme EAc[84,85]. The latter is finally hydrolysed to give the free enzyme and acetate (see Fig. 4).

In non-enzymatic ester hydrolysis, which generally proceeds *via* a $B_{Ac}2$ mechanism, the electrophilic carbonyl carbon of the ester suffers an attack by the OH ion, the basic group. Similarly, in the enzyme-catalysed hydrolysis of acetylcholine, the carbonyl carbon is probably attacked nucleophilically by the basic group B_2, and the acetylated enzyme EAc is formed. The acidic group AH first forms a hydrogen bond with the alcoholic oxygen atom and the choline residue is then cleaved off in the next step. A configurational change finally brings the acetylated group close to the basic group B_1, which catalyses the deacetylation by water or other nucleophilic substances[78,83]. The rate-determining step is deacetylation in the case of acetylcholine, acetylthiocholine, and phenyl acetate, but acetylation in the case of relatively poor substrates such as methylaminoethyl acetate[80]. Evidence for this mechanism includes the ^{18}O-exchange between the acetate and labeled water in the presence of acetylcholinesterase[87,88], and the fact that kinetic equations based on this postulated mechanism account best for the experimental values. Furthermore, the formation of an acetylated enzyme explains the observation that acetylcholinesterase can act as a transacetylating agent[83], and it is clearly analogous to the formation of a phosphorylated enzyme in the reaction with alkyl phosphates.

1. Chemical Nature of the Active Sites and Groups

a) *Anionic Site*

ω-Carboxyl groups of aminodicarboxylic acids seem the most likely carriers of negative charge on the anionic sites. Degradation studies have shown that the active center involves glutamic acid in AChE, but aspartic acid in other esterases[89,90].

b) *Esteratic Site*

A great number of findings indicates that serine, which contains an OH group and is present in all hydrolases[89,90], plays an important part in the esteratic site[91]. It has been shown, for example, that hydrolases can be inhibited stoichiometrically with diisopropyl fluorophosphate (DFP) *(7)* labeled with ^{32}P[92,93] (see also[50,57]), and that subsequent hydrolysis of the protein gives *O*-diisopropoxyphosphorylserine[94] (cf. also[95]). Though phosphorylation and acetylation with *p*-nitrophenyl acetate[96] seem to involve the serine residue, the site of acetylation in ordinary substrate cleavage is not yet certain[97].

The amino acid sequence, so far elucidated only for tripeptide units, is –Glu–Ser–Ala– in acetylcholinesterase[98] and butyrylcholinesterase, but –Asp–Ser–Gly– in several other esterases[89,90].

Under physiological conditions, free serine does not catalyse the hydrolysis of esters[99], nor does it react with alkyl phosphates[100,101]. It must therefore be activated by other amino acid groups in the enzymes. The imidazole group of histidine probably represents such an activating group[102]; this group is known to possess numerous biochemical and catalytic functions[103]. By analogy with chymotrypsin and trypsin, one may assume that each of the two basic groups B_1 and B_2 consists of an imidazole residue, and that they are brought close to each other in the protein by a conformational change[80b]. Various mechanisms have been proposed for the cooperative action of the active groups[2b,54,62,63,104,106–109]. According to the most probable mechanism, the doubly bonded nitrogen of the imidazole ring abstracts a proton from the OH group of serine, presumably in a concerted mechanism (cf.[86]). The resulting serine alkoxide anion then attacks the substrate or the alkyl phosphate nucleophilically (see below), and the acetylated serine thus formed is brought into the vicinity of the second imidazole group by a configurational change. This imidazole group abstracts a proton from water (this has already been found in the catalysis of activated esters by imidazole[91,100,105,

[81] *J. A. Cohen* and *R. A. Oosterbaan* in [3], p. 299.

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[89] *F. Sanger*, Proc. chem. Soc. (London) *1963*, 76.

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[91] *D. E. Koshland jr.*, Bull. Soc. Chim. biol. *46*, 1745 (1964).

[92] *E. F. Jansen*, *M. D. F. Nutting*, *R. Jang*, and *A. K. Balls*, J. biol. Chemistry *179*, 189, 201 (1949).

[93] *H. O. Michel* and *S. Krop*, J. biol. Chemistry *190*, 119 (1951).

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[97] *S. A. Bernhard*, *S. J. Lau*, and *H. Noller*, Biochemistry *4*, 1108 (1965).

[98] *D. C. Shaw*, unpublished, see [89].

[99] *V. I. Rozengart*, Doklady Akad. Nauk SSSR *133*, 1223 (1960); cf. Dokl. Biochem. Sect. (Engl. Transl. Biochem. Sect. Proc. Acad. Sci. USSR) *130/35*, 179 (1960/61).

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[101] *R. F. Ashbolt* and *H. N. Rydon*, Biochem. J. *66*, 237 (1957).

[102] *F. Bergmann*, *R. Segal*, *A. Shimoni*, and *M. Wurzel*, Biochem. J. *63*, 684 (1956).

[103] *E. A. Barnard* and *W. D. Stein*, Advances in Enzymol. *20*, 51 (1958).

[104] *R. M. Krupka*, Canad. J. Biochem. *42*, 677 (1964).

[105] *F. Bergmann*, *S. Rimon*, and *R. Segal*, Biochem. J. *68*, 493 (1958).

[106] *L. W. Cunningham*, Science (Washington) *125*, 1145 (1957).

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[108] a) *G. R. Porter*, *H. N. Rydon*, and *J. A. Schofield*, Nature (London) *182*, 927 (1958); b) *H. N. Rydon*, *ibid. 182*, 928 (1958).

[109] *A. P. Brestkin* and *E. V. Rozengart*, Nature (London) *205*, 388 (1965).

[110, 111]) and thus effects hydrolysis, *i.e.* deacetylation of the serine. A simple scheme of this mechanism has been given by *Krupka* [80b] (see Fig. 3).

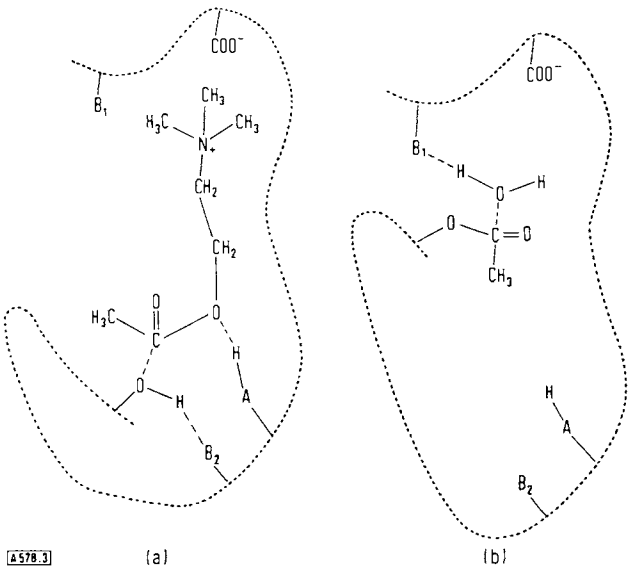


Fig. 3. Schematic representation of the active site in acetylcholinesterase. B_1 and B_2 are the basic groups (pK 6.3 and 5.5, respectively), AH is the acidic group (pK 9.2), OH and COO^- are the serine hydroxide group and the anionic active site.

(a) Enzyme-substrate (ES) complex in the case of acetylcholinesterase;

(b) Acetylated enzyme (EAc) (after *Krupka* [80b]).

Only hypotheses exist as yet about the nature of the acidic group, but various indications suggest that it is the OH group of tyrosine [63, 105]. According to *Koshland*, on the other hand, tyrosine seems to play no part in the catalysis, at least not in the case of chymotrypsin [91].

c) *Steric Configuration of the Active Center*

The protein must be present in a suitable steric configuration (*e.g.* having a "substrate cavity" [86]) in order to permit the joint attack of the active groups, which – like serine and histidine in the amino acid chain – are not adjacent. In hydrolases such as α-chymotrypsin, ribonuclease, and carboxypeptidase A, serine and histidine are brought together by a folding of the protein molecule fixed by disulfide bridges [112, 113]. According to the theory of induced fit [113, 114], the substrate, too, brings about a catalytically active configuration of the active center of the protein. The ability of the protein to fit itself to the substrate may affect the substrate specificity.

Information about the steric configuration of the active center in acetylcholinesterase has been obtained from experiments with substrates and reversibly cleavable inhibitors. In these experiments the inhibition or the rate of cleavage was ascertained in order to establish which are the ones that fit best [17, 115–119]. The protonated basic group B_1 can impede the access of a reversible inhibitor to the adjacent anionic site. The lowering of the inhibition constant for tetramethylammonium chloride, accompanying a change in the pH in the region of the dissociation constant of the first basic group B_1, indicates that the distance from the anionic site cannot exceed 5.5 Å. Since such an effect has not been found with the second basic group B_2 and the acidic group AH, these groups do not interact with the anionic site, and are situated from it at distances of 8–10 and 9 Å, respectively [80].

D. Inhibition

I. Inhibition by the Substrate and Reversible Inhibitors

When the rate of hydrolysis of acetylcholine by acetylcholinesterase is plotted against the substrate concentration, the resulting bell-shaped curve shows a strong decrease in the enzymatic activity at substrate concentrations exceeding $2.5\text{-}3 \times 10^{-3}$ M (examples are given in [2b, 54]), except with certain substrates, such as glyceryl triacetate, which lack such inhibiting action even at higher concentrations. This action of the substrate is characteristic for hydrolysis by AChE, and may be used to differentiate between the latter and other hydrolases. The above inhibition was earlier ascribed to the formation of an inactive (or weakly active [58]) ES_2 complex whose anionic and esteratic sites are occupied by two molecules of acetylcholine, so that the steric configuration impedes the activation of the ester bond [20a, 67]. However, the experimental data are not explained in a satisfactory manner by the kinetic equations based on this assumption (*e.g.* [58, 120, 121]; cf. also [54]). More feasible is the theory [119] according to which the intermediate acetylated enzyme EAc in which the anionic site is unoccupied (as in the free enzyme), combines with excess substrate to form a much less active complex EAcS. This is supported by kinetic equations proposed by *Krupka* and *Laidler* [119].

Reversible inhibitors are those which form enzyme-inhibitor complexes that can dissociate, *i.e.* inhibitors which can therefore be separated from the enzyme *e.g.* by dialysis. In the broadest sense, this group of inhibitors comprises all substances that show a more or less strong affinity for the active center of the enzyme, comprising therefore also substances such as substrates, reactivators, and cleavage products. Essentially, these substances are substituted derivatives of the ammonium ion, which, because of their structure, become attached mainly to the anionic site, similarly to

[110] *T. C. Bruice* and *G. L. Schmir*, Arch. Biochem. Biophysics *63*, 484 (1956).

[111] *M. L. Bender* and *B. W. Turnquest*, J. Amer. chem. Soc. *79*, 1652, 1656 (1957).

[112] *H. Neurath*, Sci. American *211*, No. 6, p. 68 (1964).

[113] *D. E. Koshland jr.*, Science (Washington) *142*, 1533 (1963).

[114] *D. E. Koshland jr.*, a) Proc. nat. Acad. Sci. USA *44*, 98 (1958); b) J. cellular comparat. Physiol. *54*, Suppl. *1*, 245 (1959); c) Advances in Enzymol. *22*, 45 (1960).

[115] *S. L. Friess*, J. Amer. chem. Soc. *79*, 3269 (1957).

[116] *R. M. Krupka* and *K. J. Laidler*, Nature (London) *190*, 916 (1961).

[117] *S. L. Friess* and *H. D. Baldridge*, J. Amer. chem. Soc. *78*, 2482 (1956).

[118] *I. B. Wilson* and *C. Quan*, Arch. Biochem. Biophysics *73*, 131 (1958).

[119] *R. M. Krupka* and *K. J. Laidler*, J. Amer. chem. Soc. *83*, 1445, 1448, 1454, 1458 (1961).

[120] *W. Hardegg*, Habilitation Thesis, Universität Heidelberg, 1958.

[121] *C. Marmasse*, Biochim. biophysica Acta *77*, 530 (1963).

"proper" substrates, and can thus block the formation of the ES complex and the deacetylation of EAc [124]. *Long* has listed all the compounds whose reversible inhibitory action has been investigated [122]. The substrate cleavage and the inhibition by the substrate S and reversible inhibitors I are best described by the following scheme, proposed by *Krupka* and *Laidler* [17, 119] (Fig. 4).

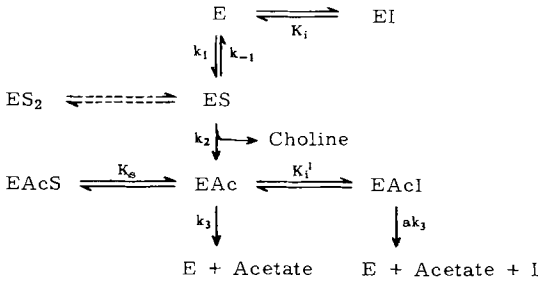


Fig. 4. Scheme for the cleaving off of the substrate and the inhibition by excess substrate [17,119].

According to the steady-state theory, the rate of the cleaving off of the substrate in the presence of inhibitors and an excess of substrate is given by the general equation:

$$v = \frac{k_2[E]_0\overline{K}[S]}{1 + K_i[I] + \overline{K}[S]\left\{1 + \frac{k_2}{k_3}\left(\frac{1 + \overline{K}'_i[I] + K_s[S]}{1 + a\overline{K}'_i[I]}\right)\right\}}$$

where $[E]_0$ is the total enzyme concentration and

$$\overline{K} = \frac{k_1}{k_{-1} + k_2}$$

The equation for inhibition by the substrate alone can be derived from this by putting [I] = O. For very small [S], the equation is simplified to the usual form:

$$v = \frac{V_{max}\,[S]}{K_m + [S]},$$

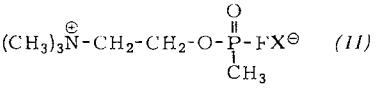
In the case of acetylcholinesterase, v_{max} and K_m can be expressed in the following way [17, 119, 123]; (cf. also [124, 125]):

$$V_{max} = \frac{k_2[E]_0}{1 + \frac{k_2}{k_3}} \text{ and } K_m = \frac{k_{-1} + k_2}{k_1\left(1 + \frac{k_2}{k_3}\right)}$$

II. Inhibition by Irreversible Inhibitors (Alkyl Phosphates) [2b,12a,12b,12d,13,126,194]

Unlike the inhibition by substrates and reversible inhibitors discussed above, the irreversible inhibition of acetylcholinesterase by the alkyl phosphates *(2)–(10)* listed in Section A is based on a phosphorylation that basically corresponds to acetylation of the enzyme in the normal enzymatic reaction. However, unlike the acetylated enzyme, the phosphorylated enzyme is hydrolysed by water very slowly, if at all [127], and only stronger nucleophilic reagents can remove the phosphoric acid residue from the enzyme and thus reactivate it [127].

Normal alkyl phosphate hydrolysis may serve as a model reaction for the phosphorylation of the enzyme. In place of the OH^- ion in the S_N2 reaction [128], we have in the enzyme a center with a relatively high electron density. This analogy is further manifested in the similarity between the activation energies: phosphorylation of the enzyme (paraoxon *(3)* [diethyl-*p*-nitrophenyl phosphate] + AChE) E = 10.6 kcal/mole [129]; hydrolysis of the alkyl phosphate (paraoxon + OH^-) E = 12.4 kcal/mole [130]. However, the alkyl phosphate reacts much faster (by several powers of ten) with the enzyme than with the OH^- ion [129, 131, 130b], and one can therefore assume that it is fixed on active sites of the enzyme in a way that favors the subsequent reaction [132]. The affinity of the inhibitor for the enzyme (and thus the inhibitory action) is increased – as with the other substrates – by the introduction of a cationic group in the alkyl phosphate, bearing in mind the distance from the anionic and the esteratic site (two CH_2 groups) (*Tammelin*'s esters, *e.g.* choline methylphosphonofluoridate *(11)* [133]):



(11)

Furthermore, the facts that the inhibition depends on pH in the same way as the acetylcholine cleavage [68], and that acetylcholine itself can compete with the inhibitor [134] justify the concept that alkyl phosphates can be regarded as particularly poor substrates, and indicate that the reaction of *e.g.* diisopropyl fluorophosphate with the esteratic site can be described analogously to ordinary substrate cleavage [15c].

The phosphorylated enzyme is converted into an unreactive form in a relatively slow secondary reaction (aging), which hampers the investigation *in vitro* and especially *in vivo* [135 to 138]. This aging is probably due to the cleaving off of an alkyl

[122] *J. P. Long* in [3], p. 374.

[123] Cf. the discussion between *G. E. Hein* and *R. M. Krupka*, *K. J. Laidler*, Nature (London) *193*, 1155 (1962).

[124] *R. M. Krupka*, Biochemistry *2*, 76 (1963); *3*, 1749 (1964); *4*, 429 (1965).

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[126] *B. Holmstedt* in [3], p. 428.

[127] *I. B. Wilson*, J. biol. Chemistry *190*, 111 (1951).

[128] a) *L. Larsson*, Svensk kem. Tidskr. *70*, 405 (1958); b) *D. F. Heath*, J. chem. Soc. (London) *1956*, 3804.

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[130] a) *J. A. A. Ketelaar*, *H. R. Gersmann*, and *K. Koopmans*, Recueil Trav. chim. Pays-Bas *71*, 1253 (1952); b) *D. F. Heath*, J. chem. Soc. (London) *1956*, 3796.

[131] *H. S. Aaron*, *H. O. Michel*, *B. Witten*, and *J. I. Miller*, J. Amer. chem. Soc. *80*, 456 (1958).

[132] Cf. [12d], p. 124.

[133] *L. E. Tammelin*, Acta chem. scand. *11*, 859 (1957).

[134] *K.-B. Augustinsson* and *D. Nachmansohn*, J. biol. Chemistry *179*, 543 (1949).

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[136] *I. B. Wilson*, Discuss. Faraday Soc. *20*, 119 (1955).

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[138] *E. Heilbronn*, Biochem. Pharmacol *12*, 25 (1963).

group from the dialkylphosphorylated enzyme, the remaining monoalkylphosphorylated enzyme anion being no longer susceptible to attack by the anion of a reactivator [139]. Isopropanol formed from the eliminated alkyl group was in fact detected [140] in a medium in which acetylcholinesterase had been inhibited by sarin *(9)* and then allowed to age (cf. [141]).

Literature data on the inhibitory action refer to the molar concentration of the inhibitor that gives a 50% inhibition of AChE, or to the negative logarithm pI_{50} of this concentration [142]. The pI_{50} values generally lie between 6 and 9 [143]. Less often, ordinary rate constants are given.

It is difficult to correlate the chemical structure with the inhibitory action, since the latter involves many factors. On the other hand, a good correlation has been found between the inhibition and Hammett's σ-constants for 17 aromatic dialkyl phosphates [144].

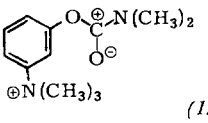
E. Reactivation [2b,12b,12d,13,145,194]

I. Development of Reactivators

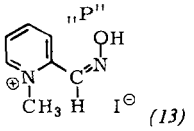
The reactivation of acetylcholinesterase by displacing the phosphate residue with nucleophilic reagents is not merely of theoretical interest, but is also the basis of an effective therapy of alkyl phosphate poisoning, which is difficult to combat with atropine alone (atropine is the pharmacodynamic antagonist of acetyl choline [146]).

The acetylated enzyme can transfer its acetyl group to hydroxylamine to form acetylhydroxamic acid [147], and it was therefore logical to assume that the phosphorylated enzyme would react analogously. Thus, *Wilson* [127] found that treatment with 0.7 M hydroxylamine solution led to a 50% reactivation of acetylcholinesterase inhibited with TEPP *(6)*, and numerous nucleophilic reagents were subsequently tested as potential reactivators [148]. However, the relatively high concentration at which hydroxylamine and reactivators without a positive charge are active does not permit their therapeutic use.

Notwithstanding its weak nucleophilic character, choline is quite a good reactivator [148]. This fact indicates that, like a substrate or an inhibitor, a reactivator must contain a cationic center in order to become attached to the anionic site of the enzyme [149]. The idea of combining with a cationic center the nucleophilic group for the displacement of the phosphate group made *Wilson* use the reversible inhibitor neostigmine *(12)* as a model reactivator. The carbamate carbon in neostigmine corresponds to the position of phosphorus ("P") in the active center of the phosphorylated enzyme, whose steric features are best satisfied by 2-(hydroxyiminomethyl)-1-methylpyridinium iodide (2-PAM), *(13)* [150] (cf. [151, 152]).



(12)



(13)

2-PAM has since been established in combination with atropine as a clinical antidote for alkyl phosphate poisoning [153, 154]. However, the large 2-PAM cation does not penetrate the blood-cerebral barrier, and cannot therefore react with inhibited AChE in the central nervous system [155].

According to *Wilson*'s hypothesis concerning the position of phosphorus in the phosphorylated enzyme, the *anti*-form of 4-(hydroxyiminoethyl)-1-methylpyridinium iodide (4-PAM) should be more active than the *syn*-form [152]. However, *Poziomek* [156] has found the opposite to be the case, and *Wilson*'s suggestions are therefore best viewed merely as working hypotheses.

The idea of tailor-made reactivators has been found very fruitful [157] and led to a new group of reactivators consisting of two hydroxyiminomethylpyridinium groups linked together by a chain [158–160] and corresponding therefore to reversible inhibitors with two positive centers. In these, the hydroxyiminomethyl group must be in the 4-position, and not in the 2-position. Thus, 1,1'-trimethylenedi-(4-hydroxyiminomethylpyridinium) dibromide (TMB-4) considerably surpasses the corresponding 2-isomer [160, 161]. However, the relatively high toxicity of TMB-4 restricts its therapeutic application [162, 165]. Oxybis-(4-hydroxyiminomethylpyri-

[139] Cf. [12d], p. 129.

[140a] *F. Berends, C. H. Posthumus, I. v. d. Sluys*, and *F. A. Deierkauf*, Biochim. biophysica Acta *34*, 576 (1959).

[140b] *T. E. Smith* and *E. Usdin*, Biochemistry *5*, 2914 (1966).

[141] *J. H. Fleisher* and *L. W. Harris*, Biochem. Pharmacol. *14*, 641 (1965).

[142] Cf. [12b], p. 77.

[143] Cf. [12b], p. 73.

[144] *T. R. Fukutu* and *R. L. Metcalf*, J. agric. Food Chem. *4*, 930 (1956).

[145] *F. Hobbiger* in [3], p. 921.

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[147] *S. Hestrin*, Biochim. biophysica Acta *4*, 310 (1950).

[148] *I. B. Wilson*, J. biol. Chemistry *199*, 113 (1952).

[149] *I. B. Wilson, S. Ginsberg*, and *E. K. Meislich*, J. Amer. chem. Soc. *77*, 4286 (1955).

[150] *I. B. Wilson*, Biochim. biophysica Acta *18*, 168 (1955).

[151] *A. F. Childs, D. R. Davies, A. L. Green*, and *J. P. Rutland*, Brit. J. Pharmacol. Chemotherapy *10*, 462 (1955).

[152] *I. B. Wilson, S. Ginsburg*, and *C. Quan*, Arch. Biochem. Biophysics *77*, 286 (1958).

[153] *W. D. Erdmann*, Dtsch. med. Wschr. *85*, 1014 (1960).

[154] *D. Grob* in [3], p. 989.

[155] *H. Kewitz* and *D. Nachmansohn*, Arch. Biochem. Biophysics *66*, 271 (1957).

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[157] *I. B. Wilson* and *S. Ginsburg*, Biochem. Pharmacol. *1*, 200 (1958).

[158] *E. J. Poziomek, B. E. Hackley*, and *G. M. Steinberg*, J. org. Chemistry *23*, 714 (1958).

[159] *F. Hobbiger, D. G. O'Sullivan*, and *P. W. Sadler*, Nature (London) *182*, 1498 (1958).

[160] *W. K. Berry, D. R. Davies*, and *A. L. Green*, Brit. J. Pharmacol. Chemotherapy *14*, 186 (1959).

[161] *F. Hobbiger* and *P. W. Sadler*, Brit. J. Pharmacol. Chemotherapy *14*, 192 (1959).

[162] a) *J. H. Wills*, Federat. Proc. *18*, 1020 (1959); b) *J. F. O'Leary, A. M. Kunkel*, and *A. H. Jones*, J. Pharmacol. exp. Therapeut. *132*, 50 (1961).

[163] Manufactured by E. Merck AG., Darmstadt.

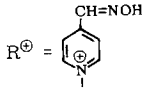
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dinium-1-methyl) dichloride (LüH6, Toxogonin®, *(14)* [163, 164] is less toxic than TMB-4 [165], therapeutically more active than 2-PAM [166–168] and can reactivate inhibited acetylcholinesterase in the central nervous system as well [169, 168b]. The reactivity of Toxogonin®, which surpasses that of TMB-4 [170], indicates that the chain connecting the two substituted pyridinium residues plays an important part in the reactivation [171]. Systematic variation of this chain has led to an antidote equalling Toxogonin® in its activity: 2,3-dihydroxybutylene[1,1'-bis-(4-hydroxyiminomethylpyridinium)] dibromide, R-21 *(15)* [172].

$$R^{\oplus}\text{-}CH_2\text{-}O\text{-}CH_2\text{-}R^{\oplus}\ 2\ Cl^{\ominus} \qquad (14)$$

$$R^{\oplus}\text{-}CH_2\text{-}CHOH\text{-}CHOH\text{-}CH_2\text{-}R^{\oplus}\ 2\ Br^{\ominus} \qquad (15)$$



II. Mechanism of the Action of Reactivators

The ability of a reactivator to reactivate AChE inhibited by an alkyl phosphate depends on factors that influence the formation of a reaction complex between the reactivator and the inhibited enzyme, and the elimination of the phosphoryl group from the enzyme.

1. The Reaction Complex

The first step of reactivation resembles the enzymatic hydrolysis of acetylcholine insofar as it involves the formation of a reaction complex EIR (EI is the inhibited enzyme and R is the reactivator), which then decomposes into free enzyme E and the phosphorylated reactivator RI [149, 137, cf. 173b]:

$$EI + R \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} EIR \xrightarrow{k_2} E + RI$$

$$\text{where } K_r = \frac{[EI]\cdot[R]}{[EIR]} = \frac{k_{-1}+k_2}{k_1}$$

If we regard the constants K_r of the reactivators in Table 2 as Michaelis constants K_m for various substrates, a comparison shows that K_r is considerably higher for uncharged reactivators, such as hydroxyiminoacetone, than for reactivators having a cationic center (*e.g.* 2-PAM). Thus, 2-PAM itself is a weak reversible inhibitor, and it can compete with cations for the anionic site [175]. A similar effect is exerted by a bulky group extending between the esteratic site and the anionic site (a group such as isopropyl in the case of AChE inhibited by diisopropyl fluorophosphate), which impedes the access of the cationic center of 2-PAM to the anionic site [136, 137, cf. 176]. A further important variable is the rate constant k_2 for the decomposition of the reaction complex EIR into the reactivated enzyme E and the phosphorylated reactivator RI. A method for the determination of k_2 has been given by *Green* and *Smith* [174].

Table 2. Equilibrium constants K_r and decomposition rate constants k_2 of the reaction complex EIR.

Reactivator	Blocking group	K_r (mole/l)	k_2 (min^{-1})
Hydroxyimino-acetone [173]	i-C_3H_7O–P(CH_3)O	1×10^{-2}	2.4×10^{-1}
Hydroxyimino-acetone [173]	$(C_2H_5O)_2PO$	2×10^{-2}	1.6×10^{-1}
2-PAM *(13)* [174]	$(C_2H_5O)_2PO$	1.4×10^{-4}	8.1×10^{-2}
2-PAM *(13)* [174]	$(i\text{-}C_3H_7O)_2PO$	8×10^{-4}	1.5×10^{-2}
3-Pyridincarbo-hydroxamic acid [149]	$(C_2H_5O)_2PO$	3.4×10^{-2}	

Compounds with two hydroxyiminomethylpyridinium groups, and particularly those with a three-membered chain (*e.g.* TMB-4 [177] and Toxogonin® [170]), are even faster reactivators than 2-PAM, possibly because of an additional bond formed with an assumed second anionic site [157], or else because of an enhanced reactivity with the phosphorylated enzyme [178]. It seems probable that the enzyme becomes attached to different groups depending on the configuration of the reactivators [172, 179]. Thus, in the case of 2-pyridinecarbohydroxamic acid, a hydrogen bond is formed with the ring nitrogen [173].

2. Elimination of Phosphoryl Group from the Enzyme

After the complex EIR has been formed, the nucleophilic group of the reactivator reacts with the electrophilic phosphorus atom, and the free enzyme is liberated [180]. The rate of reactivation is therefore determined by the electrophilicity of phosphorus [181]

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and the nucleophilicity of the attacking agent [145]. A measure of the latter is the ability of the reactivator to accelerate the hydrolysis of the alkyl phosphate in question [128a, 182–187].

With a substance whose anion delivers a nucleophilic attack, the pK_a value plays an important role. For an efficient therapy, the dissociation should be virtually complete in the physiological medium at pH 7–8. Since a low pH, which favors dissociation, reduces the nucleophilicity of the molecule, the optimum reaction rate is a function of both the pK_a and the pH. In the case of substituted hydroxamic acids, $pK_a = pH + 0.6$ [188], cf. [172].

The attack by a nucleophilic particle can be promoted by the pull exerted by the electrophilic group, and this push-pull mechanism has been accepted for the reactions of alkyl phosphates with copper(II) hydroxide [189], hydrogen peroxide [190–192], and the mono-anion of pyrocatechol [193]. In the case of Toxogonin®, *Lüttringhaus et al.* [164] have isolated the corresponding mono-anion. According to these authors the two pyridinium rings are presumably arranged in a sandwich fashion. The hypothesis of concerted action is further supported by the fact that the mono-anion of pyrocatechol is superior to those of resorcinol and hydroquinone [195], c.f. [178].

3. Rephosphorylation of the Enzyme

Acetylcholinesterase can be rephosphorylated in an undesirable reverse reaction by the phosphorylated reactivator RI formed in the reactivation of the enzyme [196], cf. [197]:

$$RI + E \rightleftharpoons EI + R$$

The most important phosphorylated reactivators fit in with the P–XYZ system of phosphorylating agents [198]. Both the α-hydroxyimino ketones and the hydroxyiminomethylpyridinium salts possess an electron acceptor Z (C=O or ring nitrogen, respectively) required for taking up the electrons from the P–X bond in the phosphorylation. The ring nitrogen is linked to the hydroxyiminomethyl group by a conjugated system Y whose UV-spectrum indicates a negative solvatochromic effect in the case of 2-PAM and 4-PAM, but not with the inactive 3-PAM, where the system is not properly conjugated [199]. Whilst the phosphorylated α-hydroxyimino ketones [200] and hydroxamic acids [201] cannot be intercepted because they decompose rapidly, hydroxyiminomethylpyridinium salts phosphorylated by sarin *(9)* – which show a structural resemblance to the highly toxic *Tammelin*'s esters *(11)* – are sufficiently stable [202] to phosphorylate and thus inhibit acetylcholinesterase [203]. This is the reason why the inhibition of cholinesterases in the plasma by Rogor® [204] might even be further aggravated by large doses of Toxogonin®. One should therefore never administer overdoses of specific antidotes [205].

Mention should be made in this connection of the important investigations concerning the conditions under which the phosphorylated oxime, or a model compound, decomposes irreversibly into non-toxic substances. Thus, with warm acetic anhydride, 2-PAM forms the nitrile [206]. The nitrile is formed similarly in boiling ethanol by 4-PAM esterified with *p*-nitrobenzoyl chloride on the hydroxyiminomethyl group [207], cf. [208]. Furthermore, pyridinium chlorides that – like Toxogonin® – contain an ethereal oxygen atom α to the ring nitrogen, lose their side chain in boiling ethanol, and form pyridine hydrochloride. Solvolysis of the corresponding benzoyloxyiminomethylpyridinium compounds leads to 4-cyanopyridinium chloride or a mixture of this and pyridine-4-aldoxime hydrochloride, depending on the solvent and the temperature [207].

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Preparation of Dichlorohexafluoropropane by Fluorination of 1,2-Dichloropropane [1]

By *M. Schmeisser, K. P. Ehlers,* and *P. Sartori* [*]

Dedicated to Prof. F. Asinger on the occasion of his 60th birthday

Hitherto little has been known of the action of elementary fluorine on chlorohydrocarbons [2]. As in electrochemical fluorination, the presence of chlorine atoms in the molecule inhibits the reaction of elementary fluorine in the substitution of hydrogen by fluorine.

We have investigated the suitability of 1,2-dichloropropane *(1)* for the preparation of 1,2-dichlorohexafluoropropane *(2)* b.p. 34.7 °C. The latter compound, which is a possible starting material for the preparation of hexafluoropropane [3], has hitherto only been prepared by complicated procedures [4].

The fluorination of *(1)* was carried out in the vapor phase at a temperature between 100–200 °C in a copper reaction furnace (diameter 80 mm, length 1150 mm) filled with copper wool, which in principle corresponds to the apparatus described by *Bigelow, Calfee,* and *Miller* [5]. Fluorine diluted with nitrogen, and a nitrogen stream loaded with *(1)* in the vapor state were fed together through the reaction furnace and the products of reaction passed over NaF to remove HF, and then finally collected in cold traps. A small excess of fluorine was used. Large amounts of CF_4, C_2F_6, and C_3F_8 were produced as well as chlorine-containing fluorination products.

The chlorine-containing fluorination products could be quantitatively frozen out at −78 °C. They were separated by fractional distillation in a Podbielniak column or by preparative gas chromatography, and identified by chemical analysis and IR spectroscopy. Isomers containing equal numbers of chlorine atoms could not be separated. The proportions of *(2)* and 1,3-dichloroperfluoropropane in the reaction mixture were determined by treatment of the mixture with zinc in ethanol, hexafluoropropene being formed from *(2)* and chlorohexafluoropropane from 1,3-dichloroperfluoropropane. As the table shows, the yield of *(2)* is dependent on temperature and is a minimum at 150–175 °C.

Therefore, *(2)* can be isolated in one step from relatively simple starting materials and in yields comparable with those obtained by the usual methods [4].

Free chlorine could not be detected in the reaction mixture. However, extensive isomerization and the formation of chlorine-free, as well as chlorine-containing, products suggest intermediary chlorine fission. Under the reaction conditions chlorine can react rapidly with fluorine to form ClF, which then reacts with CH compounds to bring about chlorine substitution and HF formation.

The analogous fluorination of propane and of butane leads to the formation of the corresponding perfluorination products C_3F_8 and C_4F_{10}, respectively, in yields of 75 to 80% [6].

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[*] Prof. Dr. M. Schmeisser, Dr. K. P. Ehlers, and Dr. P. Sartori
Insitut für Anorganische Chemie und Elektrochemie
der Technischen Hochschule
Professor-Pirlet-Str. 1
51 Aachen (Germany)

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Fluorination of $C_3H_6Cl_2$ with fluorine. 1,2-Dichloropropane (2.4 g/h) with N_2 (11 l/h) as carrier-gas; fluorine (4.85 g/h) diluted with N_2(2–3 l/h).

Temperature (°C)	Total amount of $C_3H_6Cl_2$ (g)	Total amount of chloroperfluoroalkane (g)	Proportion of the total amount of chloroperfluoroalkane (%)							
			C_3H_7Cl B.p. −2 °C	1,2-$C_3F_6Cl_2$ *(2)* B.p. 34.7 °C		1,3-$C_3F_6Cl_2$ B.p. 33.8 °C		$C_3F_5Cl_3$ B.p. 74–76 °C	$C_3F_4Cl_4$ B.p. 112–114 °C	Residue
120	103.1	48.69	22.3	33.9	8.2 [a]	9.6	2.3 [a]	3.7	13.5	17.1
135	134.3	49.78	25 0	23.6	4.5	22.1	4.8	1.0	19.9	6.0
150	115.1	46.29	14.79	20.1	4.1	14.2	3.7	1.8	32.3	4.4
175	86.4	49.51	16.48	13.9	4.1	25.2	8.8	2.1	25.2	12.4
200	81 6	49.40	18.05	28.4	8.8	20.4	7.1	0.9	24.7	5.0

[a] The numbers in these columns are yields (%) referred to amount of reacted 1,2-dichloropropane.

8,9-Diacetylsesquifulvalene

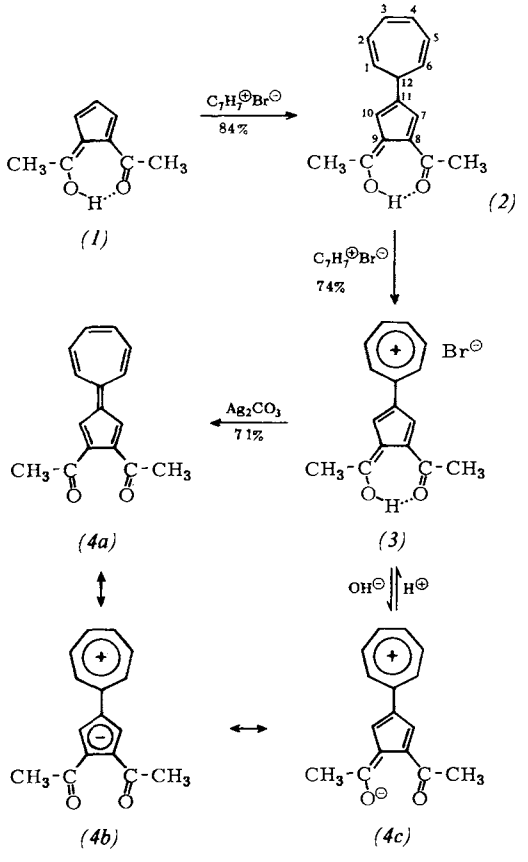
By *E. Koerner von Gustorf, M. C. Henry,* and *P. V. Kennedy* [*]

Dedicated to Professor G. Wittig on his 70th Birthday

8,9-Disubstituted sesquifulvalenes have not hitherto been prepared. We have found that 8,9-diacetylsesquifulvalene is accessible in good yield by the reaction sequence *(1)* → *(4)*.

When tropylium bromide in CH_3OH is added dropwise to 1,5-diacetylcyclopentadiene [1] (whose existence in the tautomeric fulvene form *(1)* is confirmed by ^1H-NMR studies [2]), the product *(2)* is precipitated as yellow needles (m.p. 135.5 – 136.5 °C). Small amounts of admixed *(3)* can be readily removed since *(3)* is insoluble in ether. Compound *(3)* is formed by hydride transfer on addition of *(2)* in ether to tropylium bromide in CH_3OH and separates as carmine-red platelets (decomp. 230 °C). Shaking *(3)* with an excess of Ag_2CO_3 in CH_3OH affords analytically pure, dark red 8,9-diacetylsesquifulvalene *(4)* [m.p. 127–128 °C (decomp.)], which is stable in air.

The increased or decreased shielding of the protons of the five- and seven-membered rings shown by the NMR data indicates participation of dipolar resonance structures such as *(4b)* and *(4c)* in the ground state of *(4)*. Protonation of *(4)* occurs mainly on the carbonyl-oxygen; the ^1H-NMR spectra of *(3)* and *(4)* are thus identical in CF_3COOH.



^{1}H—NMR data (δ values; tetramethylsilane as internal standard) [6].

	(2) in CCl_4	(4) in $CDCl_3$	(3), (4) in CF_3COOH
2 CH_3	2.51 (s) [a]	2.40 (s)	2.80 (s)
—OH···O=C	17.8 (s)	—	below CF_3COOH
H(7), H(10)	7.18 (s)	6.92 (s)	8.25 (s)
H(1), H(6)	5.3 (m)	6.7 (m)	8.5 (m)
H(2), H(5)	6.2 (m)		
H(3), H(4)	6.65 (m)	7.4 (m)	9.0 (m)
H(12)	2.6 (m)	—	—

[a] s = singlet, m = multiplet.

The shapes and chemical shifts of the signals for the protons in the seven-membered ring of *(3)* correspond to those of 7,8,9,10-tetraphenylsesquifulvalene in CF_3COOH [3]. Compounds *(3)* and *(4)* are water-soluble (after wetting with CH_3OH). The basicity of water suffices to convert *(3)* into *(4)*. Protonation of *(4)* (λ_{max} = 498 mμ; log ε = 4.596) [4] to *(3)* (λ_{max} = 467 mμ; log ε = 4.568) [4] (*e.g.* with HCl) in an aqueous system is accompanied by a color change from reddish-orange to yellow. Since alternate deprotonation (*e.g.*, by dilute NH_3) and protonation can be repeated indefinitely, this system can be used as a pH indicator. Concentrated NaOH solution decolorizes *(4)*, probably by attack of the double bond between C-11 and C-12; this process is also reversible.

1,5-Dibenzoylcyclopentadiene reacts with tropylium bromide [5] in the same way as *(1)*.

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[*] Prof. Dr. E. Koerner von Gustorf and P. V. Kennedy
Boston College, Department of Chemistry
Chestnut Hill, Mass. 02167, (U.S.A.)
Dr. M. C. Henry
U.S. Army Natick Laboratories
Natick, Mass. 07162, (U.S.A.)

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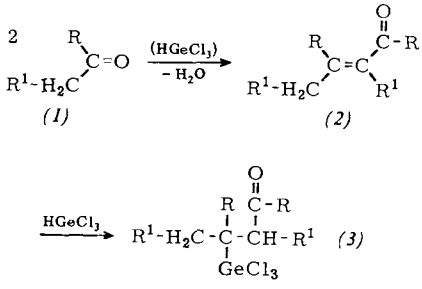
[6] We thank *J. C. Hogan* and *F. H. Bissett* for the spectra.

Reactions of Trichlorogermane with Ketones and Alcohols

By *O. M. Nefedov, S. P. Kolesnikov*, and *B. L. Perlmutter* [*]

Dedicated to Professor G. Wittig on his 70th Birthday

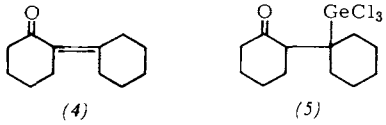
Under the influence of $HGeCl_3$, ketones of type *(1)* condense to give β-unsaturated ketones *(2)*, which readily add trichlorogermane with formation of trichlorogermyl ketones *(3)*.



R = Alkyl or Aryl; R^1 = H, Alkyl, or Aryl.

For instance, heating 0.22 mole of $C_6H_5COCH_3$ with 0.1 mole of $HGeCl_3$ (160 °C, 30 min) gives a 96 % yield of 1,3-diphenyl-3-(trichlorogermyl)-1-butanone *(3)*, R = C_6H_5, R^1 = H; m.p. 172–174 °C (from C_6H_6), IR spectrum $\nu_{C=O}$ = 1670 cm^{-1}, NMR spectrum δ = 1.45 (singlet, CH_3 group), 3.05 (quartet, CH_2 group), and 7.3 to 8.5 (C_6H_5 groups) in the ratio 3:2:10.

Similarly, 0.51 mole of cyclohexanone and 0.085 mole of $HGeCl_3$ afford a 97 % yield of 2-(1′-trichlorogermylcyclohexyl)cyclohexanone *(5)*, m.p. 174–176 °C (from C_6H_6), IR spectrum $\nu_{C=O}$ = 1710 cm^{-1}, together with 2-cyclohexylidenecyclohexanone *(4)* (4.5 g).



The trichlorogermyl ketone *(5)* is also formed on treatment of $HGeCl_3$ with 1-methoxycyclohexene (yield 35 %), with *(4)* (yield 85 %), or with 2-(1′-chlorocyclohexyl)cyclohexanone (yield 65 %), or by treatment of the last-mentioned ketone with the dioxane-germanium dichloride complex $C_4H_8O_2 \cdot GeCl_2$ (yield 60 %).

Reaction of 0.22 mole of cycloheptanone with 0.1 mole of $HGeCl_3$ gives a 98 % yield of 2-(1′-trichlorogermylcycloheptyl)cycloheptanone, m.p. 112–115 °C (from C_6H_6), IR spectrum $\nu_{C=O}$ = 1680 cm^{-1}.

Ketones that cannot condense in this way react differently with $HGeCl_3$. For example, use of $(C_6H_5)_2CO$ leads to $(C_6H_5)_2CHGeCl_3$ *(6)* [1] [yield 14 %, m.p. 78–79 °C (from CCl_4 and C_6H_6), b.p. 147–152 °C/0.5 mm] and polymeric products. NMR spectrum of *(6)*: δ = 4.6 (singlet, CH group) and 7.2 ppm (singlet, C_6H_5 groups) in the ratio 1:10. Forma-

tion of *(6)* is explained by the strong reducing action of $HGeCl_3$ [2]. The alcohol *(7)* is probably formed first and then condenses to give the ether *(8)*. Under the influence of $HGeCl_3$ ethers can decompose to alkyl- or arylalkyl-trichlorogermanes and alcohols [3]. In fact, the reaction of the alcohol *(7)* with $HGeCl_3$ also gives the compound *(6)* (yield 89%).

$$2\ (C_6H_5)_2CO \xrightarrow{(HGeCl_3)} 2\ (C_6H_5)_2CHOH \xrightarrow[-H_2O]{(HGeCl_3)}$$
(7)

$$(C_6H_5)_2CH\text{-}O\text{-}CH(C_6H_5)_2 \xrightarrow{HGeCl_3} (C_6H_5)_2CHGeCl_3 + (7)$$
(8) *(6)*

Other alcohols react similarly with trichlorogermane. Thus t-C_4H_9OH gives t-$C_4H_9GeCl_3$ (70 % yield), s-C_4H_9OH gives s-$C_4H_9GeCl_3$ (42 % yield), n-C_4H_9OH gives n-$C_4H_9GeCl_3$ (46.5 % yield), and CH_3OH gives CH_3GeCl_3 (47 % yield).

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[*] Dr. O. M. Nefedov, Dr. S. P. Kolesnikov, and B. L. Perlmutter
N. D. Zelinskii Institute of Organic Chemistry of the U.S.S.R. Academy of Sciences
Moscow (U.S.S.R.)

[1] Reaction conditions: Refluxed for 2h (temperature raised from 140 to 190°C).

[2] *O. M. Nefedov, S. P. Kolesnikov*, and *V. I. Sheichenko*, Angew. Chem. *76*, 498 (1964); Angew. Chem. internat. Edit. *3*, 508 (1964); *O. M. Nefedov, S. P. Kolesnikov*, and *N. N. Machova*, Izvest. Akad. Nauk, Ser. chim SSSR *1964*, 2224.

[3] *O. M. Nefedov, S. P. Kolesnikov, V. I. Sheichenko*, and *Yu. N. Sheinker*, Doklady Akad. Nauk SSSR *162*, 589 (1965).

Preparation of Fluorocyclopropanes by Reductive Dechlorination of Chlorofluorocyclopropanes

By *M. Schlosser* and *G. Heinz* [*]

Dedicated to Professor G. Wittig on his 70th birthday

Recently, Japanese authors [1] reported the first preparation of fluoronorcarane from chlorofluoronorcarane and tri-n-butyltin hydride. We have found that chlorofluorocyclopropanes may be advantageously reduced by alkali metals in protonic solvents (see Table).

Chlorofluorocyclopropanes are formed when dichlorodifluoromethane is treated with a base in the presence of an olefin. In order to obtain the products in a higher state of purity we used organolithium compounds (methyl-lithium, n-butyl-lithium) as base instead of potassium t-butoxide [2].

The chlorofluorocyclopropanes were distilled in a spinning band column and then taken up in tetrahydrofuran. The resulting solution was added dropwise to a solution of a stoichiometric amount of sodium in liquid ammonia; the latter turned colorless immediately. The ammonia was removed by evaporation and the reaction product isolated by distillation or by preparative gas chromatography. Evidence of the structure of the product was provided by elemental analysis and by IR, NMR, and mass spectrometry.

Metallic lithium in t-butanol/tetrahydrofuran (1:3) [3], or sodium in methanol, will also reduce chlorofluorocyclopropanes. However, with these systems the metals must be present in excess and halogen-free cyclopropanes are formed as by-products (see Table).

The fluorine, and not the chlorine, is first partly replaced by hydrogen in what is clearly a radical side-reaction.

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[*] Priv.-Doz. Dr. M. Schlosser and Dipl.-Chem. G. Heinz
Organisch-Chemisches Institut der Universität
Tiergartenstr.
69 Heidelberg (Germany)

[1] *T. Ando, H. Yamanaka, S. Terabe, A. Horike*, and *W. Funasaka*, Tetrahedron Letters *1967*, 1123.

[2] *W. E. Parham* and *R. R. Twelves*, J. org. Chemistry *22*, 730 (1957).

[3] *S. Winstein* and *R. L. Hansen*, J. Amer. chem. Soc. *82*, 6206 (1960).

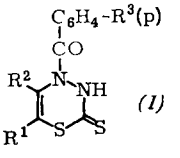
R^1	R^2	R^3	R^4	X=Cl, Z=F Yield (%)	Reducing agent	X=H, Z=F Yield (%)	*syn:anti*	X=Z=H Yield (%)
n-C_5H_{11}	H	H	H	11	Na/NH_3	76	0.6	—
					Li/t-BuOH	53	1.5	20
C_6H_5	H	CH_3	H	38	Li/t-BuOH	75	1.2	21
CH_3	CH_3	CH_3	CH_3	45	Na/NH_3	65	—	—
					Na/CH_3OH	60	—	—
					Li/t-BuOH	72	—	15
H	$-(CH_2)_4-$		H	21	Na/NH_3	74	0.5	—
					Na/CH_3OH	75	1.0	25
					Li/t-BuOH	68	1.0	32

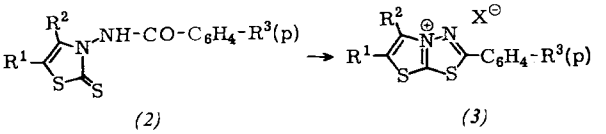
7-Methyl-4-phenyl-8*H*-1,3,5,6-dithiadiazocin-2-one, an Eight-Membered Heterocycle with Chiral Conformation

By *G. Ege* [*]

Dedicated to Prof. G. Wittig on the occasion of his 70th birthday

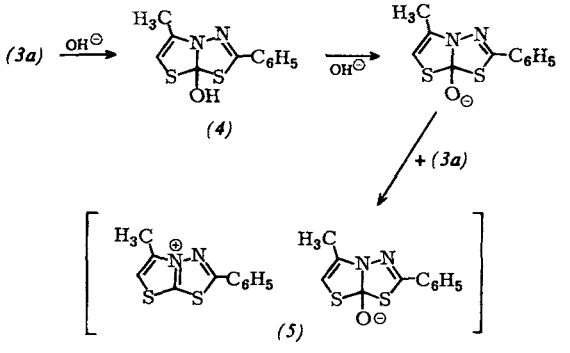
The compounds described as dihydrothiadiazinethiones *(1)* [1] have in reality the structure *(2)* [2]. These 3-benzoylaminothiazole-2-thiones *(2)* cyclize in concentrated sulfuric acid [3] at 20 °C to form the water-soluble thiazolo[2,3-*b*]-1,3,4-thiadiazolium salts *(3)*, $X^{\ominus} = HSO_4^{\ominus}$, from which the difficultly soluble perchlorates and iodides can be obtained.


(1)


(2) *(3)*

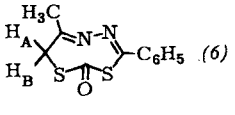
On treatment with 2N NaOH the compound *(3a)* adds hydroxide anion at the immonium double bond. The resulting hydroxy compound is, however, immediately deprotonated and reacts with the cation of *(3a)* to form the difficultly soluble salt *(5)* (m.p. 167 °C, yield 80 %).

	R^1	R^2	R^3	(3), $X^\ominus = HSO_4^\ominus$ M.p. (°C)	Yield (%)	(3), $X^\ominus = ClO_4^\ominus$ M.p. (°C)	(3), $X^\ominus = I^\ominus$ M.p. (°C)
(a)	H	CH_3	H	243	70	241	300 (decomp.)
(b)	H	C_6H_5	H	242	86		
(c)	H	CH_3	NO_2	270 (decomp.)	82		300
(d)	CH_3	CH_3	H	245	30	180	
(e)	CH_3	CH_3	NO_2	230 (decomp.)	70		



The fact that *(5)* is actually present as a salt and not as an ether follows from the NMR spectrum. The spectrum shows that the methyl group protons and olefinic protons from the cation and anion are not equivalent (two doublets at $\tau = 7.3$ and $\tau = 8.1$ for each of the three protons, a quartet at $\tau = 4.2$ for one proton, and one multiplet for eleven protons between $\tau = 1.9$ and 2.9).

When *(5)* is boiled in aqueous methanolic hydrochloric acid, the compound 7-methyl-4-phenyl-8*H*-1,3,5,6-dithiadiazocin-2-one *(6)* [colorless crystals, m.p. 120 °C, yield 90% with respect to the anion of *(5)*] is formed by transannular ring opening of the anion. The cation of *(5)* can be precipitated unchanged as the perchlorate.



The structure of *(6)* follows from the IR spectrum: a CO band at 1695 cm^{-1} and absence of absorption in the NH region.

One would expect the methylene protons, H_A and H_B, in *(6)* to be equivalent if they were to rapidly oscillate about the plane of the ring. The NMR spectrum of *(6)*, at *ca.* 20 °C, shows (see Fig. 1), however, an AB system ($\tau_A = 5.9$ and $\tau_B = 6.5$, with $J_{AB} = 11$ Hz) for the two methylene protons. The AB system is also conserved on heating the compound *(6)* to 150 °C.

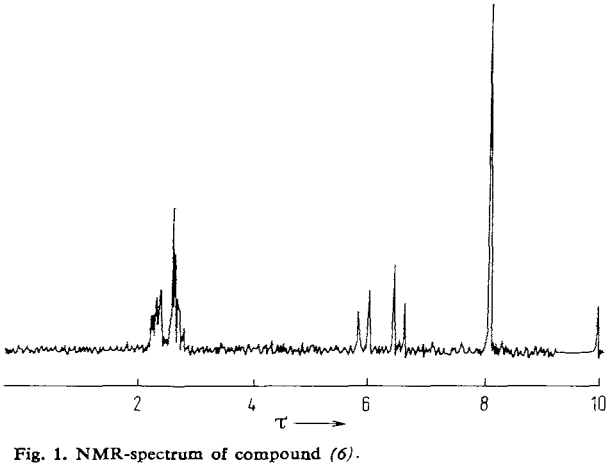


Fig. 1. NMR-spectrum of compound *(6)*.

A fixed, non-planar, and therefore chiral, conformation of the eight-membered heterocycle can thus be assumed, at least for temperatures up 150 °C. The compound *(6)* should therefore be resolvable into optical antipodes – experimental work with this aim in view is in progress.

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[*] Dr. G. Ege
Organisch-Chemisches Institut der Universität
Tiergartenstr.
69 Heidelberg (Germany)

[1] *T. Sato* and *M. Ohta*, Yakugaku Zasshi *77*, 771 (1957); Chem. Abstr. *51*, 17941 (1957).

[2] *G. Ege*, *K. Gessner*, and *H. Schildknecht*, unpublished; cf. *H. Schildknecht*, Angew. Chem. *78*, 841 (1966) and especially p. 847; Angew. Chem. internat. Edit. *5*, 751 (1966) and p. 757.

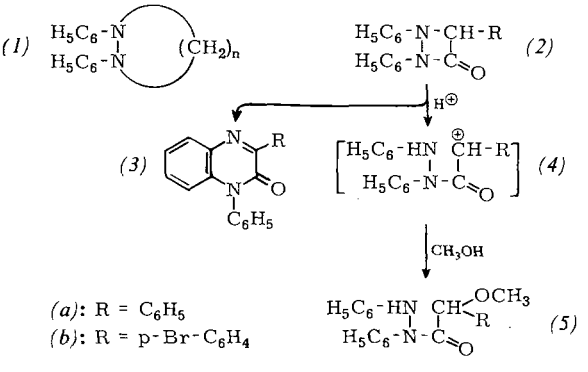
[3] Cf. The Preparation of Thiazolo[2,3-*b*]thiazolium Salts: *C. K. Bradsher*, *D. F. Lohr*, and *W. J. Jones*, Tetrahedron Letters *1965*, 1723.

ortho-Semidine Rearrangement of 1,2-Diphenyl-1,2-diazetidinone [1]

By *W. Fischer* and *E. Fahr* [*]

According to work by *Wittig et al.* [2], 1,2-diazacycloalkanes of type *(1)* undergo the *ortho*-semidine rearrangement only when *n* is at least 4. We have, however, found that the rearrangement occurs also with 1,2-diazetidinones of type *(2)*.

If the 1,2-diazetidinone *(2a)* (3 mmoles) is boiled under reflux (2 h) in methanolic solution (300 ml) with sulfuric acid (3 ml) [3], a mixture is obtained from which compound *(3a)* (m.p. 192 °C, 34% yield) separates, having been formed by an *ortho*-semidine rearrangement [4]. The structure of *(3a)* was proved by synthesis (86% yield) from *o*-aminodiphenylamine hydrochloride and phenylglyoxylic acid (equimolar amounts in a little water at room temperature). Use of preparative thin-layer chromatography (silica gel, $CHCl_3$) led to isolation, from the rearrangement mixture, of the hydrazide *(5a)* [m.p. 145 °C; yield 23%; IR (KBr), 3280 (NH), 1660 (conj. C=O) cm^{-1}; NMR ($CDCl_3$), aromatic CH and NH signals between $\tau = 2.43$ and $\tau = 3.37$, $\tau = 4.82$ (t-CH), $\tau = 6.67$ (OCH_3)], which is formed from *(4)* by rupture of the C–N bond.



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[*] Dr. W. Fischer and Prof. Dr. E. Fahr
Institut für Organische Chemie der Universität
Röntgenring 11
87 Würzburg (Germany)

[1] Part III of 1,2-Diazetidines. – Part II: *E. Fahr, W. Fischer, A. Jung,* and *L. Sauer,* Tetrahedron Letters *1967,* 161.

[2] *G. Wittig, P. Börzel, F. Neumann,* and *G. Klar,* Liebigs Ann. Chem. *691,* 109 (1966).

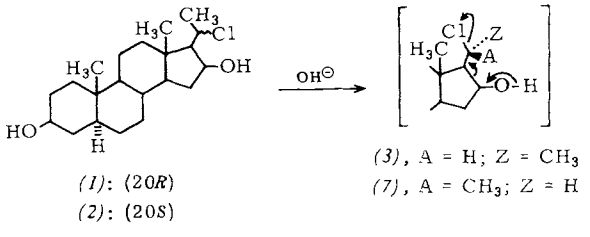
[3] Use of hydrochloric acid in place of sulfuric acid results in a reaction in which the chloride ion takes part.

[4] We obtained *(3b)* analogously from *(2b)*.

A New Fragmentation Reaction of 20-Chloro-16β-hydroxy Steroids

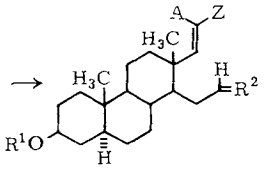
By *G. Adam*[*]

When heated with 5 % methanolic potassium hydroxide (3 h; 80 °C), 20-chloropregnan-16β-ols[1] fragment with loss of HCl and opening of ring D to form 17(20)-unsaturated 16,17-seco-16-aldehydes in 80–90 % yield. The reaction is stereospecific, its course being determined by the configuration at C-20. In this way (20*R*)-20-chloro-5α-pregnane-3β,16β-diol *(1)* affords *trans*-3β-hydroxy-16,17-seco-5α-pregn-17(20)-ene-16-aldehyde *(4)* (m.p. 121–122 °C; $[\alpha]_D^{20} = -22.3°$ ($CHCl_3$)), and the (20*S*)-stereoisomer *(2)* affords the *cis*-aldehyde *(8)* (double m.p. 82–85 and 113–116 °C; $[\alpha]_D^{18} = -9.2°$).



(1): (20*R*)
(2): (20*S*)

(3), A = H; Z = CH_3
(7), A = CH_3; Z = H



A = H, Z = CH_3:
(4), R^1 = H, R^2 = O
(5), R^1 = Ac, R^2 = O
(6), R^1 = H, R^2 = NOH

A = CH_3, Z = H:
(8), R^1 = H, R^2 = O
(9), R^1 = Ac, R^2 = O
(10), R^1 = H, R^2 = NOH

The structure of the steroid aldehydes *(4)* and *(8)* was proved as follows: In the mass spectra (negative ionization)[2] main peaks occur at *m/e* = 317 = M – 1, corresponding to a molecular formula $C_{21}H_{34}O_2$. The 100 MHz NMR spectra[2] for the *trans*- and *cis*-isomers, respectively, contain quadruplets at δ = 9.5 and 9.6 ppm (aldehyde-proton), multiplets at 5.25 and 5.15 ppm (vinyl-proton), 3.55 ppm (H on C-3), doublets centered at 1.62 and 1.71 ppm (21-methyl), and two singlets each at 0.78 and 0.87, and 0.77 and 1.08 ppm (19- and 18-methyl). The IR spectrum of *(4)* shows bands at 975 (*trans*-CH=CH–), 1678 (C=C), 1731, 2710, 2815 (aldehyde), 3025 (–CH=CH–), and 3629 cm^{-1} (OH). In the IR spectrum of *(7)* the absorption at 975 cm^{-1} is replaced by a band at 700 cm^{-1} (*cis*-CH=CH–). The two seco-steroids were also characterized as their *O*-acetyl derivatives *(5)* and *(9)* with, respectively, m.p. 84–86 °C, $[\alpha]_D^{19} = -34.2°$, and double m.p. 85–90 ° and 98–100 °C, $[\alpha]_D^{19} = -19.1°$, and as the oximes *(6)* and *(10)* with, respectively, m.p. 196–198 °C, $[\alpha]_D^{20} = -31.0°$, and m.p. 194–198 °C, $[\alpha]_D^{19} = -17.6°$.

The fragmentations observed can be regarded as special cases of olefin-forming Grob fragmentation[3]. When regard is paid to the *trans*-elimination principle and the known configurations of *(1)* and *(2)* at C-20 a synchronous reaction mechanism such as *(3)* and *(7)* can be formulated, whereby the stereospecific formation of the *trans*-aldehyde *(4)* from *(1)* and of the *cis*-aldehyde *(8)* from *(2)* is explained.

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[*] Dr. G. Adam
Institut für Kulturpflanzenforschung der Deutschen Akademie der Wissenschaften zu Berlin
X 4325 Gatersleben, Kreis Aschersleben (Germany)

[1] *G. Adam* and *K. Schreiber,* Chem. and Ind. *1965,* 989; Tetrahedron *22,* 3581 (1966).

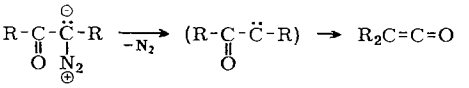
[2] I thank Dr. *R. Tümmler,* Dresden, for measurement of the mass spectra, and Dr. *W. v. Philipsborn,* Zurich, for measurement of the NMR spectra.

[3] *C. A. Grob* and *P. W. Schiess,* Angew. Chem. *79,* 1 (1967); Angew. Chem. internat. Edit. *6,* 1 (1967).

A Continuous Process for the Preparation of Diphenylketene

By *W. Ried* and *P. Junker*[*]

Up to the present, diphenylketene has been prepared either by heating a benzene solution of azibenzil to 70 °C[1] or by allowing this solution to drip, in a N_2 stream, into a flask heated to 105–110 °C[2].



R = C_6H_5, CH_3

Both methods suffer from the disadvantage that the diphenylketene already formed must be heated until all the azibenzil has decomposed and rearranged. With large batches (>0.5 mole) this leads to considerable losses since diphenylketene readily polymerizes when heated and, further, can also react with both azibenzil and the intermediate carbene. Good yields of diphenylketene are obtained, however, by use of the apparatus shown in Figure 1, by means of which the ketene formed is at once removed from the hot reaction zone.

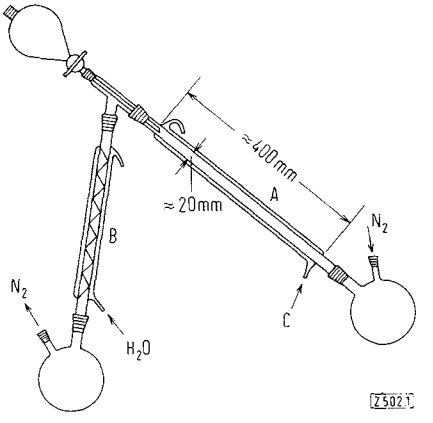


Fig. 1. Apparatus for continuous preparation of diphenylketene.

A heating fluid (*e.g.* paraffin oil), heated to 130 °C, is passed through the jacket C of the inclined condenser A, and a slow stream of N_2 is passed through the apparatus from the lower end of the heated tube. As soon as the air is removed, a benzene solution of azibenzil is added slowly from the dropping funnel. The solvent evaporates at once, while the azibenzil decomposes and rearranges; the benzene vapors are condensed in the condenser B. The rate of drip of the solution is determined so that evolution of nitrogen terminates about 5 cm above the lower end of the heated zone. The diphenylketene formed is washed out of the heated tube into the cold receiver by the reaction solution. After vacuum distillation the yield amounts to about 80 %.

The apparatus can be used also for the preparation of dimethylketene from azibutanone[3] if the reaction tube is heated at 170–180 °C. Since dimethylketene boils at 34 °C a high-boiling solvent such as tetralin or 1-methylnaphthalene must be used. This flows through the hot reaction tube while the ketene distils off and is condensed in a cold trap mounted in place of the condenser B or is used directly for further work in the gas phase. The yields of dimethylketene obtained in this way have not yet been as high as those obtained by decomposition of dimethylketene dimethylmalonyl acylal[4].

Diphenylketene:

Benzil monohydrazone (224 g, 1 mole) is mixed with yellow mercuric oxide (320 g) and anhydrous sodium sulfate (100 g) in anhydrous benzene (800 ml), methanolic KOH (1 to 2 ml) is added, and the whole is stirred for one hour with ice-cooling and then filtered. The filtrate is allowed to drip into the apparatus described (temp. of heating fluid: 130–135 °C) and the crude product that collects in the receiver is finally distilled as quickly as possible. Yield 149 g (77 %); yellow liquid, b.p. 109 °C/1 mm ([2]: 125 °C/4 mm).

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[*] Prof. Dr. W. Ried und Dipl.-Chem. P. Junker
Institut für Organische Chemie der Universität
Robert-Mayer-Strasse 7–9
6 Frankfurt/Main (Germany)

[1] *G. Schroeter*, Ber. dtsch. chem. Ges. *42*, 2346 (1909).

[2] *L. J. Smith* and *H. H. Holm*, Org. Syntheses *20*, 47 (1940).

[3] *O. Diels* and *K. Pflaumer*, Ber. dtsch. chem. Ges. *48*, 223 (1915).

[4] *H. Bestian* and *N. Günther*, Angew. Chem. *75*, 841 (1963); Angew. Chem. internat. Edit. *2*, 608 (1963).

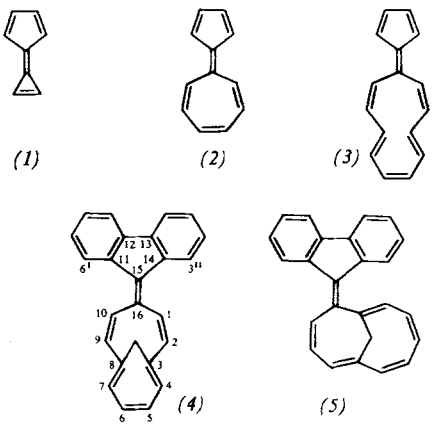
Pentahendecafulvalene

By *H. Prinzbach* and *L. Knothe*[*]

Pentahendecafulvalene *(3)* is the next higher homologue in the series calicene *(1)*[1] – sesquifulvalene *(2)*[2].

We have accomplished the first synthesis of a derivative of *(3)*, namely, 11,12;13,14-dibenzo-3,8-methanopentahendecafulvalene *(4)* in which the eleven-membered ring is bridged and the five-membered ring doubly annelated, as well as two isomers thereof to which we provisionally assign structures *(5)* and *(11)*.

When 8 mmoles of fluorenyl-lithium are treated in ether/tetrahydrofuran (1:1 v/v) at −30 °C with 6.9 mmoles of bicyclo[5.4.1]dodecapentaenylium fluoroborate[3] and the resulting mixture of hydrocarbons is oxidized with 8.1 mmoles of chloranil in carbon tetrachloride, a mixture is isolated consisting of a yellow component *(4)* and two red conponents *(5)* and *(11)*[4]. A satisfactory chromatographic separation of these components has not yet been achieved. The yellow



component can be separated from the two red ones by utilizing their differing basicities. Compounds *(5)* and *(11)* give insoluble salts with HBF_4 in ether/cyclohexane (1:10 v/v), whereas *(4)* remains in solution. *(4)* precipitates from benzene as yellow crystals, m.p. 223.5–224.5 °C, in 14 % yield. Treating the salt mixture with triethylamine in $CHCl_3$, or with $NaHCO_3$ in H_2O, regenerates *(5)* and *(11)* as dark red needles having a green sheen, m.p. 179–182 °C [from benzene/petroleum ether, 1:9 v/v; yield 16 %, content of *(5)* > 95 %]. The relative yields of the isomers can to some extent be controlled by varying the reaction temperature.

The structure of *(4)* follows from the NMR[5] and the mass spectrum[6] as well as from the result of ozonolysis which affords fluorenone in good yield.

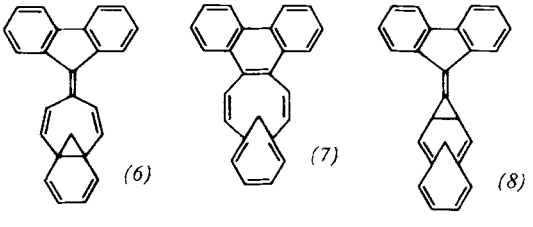
The following conclusions can be drawn from the NMR spectrum:

a) The molecule has a plane of symmetry (10 types of proton in the ratio 2:2:2:2:2:2:2:2:1:1).

b) The molecule does not exist in the norcaradiene form *(6)* (J_{gem} of the CH_2 bridge = 11.0 Hz)[7].

c) Conversion into *(7)* has not occurred; the positions of the signals of the eight "aromatic" protons is typical of the fluorene skeleton, but much too "high" for a phenanthrene ring[1] (cf. the ozonolysis).

d) The steric hindrance between protons H(1)–H(10) and H(3′)–H(6′) to be expected for the completely conjugated perimeter of *(4)* does not cause conversion into the unhindered structure *(8)*.



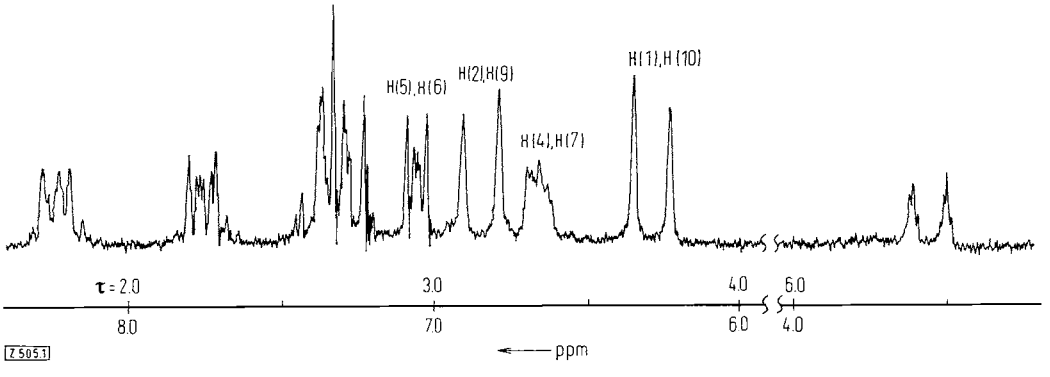


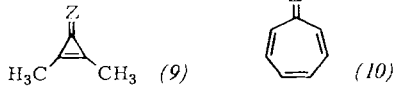
Fig. 1. NMR spectrum of *(4)* in $CDCl_3$. Tetramethylsilane as internal standard. 100 MHz, 27 °C. A further doublet with J = 11.0 Hz lies at τ = 9.80.

The mass spectrum of *(4)* includes the following strong signals: M^+ = 318 (100 %), 319 (45 %), 317 (35 %), 315 (15 %), 313 (12 %), 303 (26 %), 302 (40 %), 289 (25 %), 276 (11 %), 189 (36 %), 165 (21 %), 153 (16 %), 129 (14 %), 128 (12 %). The fact that the molecular ion gives the strongest signal indicates a stable, fully conjugated molecule. The low intensity of the fragment with *m/e* = 165 indicates further that the fluorenyl group is attached by a double bond.

IR (KI): $\tilde{\nu}$ = 1621 cm^{-1}, 1600, 1575, 1541, 1475, 1447, 1351, 1348.

UV: λ_{max} (cyclohexane) = 399 nm (ε = 20200), 342 (26800), 304 (16400, s), 294 (15840, s), 263 (40500, s), 260 (41800, s), 255 (42200), 239.6 (61500).

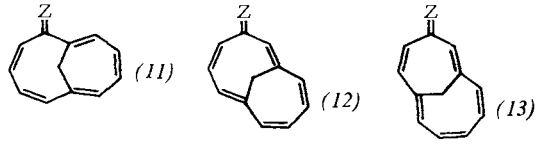
The basicity of *(4)* is surprisingly low; it is not protonated by 70 % $HClO_4$, CF_3CO_2H, or HBF_4 in ether. In the same media dibenzocalicene *(9)* [1], dibenzosesquifulvalene *(10)* [2], as well as the unsymmetrical isomers *(5)* and *(11)*, exist almost wholly as the conjugate acids.



(9) *(10)*

Z = 9-Fluorenylidene

(5) and *(11)* to *(13)* represent possible structures for the red pentahendecafulvalenes isomeric with *(4)*. Because of the



(11) *(12)* *(13)*

Z = 9-Fluorenylidene

considerable differences in chemical shift of the signals for H(6') and H(3'') and the low position of one of these signals, we consider structures *(5)* and *(11)* as the most probable. Quantum-mechanical results [8] favor structure *(5)* for the major red component.

The pentahendecafulvalenes *(4)*, *(5)*, and *(11)* are thermally very stable; they can be sublimed unchanged at 150–160 °C/0.001 mm). N–V' excitation of *(4)* causes a red shift of 26 nm compared with the system of *(10)* that is smaller by two C=C double bonds [λ_{max} (cyclohexane) = 373 nm, ε = 24000]; this and the relatively weak solvatochromic effect are of the expected order of magnitude. The basicities of *(5)* and *(11)*, which are greater than that of *(4)*, and the N–V' transitions [*(5)*, 488 nm, ε = 23000] which are at much longer wavelengths indicate a lower stability of the unsymmetrical isomers. According to our results so far, compound *(4)*, like *(10)*, but unlike *(9)*, does not react with dimethyl acetylenedicarboxylate.

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[*] Prof. Dr. H. Prinzbach
Université de Lausanne, Laboratoire de Chemie Organique
3, Place du Château, Lausanne (Switzerland)
Dipl.-Chem. L. Knothe
Chemisches Laboratorium der Universität
Albertstr. 21
78 Freiburg (Germany)

[1] *H. Prinzbach* and *U. Fischer*, Helv. chim. Acta, in press.

[2] *H. Prinzbach, D. Seip, L. Knothe*, and *W. Faisst*, Liebigs Ann. Chem. *698*, 34 (1966).

[3] We thank Prof. *E. Vogel* for experimental details and Dr. *W. Grimme* for advice.

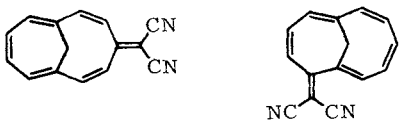
[4] Analogous results have been observed for reaction with malonodinitrile. Two compounds have been isolated so far, to which we assign the structures shown. *B. Schnellbacher*, Zulassungsarbeit zur Wissenschaftlichen Prüfung für das höhere Lehramt, Universität Freiburg, 1967.

[5] Dr. *U. Scheidegger*, Varian AG, Zürich.

[6] Dr. *H. Achenbach*, Universität Freiburg.

[7] *R. C. Cookson, T. A. Crabb, J. J. Frankel*, and *J. Hudec*, Tetrahedron, Suppl. *7*, 355 (1966).

[8] *M. J. S. Dewar, G. J. Gleicher*, and *C. C. Thompson jr.*, J. Amer. chem. Soc. *88*, 1349 (1966).

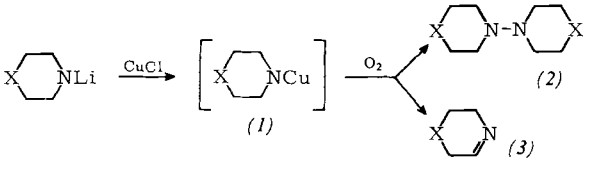


"Dimerization" of Organic Nitrogen Compounds *via* Copper-Containing Intermediates [1]

By *Th. Kauffmann, J. Albrecht, D. Berger*, and *J. Legler* [*]

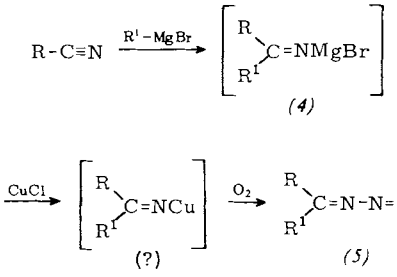
Acetylenes can be dimerized by oxidizing their copper(I) compounds with oxygen in the presence of NH_3 or amines (Glaser reaction) [2]. We have found that cyclic secondary amines, and also imines and amidines, can be dimerized analogously.

Dimerization of Amines: The secondary amines were converted by phenyl-lithium into the lithium amides, which on reaction at 20 °C with one molar equivalent of anhydrous CuCl in a mixture (1 : 1 v/v) of diethyl ether and free amine gave colorless suspensions that probably contained copper(I) amides of the type *(1)* [3]. These suspensions become dark brown when oxygen is passed into them (1 h) and a strongly exothermic reaction leads in each case to a hydrazine derivative of type *(2)* and an azomethine *(3)*. Yields, calculated on the lithium amide are: *(2)*, X = O 80 %, X = CH_2 109 %; *(3)*, X = O <5 %, X = CH_2 60 %. The yields in excess of 100 % for *(2)* + *(3)* when X = CH_2 show that the free amine enters into reaction in this case. – Under the above conditions pyrrolidine and diethylamine give almost exclusively the azomethines.



(1) *(2)* *(3)*

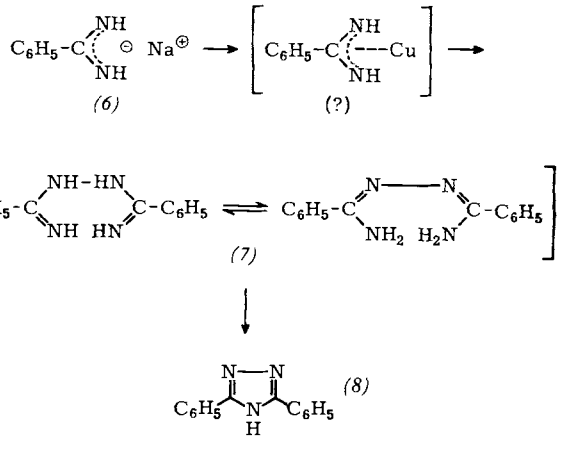
Dimerization of Imines: The colorless iminomagnesium halides *(4)* obtained by reaction of benzonitrile with a molar equivalent of Grignard reagent were treated with anhydrous CuCl in ether/tetrahydrofuran (2 : 1 v/v) at 20 °C; a yellow (R^1 = C_6H_5) or pale grey (R^1 = C_2H_5) suspension was formed. After oxygen had been passed in at 20 °C (1 h), an azine of type *(5)* could be isolated from the mixed products in each case. The best yields (94 % when R^1 = C_6H_5, 75 % when R^1 = C_2H_5; based on nitrile) were obtained when 0.05 to 0.2 mole of CuCl was used per mole of nitrile.



(4) (?) *(5)*

Dimerization of Amidines: The sodium amidines *(6)* obtained by treatment of benzonitrile with sodium amide were treated with a molar equivalent of anhydrous CuCl in 1,2-

dimethoxyethane at 20 °C. Oxygen was then passed into the yellowish-green mixture at 85 °C (15 h). The triazole *(8)* could be isolated in 40 % yield [based on *(6)*] from the black mixture. The diazabutadiene-1,4-diamine *(7)* may be a precursor of *(8)*, but attempts to isolate this compound, which rapidly loses NH_3 to form *(8)* [4], were unsuccessful. When $CuCl_2$ was used in place of CuCl the yield of *(8)* amounted to 74 %.



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[*] Prof. Dr. Th. Kauffmann, cand. chem. J. Albrecht, cand. chem. D. Berger, and cand. chem. J. Legler
Organisch-Chemisches Institut der Universität
Hindenburgplatz 55
44 Münster (Germany)

[1] Part 2 of Syntheses of Heterocycles *via* Intermediates Containing Transition Metals. *Th. Kauffmann* and *W. Sahm*, Angew. Chem. *79*, 101 (1967); Angew. Chem. internat. Edit. *6*, 85 (1967), is considered as Part 1.

[2] *C. Glaser*, Liebigs Ann. Chem. *154*, 159 (1870).

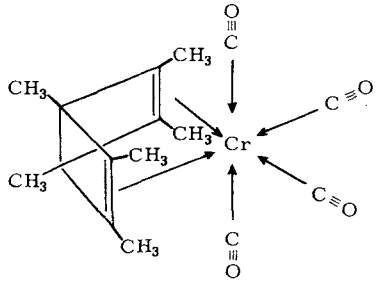
[3] These compounds, which are thermally very stable but are very sensitive to oxygen, have not yet been isolated in pure form.

[4] *A. Pinner*, Liebigs Ann. Chem. *297*, 228 (1897).

Tetracarbonyl(hexamethylbicyclo[2.2.0]hexadiene)-chromium(0)

By *E. O. Fischer*, *C. G. Kreiter*, and *W. Berngruber* [*]

Reaction of $(CH_3CN)_3Cr(CO)_3$ [1] with hexamethyl(Dewar benzene) [2] in dioxane (1.5 h at 40 °C) followed by filtration, evaporation of the filtrate to dryness, and chromatography of the residue on Al_2O_3 (Grade III) using n-hexane as eluant gave the first π-complex of the Dewar-benzene system, namely, the yellow, well crystalline compound $C_{12}H_{18}Cr(CO)_4$ *(1)* (yield *ca.* 5 %). The complex *(1)* is monomeric in organic media such as benzene, chloroform, and n-hexane in which it is also readily soluble. The composition of *(1)* has been established by means of elemental analysis of the crystalline material which sublimes unchanged at 60 °C in a high vacuum and decomposes above 115 °C as indicated by a darkening in color.



The ^1H–NMR spectrum of *(1)* indicates that hexamethylbicyclo[2.2.0]hexadiene, functions as a bidentate ligand in the complex. In $CDCl_3$ solution, the spectrum shows only two sharp signals at $\tau = 8.26$ and 9.1 (tetramethylsilane as internal standard) having the relative intensities 2:1 respectively. The chemical shifts are thus only slightly different from those of free hexamethyl(Dewar benzene) ($\tau = 8.45$ and 8.94). On warming, hexamethyl(Dewar benzene) is readily converted into hexamethylbenzene, whose $Cr(CO)_3$ complex displays only one ^1H–NMR signal at $\tau = 7.67$.

Four sharp bands at 2025, 1940, 1920, and 1900 cm^{-1} in the ν_{CO} region of the IR spectrum of *(1)* are in accord with the $Cr(CO)_4$ group and, when compared with the similarly constituted complex norbornadiene-$Cr(CO)_4$ [3] (4 ν_{CO} at 2032, 1960, 1946, and 1915 cm^{-1} in n-hexane), demonstrate a somewhat weaker binding of hexamethyl(Dewar benzene). ν_{CO} bands of hexamethylbenzene-$Cr(CO)_3$ [4], which lie at 1960 and 1890 cm^{-1}, were not found in the IR spectrum of *(1)*.

The shift of the ν(C=C) vibration at 1694 cm^{-1} (film) of free hexamethyl(Dewar benzene) to 1543 cm^{-1} (KBr disc) in the spectrum of *(1)* confirms that both the C=C double bonds are coordinated to the metal.

The mass spectrum [5] of *(1)* shows, in addition to the molecular ion $C_6(CH_3)_6Cr(CO)_4^+$ (*m/e* = 326), the characteristic fragment ions $C_6(CH_3)_6Cr(CO)_3^+$ (298), $C_6(CH_3)_6Cr(CO)_2^+$ (270), $C_6(CH_3)_6Cr(CO)^+$ (242), $C_6(CH_3)_6Cr^+$ (214), Cr^+ (52), CO^+ (28), and $C_6(CH_3)_6^+$ (162).

Further confirmation [6] of the structure is provided by the liberation of hexamethyl(Dewar benzene) when *(1)* is treated with pyridine.

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[*] Prof. E. O. Fischer, Dr. C. G. Kreiter, and W. Berngruber
Anorganisch-chemisches Laboratorium der Technischen Hochschule
Arcisstrasse 21
8 München 2 (Germany)

[1] *D. P. Tate*, *W. R. Knipple*, and *T. M. Augl*, Inorg. Chem. *1*, 433 (1962); see also *R. Prinz* and *H. Werner*, Angew. Chem. *79*, 63 (1967); Angew. Chem. internat. Edit. *6*, 91 (1967).

[2] *W. Schäfer*, Angew. Chem. *78*, 716 (1966); Angew. Chem. internat. Edit. *5*, 699 (1966).

[3] *M. A. Bennett*, *L. Pratt*, and *G. Wilkinson*, J. chem. Soc. (London) *1961*, 2037.

[4] *E. O. Fischer*, *K. Öfele*, *H. Essler*, *W. Fröhlich*, *J. P. Mortensen*, and *W. Semmlinger*, Chem. Ber. *91*, 2763 (1958).

[5] Measured by *J. Müller*, Atlas CH4, 50 eV.

[6] X-ray structural investigation in progress.

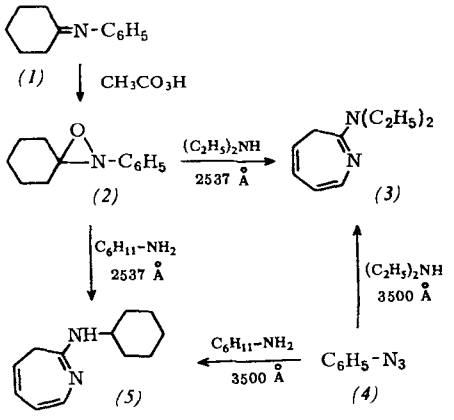
Photofragmentation of Oxaziranes

By *Ernst Meyer* and *G. W. Griffin* [*][**]

The spirooxazirane *(2)* is obtained [1] by addition of the anil *(1)* (8.6 g; 0.05 mole) in anhydrous ether (25 ml) to an anhydrous solution of peracetic acid [2] in benzene (0.05 mole) diluted with ether (25 ml) at 0 °C. After standing at room temperature for one hour, the reaction mixture is washed in turn with 10 % sulfuric acid and 10 % sodium carbonate and finally dried over potassium carbonate. The solvents are then removed by distillation under reduced pressure and the residue is dissolved in petroleum ether (b.p. 40–60 °C). On filtration of this solution through Celite and activated charcoal and subsequent concentration and cooling, compound *(2)* crystallizes out [m.p. 73–74 °C (lit. [1]: 75 °C); yield 3.0–3.5 g (36 %)].

Irradiation (24 hours) of *(2)* (3.0 g; 0.16 mole) in freshly distilled diethylamine (70 ml) [3] affords the 2-diethylamino-3*H*-azepine *(3)* (0.26 g; 10 %) which can be isolated by gas chromatography [4] after a preliminary distillation (70 to 120 °C/0.5 mm). The NMR and IR spectra are identical with those of an authentic sample prepared independently in 34 %

yield by irradiation of phenylazide (0.24 g, 0.002 mole) in diethylamine[5, 6].



Aniline is also produced upon photolysis of *(2)* but no accurate determination has been made of the yield (approximately 9 %). It is reasonable to assume that phenyl nitrene is formed as intermediate in the photolysis of *(2)* and *(4)*[7]. The photolabile compound *(5)* is formed if irradiation is carried out in cyclohexylamine.

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[*] Dr. Ernst Meyer and Prof. G. W. Griffin
Department of Chemistry
Louisiana State University in New Orleans, Lake Front
New Orleans, Louisiana, 70122 (U.S.A.)

[**] We thank the National Institutes of Health (G.M 14667-01) and the Army Research Office (Durham) for financial support of our work.

[1] *H. Krimm*, Chem. Ber. *91*, 1057 (1958); *L. Horner* and *E. Jürgens*, Chem. Ber. *90*, 2184 (1957).

[2] A solution of commercial peracetic acid (40 %) was dehydrated according to the method of *Horner* and *Jürgens* [1] by cautious addition to a benzene slurry of P_2O_5. The organic phase was decanted after 15 minutes and titrated iodometrically against a 0.1 M sodium thiosulfate solution.

[3] Irradiation conducted in 15 cm quartz tubes with degassed samples at 35 °C with low pressure mercury lamps (2537 Å).

[4] Column: 2 m × 8 mm with 30 % Silicone DC Hyvac grease as stationary phase. Temperature: 230 °C.

[5] *R. O. Lindsay* and *C. F. H. Allen* in: Organic Syntheses. Wiley, New York 1966, Coll. Vol. III, p. 710.

[6] *W. von E. Doering* and *R. A. Odum*, Tetrahedron *22*, 81 (1966) and references cited therein.

[7] The reaction may involve prior cyclization of phenyl nitrene to 7-azabicyclo[4.1.0]hepta-2,4,6-triene which subsequently reacts with the nucleophilic amine to give *(3)* or *(5)*. See [6], *R. Huisgen*, *D. Vossius*, and *M. Appl*, Chem. Ber. *92*, 2961 (1959), and *G. Smolinsky*, J. org. Chemistry *27*, 3557 (1962).

Reaction of Carbon Monosulfide and Monoselenide with Chalcogens and Halogens

By *R. Steudel*[*]

CS is formed by dissociation of CS_2 in a high-frequency discharge (0.1 mm) and can be isolated in a flow system at −190 °C and detected by low-temperature IR spectrometry[1]. By using the same experimental technique[2] it has now been found that CS undergoes a heterogeneous reaction (even at room temperature) to form SCSe and SCTe, if the walls of the discharge tube are covered with Se or Te, respectively.

In the high-frequency discharge, CSe_2 clearly gives CSe which, although it cannot be isolated, can be trapped as SeCS or SeCTe by reaction with solid sulfur or tellurium. High concentrations of mixed carbon dichalcogenides are, however, formed only on reaction of CS or CSe with gaseous chalcogens. For this purpose the discharge tube was heated until the chalcogen began to sublime. SeCTe, previously unknown, could thus be obtained in about 8 % yield (calculated on CSe_2).

For the reaction of CS with Cl_2, Br_2, or I_2 the gaseous halogen (in the proportion 0.2:1 to 0.5:1 calculated on CS_2; temperature 25 °C) was added continously behind the glowing zone of the high-frequency discharge in CS_2. Condensation was effected after a reaction time of about 0.1 sec; the thiocarbonyl halides $SCCl_2$, $SCBr_2$, and the new compound SCI_2 could thus be isolated.

SeCTe and SCI_2 are very sensitive thermally and cannot be sublimed in a high vacuum. They were identified from the following IR absorptions (at −190 °C, in a CS_2 or CSe_2 matrix), as also was $SCBr_2$ which was previously incompletely characterized (wave numbers in cm^{-1})[3]:

SeCTe: $\nu_3 = 1179$ vs, $\nu_3(Se^{13}CTe) = 1136$ w, $\nu_1 + \nu_3 = 1473$ m
$SCBr_2$: $\nu(C{=}S) = 1097$ s, $\nu(C{-}Br) = 685$ s
SCI_2: $(C{=}S) = 1062$ s, $(C{-}I) = 602$ s

The wave number of the C=S stretching vibration is particularly low for $SCCl_2$ (compared with the other thiocarbonyl halides), which can be interpreted as due to participation of a resonance structure with C−S and C=Cl bonds in the ground state of thiophosgene.

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[*] Dr. R. Steudel
Institut für Anorganische und Analytische Chemie
der Technischen Universität
Hardenbergstr. 34
1 Berlin 12 (Germany)

[1] *R. Steudel*, Z. Naturforsch. *21b*, 1106 (1966).

[2] Cf. *R. Steudel*, Tetrahedron Letters, *1967*, 1845; Z. anorg. allg. Chem. *346*, 262 (1966).

[3] m = medium, w = weak, s = strong, vs = very strong.

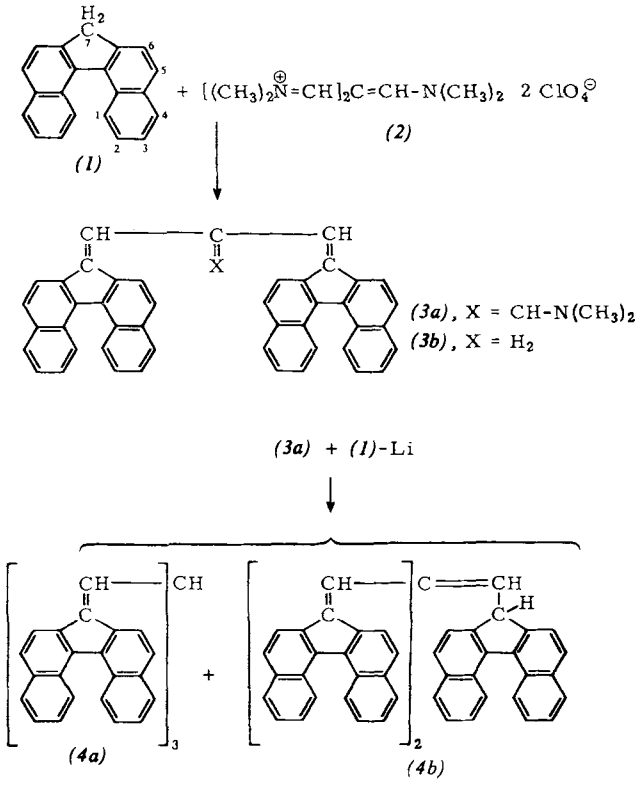
Tris-(7*H*-dibenzo[*c*,*g*]fluorenylidenemethyl)methane a New Highly Acidic Hydrocarbon [1]

By *R. Kuhn* and *D. Rewicki*[*]

7*H*-Dibenzo[*c*,*g*]fluorene *(1)* is about 4 powers of ten more acidic than fluorene[2]. Tris(biphenylylenevinyl)methane[3,4] has the highest acidity of the fluorene-substituted hydrocarbons described hitherto. It seemed to us, therefore, of interest to prepare tris-(7*H*-dibenzo[*c*,*g*]fluorenylidenemethyl)methane *(4a)*.

The hydrocarbon *(4a)* was obtained in admixture with its tautomer *(4b)* by a method given by *Jutz* and *Amschler*[4]. A concentrated solution of dibenzo[*c*,*g*]fluorene *(1)* (2 mol. equiv.) and the diperchlorate *(2)* (1 mol. equiv.) in pyridine was treated with 3 N $NaOCH_3$ solution (2.3 mol. equiv.). After warming the reaction mixture for a short time the dimethylamino compound *(3a)* was precipitated as dark red crystals, m.p. 265–270 °C, $\lambda_{max} = 506$ nm, $\log \varepsilon = 4.70$ (in tetrahydrofuran), in 80 % yield. Analyses, molecular-weight determinations, and the NMR spectrum of the chromatographically homogeneous substance agreed with formula *(3a)*. The dibenzofluorene *(1)* (1.7 mol. equiv.) was converted in tetrahydrofuran and under nitrogen into its lithium salt by means of 1 N ethereal phenyl-lithium solution. The dimethylamino compound *(3a)* (1 mol. equiv.) was added to this solution and the whole was boiled for 1 h under reflux. The resulting dark green solution was decolorized with O_2-free 2 N HCl and then extracted with benzene. On removal of the benzene and recrystallization of the residue from benzene/petroleum ether (8:2 v/v) a 65 % yield of the orange-brown hydrocarbon $C_{67}H_{40}$ was obtained that decomposed at 210 to 215 °C. Analyses and molecular-weight determinations agreed with this molecular formula. A thin-layer chromato-

gram [SiO_2; solvent, benzene/cyclohexane (1:9)] showed a double spot, which is attributed to presence of the mixture of tautomers *(4a)/(4b)*.



The NMR spectrum of the mixture (in $CDCl_3$) includes two doublets (τ = 3.64 and 4.64 ppm, J = 10 Hz), corresponding to the >C=CH–CH< group of *(4b)*, as well as a multiplet (τ = 1.2–3.0 ppm).

In dimethyl sulfoxide (DMSO) the hydrocarbons *(4)* give a deep green carbanion when treated with bases (*e.g.* NaOH, tri-n-propylamine). This anion (λ_{max} = 697 nm, log ε = 5.15) is fairly stable to oxygen but on oxidation with $K_3Fe(CN)_6$ it affords the radical tris-(7*H*-dibenzo[*c*,*g*]fluorenylidenemethyl)methyl (λ_{max} = *ca.* 860, 545 nm in benzene) which is carmine-red in solution but brownish-red in the crystalline state. This radical is sensitive to oxygen. Its ESR spectrum[5] in benzene shows four lines with relative intensities 1:3:3:1 (a_H = *ca.* 7 gauss), corresponding to coupling of the radical electron with the three equivalent vinyl protons. In the solid state the radical is partly monomeric.

As expected, the hydrocarbons *(4)* have high acidity. A 10^{-5} M solution in carefully purified DMSO is almost completely dissociated even without addition of base. A 10^3-fold molar excess of HCl in DMSO/water (85:15 mol.-%) depresses the dissociation but does not suffice to decolorize the green solution. We have determined the relative acidities of some highly acidic hydrocarbons by spectrophotometric measurements in various solvents (DMSO/water/HCl, DMSO/glacial acetic acid/sodium acetate, DMSO/tri-n-propylamine, DMSO/ethanol/sodium methoxide) and by means of 9-cyanofluorene (pK = 11.4)[6] have derived the following pK values (referred to water)[2].

Hydrocarbon [a]	pK value
BiphCH–C_6H_5	19.6 (18.6 [6])
BiphC=CH–HCBiph	14.2
[BiphC=CH]$_2$$CH_2$	12.3 [b]
BiphCH–CN	11.4 [6]
[BiphC=CH]$_3$CH	10.4 [b]
(3b)	8.2 [b]
(4a) + *(4b)*	5.9 [b]

[a] Biph = [b] Gross pK value.

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[*] Prof. Dr. R. Kuhn
Max-Planck-Institut für Medizinische Forschung,
Institut für Chemie
Jahnstr. 29
69 Heidelberg (Germany)
Dr. D. Rewicki
Institut für Organische Chemie der Freien Universität
Thielallee 63/67
1 Berlin 33 (Germany)

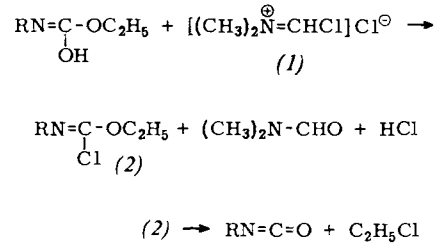
[1] Part X of Highly Acidic Hydrocarbons. – Part IX: *R. Kuhn* and *D. Rewicki*, Liebigs Ann. Chem., in press.
[2] *R. Kuhn* and *D. Rewicki*, Liebigs Ann. Chem., in press.
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Preparation of Isocyanates from Carbamates by Reaction with Phosgene

By *H. Ulrich*, *B. Tucker*, and *A. A. R. Saytgh*[*]

The synthesis of isocyanates from carbamates by means of phosphorus pentachloride[1] or pyrocatechol-phosphorus trichloride[2] has been recorded. However, it often involves difficulties in separating the isocyanates from the phosphorus oxide chlorides that are also formed[1]. In the case of alkylcarbamates, use of phosgene in place of phosphorus chlorides would result in formation of gaseous or low-boiling inert by-products. However, on reaction of ethylurethane with phosgene, carbonyldiurethane is the main product and carbamoyl chloride is formed only in small amount[1].

We have now found that reaction of carbamates in an inert solvent containing *N*,*N*-dimethylformamide (DMF) as catalyst gives isocyanates and alkyl chlorides. Reaction occurs even at low temperatures, and thus there is no reason to assume dissociation of the carbamates. The formimidoyl chloride *(1)* formed from phosgene and DMF apparently reacts with the enolic form of the carbamates, with formation of chloroformimidates *(2)* and regeneration of DMF. Thermolysis of the chloroformimidates to yield isocyanates and alkyl chlorides is known[3].



R	Solvent	Isocyanate B.p. (°C/mm)	Isocyanate Yield (%)
$CCl_3CH(OH)$	Chlorobenzene	41–54/7.5 [a]	13.2
CCl_3CHCl	Toluene	68–72/20 [a]	48.2
CH_2=CH–CH_2	*o*-Dichlorobenzene	85	57.2
C_6H_5–CH_2	Toluene	80/7	65.4
m-Cl–C_6H_4	Chlorobenzene	58–62/2.2	40.0

[a] The same isocyanate with R = CCl_3CHCl is obtained in these two cases.

Experimental:

Phosgene (1 g/min) is passed for 225 min into a boiling solution of 8.9 g (0.05 mole) of ethyl *N*-benzylcarbamate and

0.44 g of *N,N*-dimethylformamide in 90 ml of toluene. After removal of the excess of phosgene in a stream of nitrogen and rectification, 4.35 g (65.4 %) of benzyl isocyanate, b.p. 80 °C/7 mm, is obtained. No isocyanate is formed in the absence of catalyst under otherwise similar conditions.

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[*] Dr. H. Ulrich, B. Tucker, and Dr. A. A. R. Sayigh
The Upjohn Company, D. S. Gilmore Research Laboratories
North Haven, Conn. (U.S.A.)

[1] *O. Folin*, Amer. chem. J. *19*, 323 (1897).

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Preparation of Hexaazidophosphates

By *H. W. Roesky*[*]

We recently reported the preparation of the tetrachlorodicyanophosphate ion $[PCl_4(CN)_2]^{\ominus}$[1]. We have now accomplished complete substitution at the phosphorus atom by the more electronegative azide group and been able to prepare the hexaazidophosphate ion $[P(N_3)_6]^{\ominus}$ for the first time.

For the synthesis, sodium azide is added slowly, with vigorous stirring, to phosphorus pentachloride in anhydrous acetonitrile (molar ratio $PCl_5:NaN_3 = 1:10$). The reaction is slightly exothermic. Stirring is continued for 10 minutes at room temperature and an excess of 5 % aqueous tetraphenylphosphonium chloride solution is then added dropwise. A yellow viscous oil separates which can be reprecipitated from acetone/water. 1 g of PCl_5 gives 0.2 g of $(C_6H_5)_4P^{\oplus}[P(N_3)_6]^{\ominus}$. Tetraphenylarsonium chloride gives $(C_6H_5)_4As^{\oplus}[P(N_3)_6]^{\ominus}$ under the same conditions. All operations are carried out under a rapid current of dry nitrogen. The substances explode violently on slight warming.

The purest samples are obtained by separating the oil immediately after its preparation and drying it over P_4O_{10} in a vacuum desiccator. When moist, the compounds slowly evolve N_3H. The IR spectrum of $(C_6H_5)_4P[P(N_3)_6]$ in the NaCl region shows strong bands at 2150, 1250 with a shoulder, and 755 cm^{-1}, which are ascribed to $\nu_{as}(N_3)$, $\nu_s(N_3)$, and $\nu(P-N)$ vibrations. Further strong bands at 560 and 585 cm^{-1} are ascribed to deformation vibrations.

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[*] Dr. H. W. Roesky
Anorganisch-Chemisches Institut der Universität
Hospitalstr. 8–9
34 Göttingen (Germany)

[1] *H. W. Roesky*, Angew. Chem. *79*, 316 (1967); Angew. Chem. internat. Edit. *6*, 363 (1967).

Tungsten Trichloride $[W_6Cl_{12}]Cl_6$

By *R. Siepmann, H.-G. v. Schnering*, and *H. Schäfer*[*]

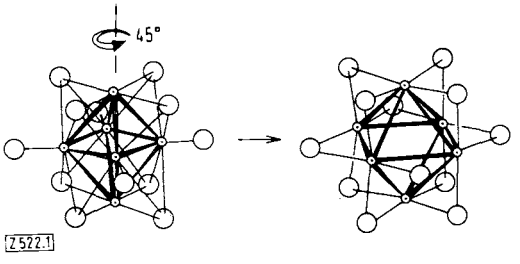
Compounds with the groups $[M_6X_8]$ and $[M_6X_{12}]$, where X = halogen, are known for the heavy transition metals[1]. When M = Mo or W the first type is regularly formed, and when M = Nb, Ta, Pd, or Pt the second.

Two exceptions to this rule are now known: (i) the recently discovered[2] iodide $[Nb_6I_8]I_{6/2}$ and (ii) the chloride $[W_6Cl_{12}]Cl_6$, which is described below.

Tungsten dichloride $[W_6Cl_8]Cl_{2}Cl_{4/2}$[1,3] reacts with liquid chlorine at *ca.* 100 °C, forming a black substance that contains 3 chlorine atoms per tungsten atom and gives sharp X-ray diagrams. The WCl_6 formed simultaneously is extracted with liquid chlorine at *ca.* 40 °C. Structural elements of the starting material apparently withstand this vigorous reaction with Cl_2. WCl_4 is converted completely into WCl_6 under similar conditions. The trichloride obtained is soluble in a small amount of warm $(CH_3)_2SO$, giving a dark brown solution. If this solution is treated with dilute aqueous H_2SO_4 and Na_2SO_4, only about 2.5/18 of the Cl becomes titratable with Ag_2SO_4. More AgCl is precipitated only on warming, and the W complex is thereby destroyed with precipitation of elemental Ag. The firm binding of the halogen is characteristic of the groups $[M_6X_8]$ and $[M_6X_{12}]$.

The structure of the trichloride was determined from Guinier measurements (by comparison with the Pt_6Cl_{12} structure). The material crystallizes in the hexagonal rhombohedral form with $a = 14.91$ Å, $c = 8.45$ Å, $c/a = 0.568$, $a_{rh} = 9.05$ Å, $\alpha_{rh} = 110.8°$, in the space group $R\bar{3}$-C_{3i}^2. The unit cell contains three formula units W_6Cl_{18} (X-ray density 5.33 g/cm^3). According to detailed calculation of intensities (trial-and-error procedure) the atoms have the following positions [position 18(f)]: 18 W with $x = 0.120$; $y = 0.016$; $z = 0.140$; 18 Cl_I with $x = 0.134$; $y = 0.018$; $z = -0.310$; 18 Cl_{II} with $x = 0.249$; $y = 0.151$; $z = 0$; and 18 Cl_{III} with $x = 0.268$; $y = 0.035$; $z = 0.310$. The W parameters were determined by comparison of intensities, the Cl parameters by consideration of bond distances. The structure contains discrete molecules $[W_6Cl_{12}^i]Cl_6^a$, which are arranged in a (distorted) body-centered cube. Interatomic distances are: $W-W = 2.9_2$, $W-Cl^i = 2.3_0$, $W-Cl^a = 2.5_2$, all $Cl-Cl > 3.6$ Å.

Conversion of the grouping $[M_6X_8]$ into $[M_6X_{12}]$ can occur in single steps by changing positions of X. However, the conversion $[M_6X_8]X_4 \rightarrow [M_6X_{12}]$ is also possible if the halogen sphere and the M_6 octahedron rotate in one step by 45 ° relative to each other (see Figure).



It is interesting that analogous "conversion" of the cationic group does not occur when Br_2 reacts with "tungsten dibromide" $[W_6Br_8]Br_2Br_{4/2}$; in this case the system changes with formation of polybromide.

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[*] Dipl.-Chem. R. Siepmann, Prof. Dr. H.-G. v. Schnering, and Prof. Dr. H. Schäfer
Anorganisch-Chemisches Institut der Universität
Hindenburgplatz 55
44 Münster (Germany)

[1] *H. Schäfer* and *H.-G. v. Schnering*, Angew. Chem. *76*, 833 (1964).

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Detection of the Molecules W_2Cl_6 and W_3Cl_9 in the Gaseous State

By *K. Rinke* and *H. Schäfer*[*]

The solid lower tungsten halides are of particular interest because of the formation of W–W bonds[1,2]. These bonds are probably essential also for the stability of the molecules

W_2Cl_6 and W_3Cl_9 that have now been observed in the mass spectrometer.

The Table shows the compounds studied and the relative ion intensities observed (a dash denotes not observed). Isotopic distribution was taken into account. The smaller fragments are not given for electron energies of 50 eV; for 12 and 15.5 eV the Table contains, however, all the $W_xCl_y^+$ ions observed.

No.	Substance	Approx. sample temp. (°C)	Electron energy (eV) uncorr.	Relative ion intensities						
				WCl_5^+	WCl_4^+	WCl_3^+	$W_2Cl_5^+$	$W_2Cl_6^+$	$W_3Cl_8^+$	$W_3Cl_9^+$
1	WCl_5	< 150	50	13	100	27	—	—	—	—
2		< 150	12	100	—	—	—	—	—	—
3	WCl_4	300	50	9	97	100	26	44	0.02	0.5
4		350	12	64	85	—	—	100	—	1
5	$WCl_{3.4}$ [a]	300—350	50	11	100	52	12	19	0.01	0.5
6	$[W_6Cl_{12}]Cl_6$	300—350	50	11	100	44	6	10	0.02	0.1
7		300	12	100	47	—	—	29	—	0.5
8	$K_3W_2Cl_9$	300	50	8	94	100	10	17	—	0.05
9		300	15.5	38	91	—	—	100	—	—
10	$[W_6Cl_8]Cl_4$	400	50	4	57	100	20	36	—	< 0.05
11		400	12	3	100	—	—	22	—	—

[a] $WCl_{3.4}$ is a material, amorphous to X-rays, containing 60.4% of W and 39.8% of Cl, obtained by *R. Siepmann* [2].

The products of hydrolysis WO_2Cl_2 and $WOCl_3$ occurred in the mass spectrum as well as the chlorides, but the results are not invalidated thereby.

The substances were placed in graphite crucibles (WCl_5 in a glass capillary) and heated in the ion source of the mass spectrometer (CH 4 from Fried. Krupp, MAT, Bremen). The measuring range of the apparatus was up to mass number 1350. The ions recorded were identified by their mass numbers and isotopic distribution. Even the W_3Cl^+ ion group with its low intensity could be resolved (Fig. 1).

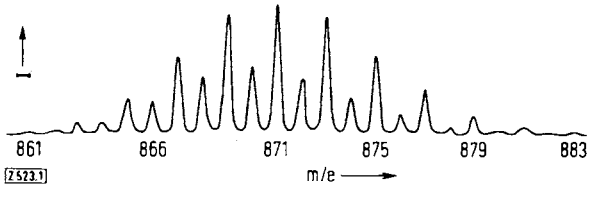


Fig. 1. $W_3Cl_9^+$ ion group. Ordinate: Ion current.

Only the ions WCl_5^+, WCl_4^+, $W_2Cl_6^+$, and $W_3Cl_9^+$ observed at low electron energies (*ca.* 12 eV) are to be considered as primary ionized gas molecules. All the other ions are fragments of the evaporated parent molecules. This follows from a study of the measured appearance potentials when WCl_4 was heated (reference value: ionization energy of argon 15.8 eV): WCl_5^+ 9.1 eV, WCl_4^+ 8.0 eV, WCl_3^+ 11.8 eV, $W_2Cl_6^+$ 9.5 eV, $W_2Cl_5^+$ 11.9 eV, $W_3Cl_9^+$ 9.3 eV.

Conclusions:

WCl_5 sublimes without decomposition (Experiment 2). W_2Cl_{10} was not observed although dimers were assumed from measurements of equilibria [3] (disputable; cf. reaction entropy).

WCl_4 decomposes to some extent on volatilization (Experiments 3 and 4). Disproportionation leads to the molecules WCl_5, W_2Cl_6, and some W_3Cl_9.

The other compounds (Experiments 5—11) give the same gaseous products as does WCl_4.

It is important that the monomeric WCl_3 does not occur alongside the considerable concentrations of W_2Cl_6. The dimer is obviously considerably more stable against thermal decomposition to monomers than is, *e.g.*, Al_2Cl_6 or Fe_2Cl_6. Further, all the chlorine-deficient fragment ions, such as W_2Cl^+ to $W_2Cl_5^+$ and $W_3Cl_3^+$ to $W_3Cl_8^+$, observed to be formed from W_2Cl_6 and $W_3Cl_9^+$ at 50 eV gave considerably lower intensities than did the corresponding parent ions $W_2Cl_6^+$ and $W_3Cl_9^+$. In this respect W_2Cl_6 and W_3Cl_9 are comparable with the halides Re_3Cl_9 [4,5], Re_3Br_9 [5,6], Tc_3Cl_9 [6], and Cu_3Cl_3 [7]. Experiments with $MoCl_5$, $MoCl_4$, $MoCl_3$, and Mo_6Cl_{12} gave no indication of the occurrence of polymeric molecules in the gas phase [8].

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[*] Dr. K. Rinke and Prof. Dr. H. Schäfer
Anorganisch-Chemisches Institut der Universität
Hindenburgplatz 55
44 Münster (Germany)

[1] *H. Schäfer* and *H.-G. v. Schnering*, Angew. Chem. *76*, 833 (1964).

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[8] We thank Mr. *H. Rabeneck* for his help.

Erratum

In the communication "Synthesis and Template Properties of Deoxyoligonucleotides with Repeating Triplet Sequences" by *F. Cramer*, *W. Frölke*, and *H. Matzura*, Volume 6, June 1967, the following correction should be made.

On page 562, right-hand column, line 30, "0.05 Mole of each trinucleotide" should read "0.50 mmole of each trinucleotide".

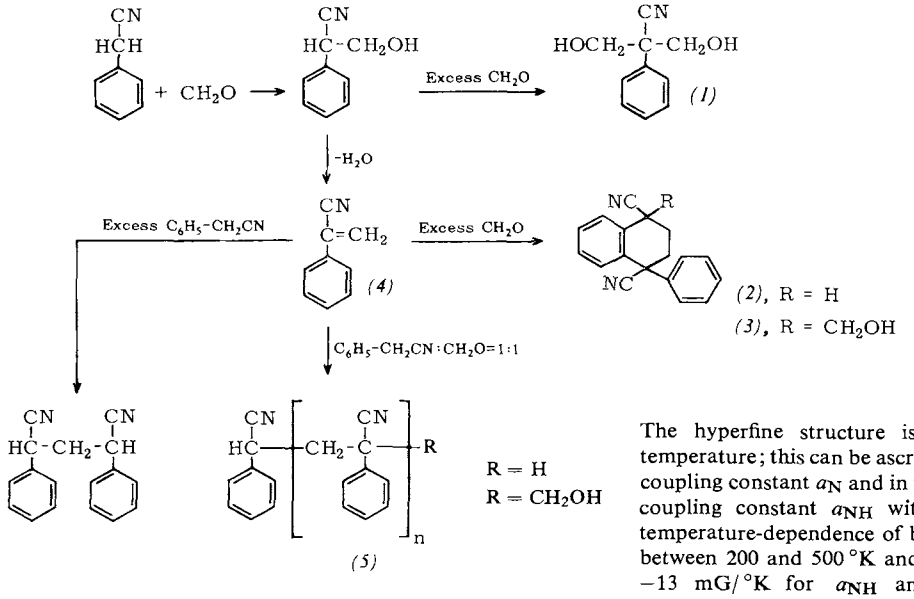
Cross-Linked Polymers from α,α'-*p*-Phenylenediacrylonitrile

By *W. Funke*[*]

p-Phenylenediacetonitrile reacts with formaldehyde (molar ratio 1:2) in a homogeneous medium (nitrile 0.128 mmole per ml of CH_3OH; CH_3ONa 0.57 mole per mole of nitrile; *ca.* 65 °C; 1 h) as well as in heterogeneous medium (nitrile 0.04 mmole per ml of H_2O; NaOH 0.22 mole per mole of nitrile; 60–100 °C; 1 h), yielding α,α'-*p*-phenylenediacrylonitrile which, however, like the α-cyanostyrene that arises from phenylacetonitrile and formaldehyde, cannot be isolated because it immediately polymerises anionically[1].

Unlike the products formed in a homogeneous medium, the cross-linked polymers of α,α'-*p*-phenylenediacrylonitrile that are obtained from a heterogeneous medium contain only ≥CH and $-CH_2OH$ as end-groups, so that quantitative determination of the end-groups and study of the initiation and termination steps would appear to be simpler. Nevertheless, quantitative analysis of the end-groups is not completely satisfactory for the cross-linked polymers, so that the end-groups were investigated for the linear polymers *(5)* prepared from phenylacetonitrile and formaldehyde *via* α-cyanostyrene. It has been shown earlier that, for reactions in a homogeneous medium, these linear polymers are good models for the cross-linked polymers.

The hydroxymethyl end-groups were determined by titration with phenyl isocyanate and by nuclear resonance spectroscopy. The ratio of hydroxymethyl to phenyl groups was calculated from the oxygen and nitrogen contents. The ratio of ≥CH to phenyl groups was evaluated by nuclear resonance spectroscopy. In this way the ≥CH/CH_2OH ratio was found to be 2.7 to 3.0, whence it is concluded that the phenylacetonitrile anion is the preferred initiator for anionic polymerization of the intermediate monomer, even in the presence of water, and that addition of a proton to the anionic end of the chain in a termination reaction is not the only way in which the ≥CH end-groups are formed.



When a large excess of formaldehyde (molar ratio 10:1) was used in a heterogeneous medium at 64 °C, α,α-bis(hydroxymethyl)phenylacetonitrile *(1)* was isolated, and dimeric α-cyanostyrene *(2)* and its formaldehyde adduct *(3)* were identified. When a shorter reaction time (10 min) was used, larger amounts of α-cyanostyrene *(4)* were identified by hydrogenation, IR spectra, and formation of the dimer.

Lecture at the Chemischen Werken Hüls A.-G., Marl (Germany) on December 7th, 1966 [VB 48 IE]
German version: Angew. Chem. *79*, 624 (1967)

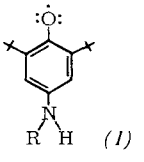
[*] Doz. Dr. W. Funke
Forschungsinstitut für Pigmente und Lacke e.V.
Wiederholdstraße 10/1
7 Stuttgart N (Germany)

[1] *W. Funke*, Makromolekulare Chem. *93*, 33 (1966).

Detection of Mesomeric Limiting Structures by Electron Spin Resonance

By *H. B. Stegmann* and *K. Scheffler*[*]

4-Amino-2,6-di-t-butylphenols can be converted into stable paramagnetic compounds by oxidation with alkaline ferricyanide solution or by heavy-metal oxides in solvents such as alcohols, ether, benzene, or pyridine.



(1)

R = H, CH_3, $CH(CH_3)_2$, C_6H_5

In the ESR spectra of these radicals, a hyperfine structure is recognizable that is to be attributed to interaction of the unpaired electron with the nitrogen, as well as with the protons of the amino group and of the substituent R. This indicates that in descriptions of such systems, in addition to the usual mesomeric limiting structures of aroxyls, structures must be considered in which there is an appreciable spin density at the nitrogen atom.

The hyperfine structure is very strongly dependent on temperature; this can be ascribed to a decrease in the nitrogen coupling constant a_N and in the splitting of the amino-proton coupling constant a_{NH} with increasing temperature. The temperature-dependence of both coupling constants is linear between 200 and 500 °K and when R = H the gradients are −13 mG/°K for a_{NH} and −1.3 mG/°K for a_N. The relationships can be best described, qualitatively, by a model in which the amino group carries out hindered rotation around the $C_{arom.}$-N bond. The hindering potential is derived, not from the steric situation, but from the gain in delocalization energy connected with the orientation of the molecule at low temperatures.

In experimental study of 4-amino-2,5-di-t-butylphenoxyl, qualitatively and quantitatively the same temperature-dependence for nitrogen and amino-protons was observed even though the steric environment had been considerably altered. Further, an increase in spin density in the aroxyl ring can be assumed from the increase, with temperature, of the coupling parameters of the proton in position 6. Thus aminoaroxyls can be described as mesomeric radicals in which limiting structures that account for free electron density on the nitrogen contribute a considerable part, although with rising temperature these limiting forms decrease significantly in favor of "aroxyl structures".

Lecture at Isny/Allgäu on January 25th, 1967 [VB 62 IE]
German version: Angew. Chem. 79, 625 (1967)

[*] Dr. H. B. Stegmann and Dr. K. Scheffler
Chemisches Institut der Universität
Wilhelmstr. 33
74 Tübingen (Germany)

Active Transport of Ions through Biogenic Membranes

By *E. Broda*[*]

Active transport is the movement of a solute against the gradient of the electrochemical potential; it is observed only at biogenic membranes. For instance, NaCl is enriched on the inner side of surviving frog skin; thus separation occurs if an NaCl solution is divided by a frog skin. Experiments with other salts, and in particular experiments by *Ussing* and *Zerahn*'s "short circuit" method [1], have shown that, in the frog skin, active transport is specific for sodium – the counterion follows the resulting potential difference. According to *Ussing* the electrical potential between the two sides of frog skin first observed by *DuBois-Reymond* in 1848 is to be ascribed to active transport.

Active transport increases the total free energy of the solutions separated by the membrane, and decreases their entropy. Clearly a compensating decrease in free energy and increase in entropy results from metabolic processes in the membrane. Presumably it is adenosine triphosphate formed in metabolism that drives the "ion pump", and its efficiency is found to be considerable (*ca.* one half). The unknown endogenous substrate can be replaced experimentally by a defined exogenous substrate (radioglucose). The CO_2 formed can be measured with a gas counter and a consumption of 10^{-12} mole cm^{-2} h^{-1} can be determined. The share of the glucose in transport work, as found experimentally, can be represented over five powers of ten in glucose concentration by a mechanism according to which glucose-6-phosphate resulting from hexokinase reaction competes with endogenous (non-radioactive) glucose-6-phosphate.

Apparently all biogenic membranes are capable of specific active transport of some substance or other (even neutral molecules), and by participation of "passive" diffusion in the opposite direction this leads finally to a stationary state.

Radiochemical experiments with *Chlorella* algae show that the energy for transport of potassium (uptake from the nutrient solution) is made available either by respiration or by illumination (photophosphorylation). The mechanism for transport of potassium is largely specific for that element (and for rubidium). Bromide is also subject to active transport by the algae; the bromide transport system can also bring chloride into the interior of the cells, but not other anions. It is at present not clear why glucose inhibits active transport of bromide; this is not due to an osmotic effect since galactose and mannitol are ineffective. Trace elements also, *e.g.* zinc, can be enriched actively by algae. However, proof is more difficult with polyvalent cations as these are also taken up strongly by ion exchange, *i.e.* a passive process.

The stationary states brought about by active transport are a special case of the dynamic states characteristic of life. There is a further special case when organic compounds occur in organisms in stationary concentrations that surpass those given by equilibria; an example is the coexistence of serum albumin with the amino acids of which it is composed. Supply of free energy (for albumin by way of adenosine triphosphate) is necessary also for preservation of these dynamic conditions.

Since work is required for the maintainance of stationary states, even in conditions of strongly depressed life activity, we have measured the respiration of spores of *Bacillus cereus*. It corresponded (in water at 30 °C) to a half-life for "self consumption" of several hundred years, and was smaller by powers of ten than the respiration of the vegitative forms. At 19 °C or in the dry condition, the respiration of the spores was immeasurably small, but it was much increased by exogenous glucose or dinitrophenol. It is possible that on further improvement of the sensitivity of the radiochemical methods an energy metabolism can be demonstrated in all cryptobiotic systems.

Colloquium at Berlin-Dahlem (Germany)
on February 7th, 1967 [VB 68 IE]
German version: Angew. Chem. 79, 624 (1967)

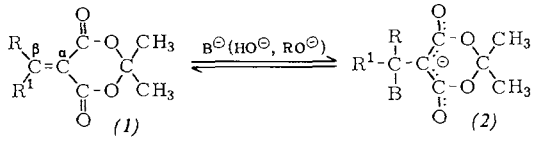
[*] Prof. Dr. E. Broda
Institut für Physikalische Chemie der Universität
Währingerstr. 42
Wien IX (Austria)

[1] *H. H. Ussing* and *K. Zerahn*, Acta physiol. scand. *23*, 110 (1951).

A New Class of Lewis Acids

By *F. Wessely*[*]

Condensation products from cyclic malonyl acylals *(1)* and aldehydes or open-chain or cyclic ketones can be titrated as monoprotic acids. Chemical and physicochemical measurements as well as quantum mechanical calculation (after *Polansky et al.*) show that an $HO^{\ominus}$ or alkoxide ion $B^{\ominus}$ is attached to the β-carbon atom with formation of the anion *(2)*, which is stabilized by delocalization of the negative charge.

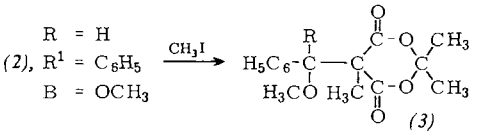


(1) *(2)*

The evidence is:

1a) In most cases, *e.g.* R = H, R^1 = alkyl or aryl, compound *(1)* yields no CH_4 with the Zerewitinoff reagent.

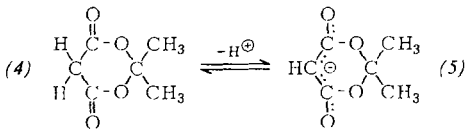
1b) Formation of compound *(3)* is proved by degradation reactions.



(3)

1c) Alkaline solutions of compounds *(1)* cannot be catalytically hydrogenated.

2a) Compounds *(1)* in neutral solution give a UV spectrum that changes characteristically when the anion is formed in alkaline solution. A band is formed that is peculiar to the anion *(5)* of Meldrum's acid *(4)*. This anion is also stabilized by delocalization of the negative charge.

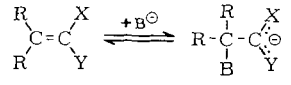


2b) Addition of $CD_3O^{\ominus}$ in CD_3OD shifts the signal of the olefinic proton in the ^1H–NMR spectra of *(1)*, R = H, $R^1 = C_6H_5$ or $(CH_3)_3C$, to higher field, to the region where the signals of aliphatic ethers appear.

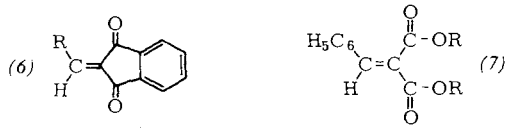
3a) The calculated π-electron densities (molecular diagrams) show maxima of positive charge on the β-carbon atom or on the two carbonyl-carbon atoms of *(1)*. The positive charge on the carbonyl-carbon atoms is the greater, but the activation energies are appreciably less favorable than for addition to the β-carbon atom.

3b) Calculations of the π-electron activation energy by the Pariser-Parr method give excellent agreement with the values found experimentally.

Thus in compounds *(1)* a partial positive charge is preformed on the β-carbon atom by the electron-acceptor groups. One may therefore regard these compounds as pseudo-Lewis acids:



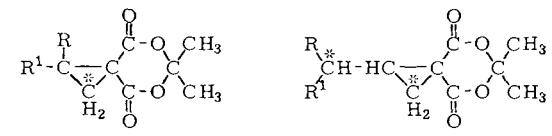
Delocalization of the π-electrons in the acceptor system is of decisive importance. In this way one can understand why, for instance, compound *(6)* also acts as an electrically neutral



Lewis acid, whereas the benzylidenemalonic ester *(7)* has no Lewis acid character; in the latter case the two C=O groups must be brought into a coplanar position to achieve maximal delocalization, and thus the entropy factor has an appreciable negative value.

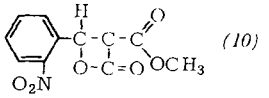
In 99 % methanol the pK_L values for the compounds studied lie between 6 and 11 according to the nature of the substituents.

A further interesting reaction has been found in the effect of ethereal diazomethane on methanolic solutions of compounds of type *(1)*. Whereas compound *(4)* reacts violently with formation of dimethyl malonate and acetone, compounds of type *(1)* give cyclopropane derivatives (immediate reaction at −70 °C; no formation of polymethylenes) with inclusion of one [*(8)*] or two [*(9)*] CH_2 groups. In the latter case, which occurs particularly with aromatic substituents (R^1 = aryl), an anionotropic migration is a prerequisite. The C atoms marked with an asterisk in formulae *(8)* and *(9)* originate in the diazomethane. A reaction can also be achieved with other diazo compounds, *e.g.* diazoacetic ester.



(8) *(9)*, R = H, R^1 = Aryl

In attempts to establish the migratory aptitude of the group R^1 of *(1)* an unusual and hitherto unexplained solvent effect was observed: If *(1)*, R = H, $R^1 = p\text{-}NO_2\text{–}C_6H_4$, is treated with diazomethane solution in methanol, *(8)* is formed in 80 % yield; in chloroform, however, *(9)* is obtained in 80 % yield. Steric reasons account for the formation of the lactone *(10)* when the 2-nitrobenzylidene compound *(1)*, R = H, $R^1 = o\text{-}NO_2\text{–}C_6H_4$, in methanol is treated with ethereal diazomethane solution; *(10)* is formed in 65 % yield.



(10)

Lecture at Mainz (Germany) on February 9th, 1967 [VB 69 IE]
German version: Angew. Chem. *69*, 652 (1967)

[*] Prof. Dr. F. Wessely
Organisch-Chemisches Institut der Universität
Währinger Str. 38
A-1090 Wien (Austria)

Relations between Structure and Thermodynamic and Chemical Properties of Molten Halides

By *H. Kühnl* [*]

The type of chloro complex formed on dissolution of chlorides of multivalent metals in alkali chloride melts can be predicted qualitatively from a consideration of the liquidus curves of the phase diagrams. A suitable method for this purpose was developed by *Flood et al.* from a simple quasi-lattice model and leads to the assumption that metal dichlorides dissolve as $(MCl_4)^{2-}$ complexes in chloride melts whose cations are equal in size to, or larger than, K^+, whereas metal trichlorides dissolve as $(MCl_6)^{3-}$ ions. This assumption accords with results of spectroscopic measurements by *D. M. Green et al.* Exceptions are $TiCl_2$ and VCl_2, from which polynuclear complexes are formed, and $AlCl_3$ and $FeCl_3$, which must occur as dimers of the type $(M_2Cl_8)^{2-}$. Smaller cations, *e.g.* Na^+, in the chloride melt lead to lower mean coordination numbers for the complexes.

The influence of the carrier melt on the stability of the complexes was measured for solutions of $FeCl_2$ and $FeBr_2$ in molten alkali and alkaline-earth chloride or bromide mixtures. For this purpose EMF measurements were used to determine activity coefficients and partial solution enthalpies for the iron(II) halide at 800–950 °C at concentrations up to 10 mole-%. The influence of the cations and anions of the solvent on the thermodynamic values can always be represented as a continuous function of the mean ion potential if the latter is defined as the sum of the mole-fractional contributions of the quotient ionic charge/ionic radius. The lower the cation potential of the melt and the higher the anion potential, the more strongly will the Fe(II) halides be bound in the complex. Changes in the anion potential are ten to fifteen times more effective than changes in the cation potential, since the anions exert their effect on the iron(II) from the first coordination sphere and the cations only from the second.

The effect of composition and compound formation on the chemical behavior is shown by reactions of alkali chloride/aluminum chloride melts with oxides or oxo salts. For instance, CrO_2Cl_2 is formed when $K_2Cr_2O_7$ is added to $LiAlCl_4$ at 120 °C. Anhydrous $CrCl_3$ is precipitated from $NaAlCl_4$ at 160–180 °C, with evolution of chlorine, and at higher temperatures some Cr_2O_3 is obtained. WO_3 and Na_2WO_4 react with an equimolar $NaCl/AlCl_3$ melt to afford WO_2Cl_2 which can be readily isolated by sublimation; an excess of $AlCl_3$ leads to pure $WOCl_4$. Under the same conditions MoO_3 yields either MoO_2Cl_2 or a complex mixture of volatile Mo(VI) and Mo(V) oxide chlorides containing some $AlCl_3$.

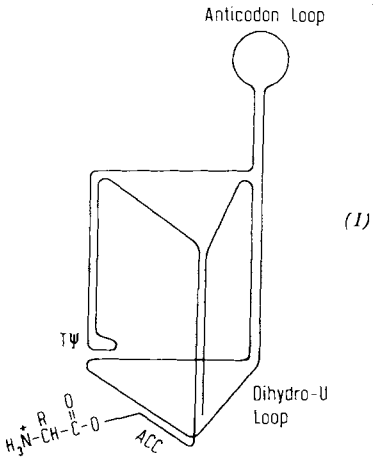
Lecture at Kiel (Germany) on February 23rd, 1967 [VB 72 IE]
German version: Angew. Chem. *79*, 653 (1967)

[*] Prof. Dr. H. Kühnl
Institut für Anorganische Chemie
der Technischen Hochschule
Callinstr. 46
3 Hannover 1 (Germany)

Determination of the Secondary and Tertiary Structure of Nucleic Acids by Chemical Methods

By *F. Cramer* [*]

The number of adenosine residues that are not base-paired [1] can be determined for transfer ribonucleic acid (t-RNA) by



(1)

N-oxidation of the adenine groups. From the degree of oxidation at 20 and 40 °C (difference: 4.5 base pairs) and from the changes in physical properties it can be concluded that the tertiary structure of t-RNA is destroyed by warming from 20 to 40 °C. The model *(1)* is proposed for the tertiary structure common to all t-RNA's. This structure arises by folding together of three base-paired regions, namely, the dihydro-U region, the TΨ region, and the CCA end region. Only the anticodon region is not drawn into the tertiary structure. In this way the molecule achieves a rigid structure which in particular holds the CCA end in a fixed position and enables the specific recognition of the t-RNA by the aminoacyl transferase.

Lecture in Strasbourg and Zürich on March 8th and 10th, 1967
[VB 77 IE]
German version: Angew. Chem. *79*, 624 (1967)

[*] Prof. Dr. F. Cramer
Max-Planck-Institut für experimentelle Medizin
Abteilung Chemie
Hermann-Rein-Str. 3
34 Göttingen (Germany)

[1] *H. Doepner, H. Seidel,* and *F. Cramer,* Angew. Chem. *78*, 601, 682 (1966); Angew. Chem. internat. Edit. *5*, 591, 671 (1966).

SELECTED ABSTRACTS

Maya blue, a pigment which was used by the Mayas in Yucatan during the final pre-Spanish era of their civilization, has been investigated by *H. Van Olphen.* The pigment is strikingly stable and is decomposed neither by treatment with hot concentrated mineral acids nor by heating to *ca.* 520 °C. The main constituent is the colorless mineral attapulgite and the pigment is probably an adsorption complex of this mineral and natural indigo (< 0.5 %). A synthetic equivalent can be prepared by mixing attapulgite with indoxyl ester or indigo, or by vat dying with reduced indigo and subsequent heating to 75–150 °C. The dye is adsorbed on the outermost surface of the mineral particles. A similar pigment can be produced from sepiolite and indigo. / Science (Washington) *154*, 645 (1966) / –Ma. [Rd 642 IE]

A new synthesis of esters of halogenoacids from esters of hydroxy acids under mild, almost neutral, conditions has been described by *J. B. Lee* and *I. M. Downie.* A hydroxy acid ester is heated rapidly to *ca.* 80 °C with a tertiary phosphine (triphenylphosphine) in CCl_4 or CBr_4. A rapid reaction ensues in which triphenylphosphine oxide, chloro- (or bromo-)esters, and $CHCl_3$ (or $CHBr_3$) are formed. If moisture is excluded, the reaction proceeds in a neutral medium. Inversion occurs at the reaction center. The reaction probably proceeds *via* an ion *(2)* which reacts with the

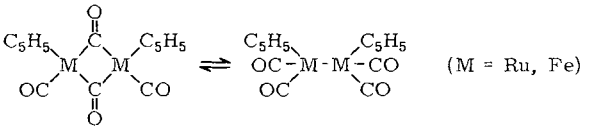
$$\underset{(3)}{R{-}CHOH{-}COOR'} + \underset{(2)}{[(C_6H_5)_3P^{\oplus}CHal_3]\,Hal^{\ominus}} \rightarrow$$

$$\underset{(4)}{[(C_6H_5)_3P^{\oplus}OCHR{-}COOR']\,Hal^{\ominus}} \xrightarrow{-HCHal_3} R{-}\underset{Hal}{CH}{-}COOR' + (C_6H_5)_3PO$$

(1)

hydroxy compound *(3)* to form anionic intermediate *(4)* that decomposes to give the haloester *(1)*. / Tetrahedron *23*, 359 (1967) / –Ma. [Rd 643 IE]

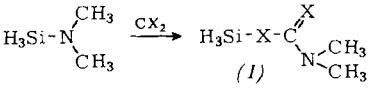
Isomerism in metal complexes has been studied by *R. D. Fischer, A. Vogler,* and *K. Noack.* Analysis of the C–O vibrations of $[C_5H_5Ru(CO)_2]_2$ and $[C_5H_5Fe(CO)_2]_2$ between –100 °C and 100 °C showed that solutions of both complexes contain equilibrium mixtures of two isomers. At low temperatures form *(a)*, which was formerly thought to be the only form, is more stable, while form *(b)* is more stable at high temperatures.



(a) *(b)*

In the Fe complex, form *(a)* still predominates strongly at room temperature, whereas in the Ru complex the two isomers are present in approximately equal quantities. The homologous Os compound, on the other hand, exists only in form *(b)*, both in solution and in the solid phase. Forms *(a)* and *(b)* appear to exist in solution entirely in the *cis* configuration; in any case, they have lost the center of symmetry of the *trans* configuration that apparently exists in the crystalline form. The tendency of the practically free molecules to adopt the *cis* configuration could be due to π or δ components in the metal-metal bond. / J. organometallic Chem. *7*, 135 (1967) / –Sch. [Rd 660 IE]

The reactions of some silylamines with CO_2, COS, and CS_2 were studied by *E. A. V. Ebsworth, G. Rocktäschel,* and *J. C. Thompson. N,N*-Dimethylsilylamine reacts to form unstable silyl *N,N*-dimethyl-carbamates, -thiocarbamates, and -dithiocarbamates.



(1)

The solid white compounds, whose IR, UV, and NMR spectra (SiH resonance and ^{29}SiH coupling) indicate the structure *(1)*, lose SiH_4 on standing. In the thiocarbamate, the silyl group is presumably attached exclusively to the oxygen. Trisilylamine and methyldisilylamine do not react with CO_2, COS, or CS_2, even at 30 atm. / J. chem. Soc. (London) A 1967, 362 / –Bu. [Rd 673 IE]

Halogenated 1,3-dicyano- and 1,3,5-tricyanobenzenes have been synthesized by *K. Wallenfels, F. Witzler,* and *K. Friedrich.* These compounds are particularly interesting in that they have a reactivity similar to that of the corresponding polynitro compounds, but do not exert the troublesome oxidizing action of the latter. The synthesis can be illustrated by the preparation of 2,4,6-tricyanofluorobenzene (m.p. 98–99 °C). The treatment of bromomesitylene with $KMnO_4$ yields bromotrimesic acid, the amide of which (prepared *via* the acyl chloride) is dehydrated with $POCl_3$ (yield 55–60%). The bromo compound is converted into 2,4,6-tricyanofluorobenzene by sublimation through a hot layer of active fluorides (KF; CsF, pure, or mixed with BaF_2 or MgF_2). This method of fluorination can also be used with *e.g.* 1,2-dichloro-1,2-dicyanoethylene. 2,4-Dicyanofluorobenzene (m.p. 82–84 °C), 1,3,5-trifluoro-2,4,6-tricyanobenzene (m.p. 148–150 °C), and their chlorinated precursors were also synthesized. All the fluorinated compounds very readily undergo nucleophilic substitution, though more slowly than the corresponding nitro compounds. / Tetrahedron 23, 1353, 1359, 1845 (1967) / –Bu. [Rd 674 IE]

The bonding of ^{32}P-labeled trinucleotides to t-RNA was detected by *G. Högenauer.* The bonding of ^{14}C-aminoacyl-t-RNA to ribosomes in the presence of trinucleotides had already been used by various research groups for the assignment of the amino acid trinucleotide codon. t-RNA-trinucleotide interactions have now also been observed in the absence of ribosomes. During the chromatography of ^{32}P–AAG (also AUG, ACG, CAG, and UUG) together with a t-RNA mixture from yeast on Sephadex G 50, a part of the radioactivity that was proportional to the quantity of ^{32}P–AAG used was always found with the high molecular weight t-RNA; this was not the case when mono- and dinucleotides were used. Fixed ^{32}P–AAG could not be displaced from the t-RNA even by a 2×10^6-fold excess of AAG-free trinucleotides. The trinucleotide-t-RNA complex is so stable that no decomposition occurs during chromatography on 30 to 40 cm Sephadex columns at pH = 7 and +2 °C. / Hoppe-Seylers Z. physiol. Chem. *348*, 227 (1967) / –Hö. [Rd 680 IE]

Two new u-amino acids having a bacteriostatic action have been isolated by *A. D. Argoudelis et al.* from the culture media of *Streptomyces* strains; they are 2-amino-3-dimethylaminopropionic acid *(1)* and 2-amino-4,4-dichlorobutyric acid *(2)*. 2.5 g of crystalline *(1)* could be obtained from 240 l of culture medium with the aid of ion-exchange chromatography, while 400 mg of *(2)* were obtained from 290 l by a Craig distribution (n-butanol/water). The bacteriostatic activity was used as a purity check. The structure was determined with the aid of IR spectra and NMR data. *(1)* was found to be identical (thin-layer and paper-chromatography; NMR-spectrum; biological action) with synthetic DL material; *(2)* was reduced with sodium borohydride, and the reduction product was identical with homoserine on paper and thin layer chromatography, in Craig distribution, and in the amino-acid analyser. Since the specific rotation of the protonated form is more positive than that of the neutral form [*(1)*: $[\alpha]_D^{25} = +48.3°$; *(2)*: $[\alpha]_D^{25} = +33.6°$] it was concluded that both substances are in the L form. *(1)* and *(2)* are moderately toxic to mice; the effects were observed on subcutaneous injection of more than 80 and 25 mg/kg respectively. The bacteriostatic and toxic effect is probably due to leucine antagonism. / Biochemistry *6*, 165 (1967) / –Hö. [Rd 681 IE]

Enzyme-bound coenzyme A has been detected by *L. B. Hersh* and *W. A. Jencks* in succinyl-CoA: 3-oxoacid CoA-transferase (E.C. 2.8.3.5). The enzyme (E) catalyses the reversible transfer of CoA from succinyl-CoA to acetoacetate. The reaction takes place in two steps I and II.

$$E + \text{succinyl-CoA} \rightleftharpoons E\cdots\text{succinyl-CoA} \rightleftharpoons E\text{–CoA} + \text{succinate} \quad \text{I}$$

$$E\text{–CoA} + \text{acetoacetate} \rightleftharpoons E\cdots\text{acetoacetyl-CoA} \rightleftharpoons E + \text{acetoacetyl-CoA} \quad \text{II}$$

When the enzyme and [1,3-^{14}C]-acetoacetyl-CoA are chromatographed on Sephadex G 50, CoA is found together with the enzyme activity, while the radioactivity is found in the low molecular weight fraction. If the same experiment is carried out with succinate, no CoA bound to high molecular weight substances can be detected. When the E–CoA isolated on Sephadex was incubated with succinate, the CoA was quantitatively transferred to the succinate. The half-lives of the decomposition of the E–CoA at pH = 6.5, 7.4, and 8.0 are 42, 30, and 14 min respectively; the complex is stable for more than an hour in 0.1 M HCl. / J. biol. Chem. *242*, 339 (1967) / –Hö. [Rd 682 IE]

Effective hydrogenation catalysts obtained by reduction of Pt^{IV} salts with solvents are reported by *G. Henrici-Olivé* and *S. Olivé.* Such catalysts were obtained *e.g.* from solutions of $PtCl_4$ in solvents having electron-donor properties (alcohols such as methanol and isopropanol, esters such as ethyl acetate, and ethers such as propylene oxide and tetrahydrofuran). Support materials such as silica gel or alumina are soaked with a solution of the type described, the excess solvent is distilled off (about 25 °C in vacuum), and the dried material is heated (reduction of the Pt_{IV} solvate) for about 1 hour at 150 to 200 °C to obtain optimum catalyst activity (best concentration of Pt_{IV} on the support: 0.1 to 0.3 wt.-%). Hydrogenation rates of up to 250 moles of H_2 per g-atom of Pt per min were obtained with 1-octene. Solutions of $PtCl_4$ in propylene oxide become black-brown on prolonged standing at 20 °C or when heated for a short time at 90 °C; the stable, highly viscous solution obtained on concentration can be used, even in toluene or cyclohexane, for hydrogenations under very mild conditions. Aldehydes cannot be used for the production of these catalysts; the deposition of Pt is hindered by even small quantities of water in the solvent. / Chimia *21*, 87 (1967) / –Jg. [Rd 688/IE]

Dialkyltin dithiolates have been prepared from dialkyltin dialkoxides and oxides by *D. Sukhani, V. D. Gupta,* and *R. C. Mehrotra.* Unlike the alkoxides of Al, Ti, and Zr, dialkyltin dialkoxides react readily with thiols (molar ratio 1:2) when refluxed in anhydrous benzene (yield 90 to 99%) *e.g.*:

$$(C_4H_9)_2Sn(OC_2H_5)_2 + 2\ RSH \rightarrow (C_4H_9)_2Sn(SR)_2 + 2\ C_6H_5OH$$

Dialkyltin oxides react in a similar manner if the water formed is removed by azeotropic distillation

$$(C_4H_9)_2SnO + 2\ RSH \rightarrow (C_4H_9)_2Sn(SR)_2 + H_2O$$

R = C_2H_5, C_3H_7, C_4H_9, i-C_4H_9, t-C_4H_9, $C_{12}H_{25}$, C_6H_5, $C_6H_5CH_2$

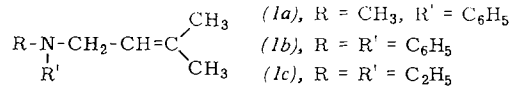
Apart from the dodecyl derivative (decomp.), the thiolates can be distilled at 0.1 to 1 mm Hg. Ebullioscopic measurements indicate that they are monomeric in benzene. Unlike the Si–S bond, the Sn–S bond is highly resistant to hydrolysis. Attempts to isolate $(C_4H_9)_2Sn(OC_2H_5)SR$ led to dismutation. Cleavage into the starting components takes place only on heating for about 200 hours with a large excess of alcohol in the presence of *p*-toluenesulfonic acid as catalyst. With this catalyst, higher thiols (molar ratio 2:1) can be introduced on removal of the lower thiol by azeotropic distillation (in cyclohexane), *e.g.*:

$$(C_4H_9)_2Sn(SC_3H_7)_2 + 2\ RSH \rightarrow (C_4H_9)_2Sn(SR)_2 + 2\ C_3H_7SH$$

R = dodecyl, 2-tolyl.

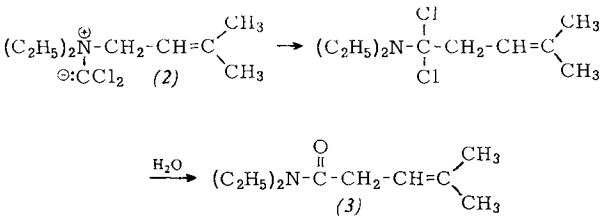
/ J. organometallic Chem. *7*, 85 (1967) / –Jg. [Rd 691 IE]

The reaction of allylamines with dichlorocarbene has been studied by *W. E. Parham* and *J. R. Potoski*. Dichlorocarbene is produced from potassium t-butoxide/chloroform method (I), n-butyl-lithium/carbon tetrachloride method (II), and ethyl trichloroacetate/sodium methoxide method (III). The



(1a), R = CH_3, R' = C_6H_5
(1b), R = R' = C_6H_5
(1c), R = R' = C_2H_5

allylamines, *e.g. (1a)*, unlike the analogous allyl sulfides, give the dichlorocyclopropane derivatives, the yield of which increases with decreasing basicity of the amine. For *(1a)* the yields obtained by methods I, II, and III are 28 %, 26 %, and 18 %, while for *(1b)*, methods I and II give yields of 45 % and 73 %. When *(1c)* is used as the starting material, the reaction leads to the dichlorocyclopropane derivative (5 %) together with an amide *(5)* (yield 7 %; n_D^{25} = 1.4680), the formation of which can be explained by Stevens rearrangement of the ylide *(2)*. This rearrangement is more important



(2) *(3)*

in the reactions of the allyl sulfides, since the sulfur ylide is resonance-stabilized owing to the participation of the d orbitals of sulfur: $R_2\overset{\oplus}{S}-\overset{\ominus}{C}\!\!\swarrow \leftrightarrow R_2S{=}C\!\!\swarrow$. / J. org. Chemistry *32*, 275 (1967) / –WG. [Rd 703a IE]

BOOK REVIEWS

Klinik und Therapie der Vergiftungen. (Clinical treatment and therapy of poisoning) by *S. Moeschlin*. Georg Thieme Verlag, Stuttgart 1964. 4th revised and enlarged Edit., 750 pp., 99 figures. Reprinted unchanged 1965; cloth, DM 66.–.

In 1951, *Moeschlin* wrote the first German-language reference book on poisoning for clinicians. According to the preface, the reason for writing the book was the "occurrence of a very large number of new poisons in industry and in the pharmacopoeia". In the second and third additions, the author "included many drugs in response to numerous requests by colleagues", and the fourth edition, published in 1964, included a "Section on plastic substances".

According to the preface, "the arrangement into groups of poisons follows practical rather than strictly chemical principles": After general discussions on poisoning, the fundamentals of the therapy of poisoning,*etc.*,some 200 pages are devoted to "Poisoning by inorganic substances", and the next 305 pages to "Poisoning by organic compounds", including analgesics and antipyretics, as well as "Plastics and resins", soporifics, insecticides, the "principal chemical warfare agents", and vitamins and hormones. This is followed by 60 pages on "Plant poisons and their derivatives", 35 pages on "Analeptics", "Antihistamines", and "Antibiotics", and finally about 50 pages on toadstool poisons and animal venoms. The book closes with a list of "Guiding symptoms in cases of poisoning" (40 pages) and a 34-page subject index.

For each substance the use, the acute and chronic poisoning symptoms (with many of the author's own cases), and the methods of identifying the substance in poisoning cases are described briefly, and in most cases numerous suggested treatments are added.

In the past 15 years, "Moeschlin" has become a "Bible' to many clinicians dealing with cases of poisoning, although this faith is not always justified.

It is of less concern to the reader of this journal that too little space is given to general treatments and too much to antidotes. The chemist is more interested in whether the book will provide him with information about substances that are injurious to health and about the prevention of poisoning by potentially dangerous chemicals. Unfortunately, the first edition contained incorrect information which had been taken directly from compilations by uncritical authors (particularly in connection with occupational diseases), and this information has been included unchanged in subsequent editions. It is impossible in a short review to mention the numerous errors, incorrect chemical data, and doubtful treatments contained in the book, and only a few examples will be given here:

It is generally known nowadays that benzene is a dangerous hemotoxin and that toluene and xylene are not, since alkylbenzenes are rapidly detoxicated by side-chain oxidation. However, *Moeschlin* states on p. 351: "It was *formerly* thought, mainly on the basis of animal experiments, that toluene and xylene are relatively safe for humans.... However, from various observations on similar chronic poisoning phenomena in persons working with pure toluene or xylene and from positive animal experiments, *today* it must be concluded that toluene and xylene are substantially equivalent to benzene in their toxic action". The "recent" literature data included were published in 1929, 1933, 1939, and 1942. Moreover, the author cannot quote a single case of blood damage in humans as a result of working with pure toluene and xylene. It is only too well known that toluene and xylene were formerly often contaminated with benzene. However, according to *Moeschlin*, "only the quantity of these methylated benzenes absorbed is generally rather smaller, owing to their higher boiling point". Chemists will have their own ideas about the hypothesis presented on p. 352, with a structural formula, according to which benzene acts by direct addition to cysteine (*via* an –S– bond), so leading to a marked cysteine deficiency and a secondary cytochrome deficiency

Under Benzene derivatives" (p. 371), the book surprisingly includes naphthalene, naphthol, thymol, and phenolphthalein, which are reported to cause hemolysis and methemoglobin formation, "like aniline and nitrobenzene". Under nitrobenzene (p. 387) and aniline (p. 399), it is not pointed out that methemoglobin formation is promoted by alcohol. In a case of acute dinitrobenzene poisoning (p. 392), on the other hand, one glass of beer six weeks later is reported to cause a relapse. The author's explanation is that the dinitrobenzene "was stored in adipose tissue, and can be remobilized by fat-soluble agents (alcohol)". (The alcohol concentration in the blood after a glass of beer cannot be much more than 0.03 %).

According to *Moeschlin*, the narcotic Halothan® (= fluothane) which can allegedly cause acute yellow dystrophy of the liver, can no longer be used as an anesthetic (p. 338). Substances such as α,β-dichlorodiethyl ether and even ethylene chlorohydrin (p. 344), "should no longer be used in industry in any circumstances". Such statements are somewhat too strong. *Moeschlin* should have protested against the use of benzene and carbon tetrachloride as solvents in the home. Substances such as carbon tetrachloride and methyl bromide are prohibited from use in fire extinguishers (in Germany at least), though *Moeschlin* repeatedly states that they (and even methyl chloride) are used in fire extinguishers, and does not object; he should have demanded a ban in this case.

In the bizarre treatment of "Smog" (pp. 374–277), "18 very toxic nitroolefins" in Los Angeles are confused with the carcinogenic hydrocarbons. Here the author (p. 355) claims that "about 300 to 500 new chemical substances are released for general use every year; in the production of these many by-products are formed, the major part of which passes into the atmosphere".

The new short section on "Plastics and resins" (p. 455) is full of errors. ε-Caprolactam is reported to have a sensitizing action, and the "danger of sensitization is greatest during the manufacture of plastics, and less during use of the finished commercial products".

According to the book, in one place "toluene diisocyanate is not a highly toxic substance", whereas, *e.g.*, it is correctly stated on p. 458 that "isocyanates, *e.g.* Desmodur®, are highly toxic substances, the inhalation of which leads to necrosis of the mucous membranes and possibly to fatal bronchiolitis".

A most surprising section is that on p. 457 dealing with the "Toxic effects of inhalation of liquid particles of plastic into the lungs". With reference to the alleged cases of thesaurosis (= storing-up) due to hair sprays containing polyvinylpyrrolidone (*Bergmann* 1958), *Moeschlin* states: "The inhaled particles solidify in the alveoli of the lungs to form solid particles of plastic, which can only be partly eliminated in the sputum" (polyvinylpyrrolidone is water-soluble). *Moeschlin* is evidently unaware of the fact that most of these "cases" were incorrectly diagnosed (Boeck's morbus). On the contrary, he concludes that "hair sprays containing liquid plastics should be prohibited". (In fact, some of the so-called "cases of thesaurosis" were due to allergic reactions to shellac, *i.e.* a *natural* resin in the hair spray!).

Methyl violet in indelible pencils is claimed to have "a strong toxic action on tissue, owing to its alkaline reaction". The "immediate excision of the injured part" (*e.g.* of the hand) suggested by *Moeschlin* has long been recognised as foolish. On p. 403 the author refers to the "frequent production of keratitis and conjunctivitis by numerous aniline dyes" (references from 1905 and 1906!).

Though any number of such errors could be quoted, the positive points should also be mentioned. An excellent reference list is given at the end of each chapter and, since the various authors are named in the text, the physician can at least check the often doubtful statements about cases of poisoning. Thus the book could be useful if read very critically. In a future edition, the entire contents should be critically sifted and brought up to date by the inclusion of the latest literature, particularly on industrial toxicology.

The author should preferably enlist the aid of a toxicologist who is familiar with chemistry, in order that the deserving work put into the book over the past 15 years may finally enable the clinician, with the aid of this bible, to diagnose, assess, and treat poisoning. *H. Oettel* [NB 564 IE]

Advances in High Pressure Research, Vol. 1. Edited by *R. S. Bradley*, Academic Press, London-New York 1966. 1st Edit., x, 396 pp., numerous figures and tables, 100 s.

Up to 1952, *Bridgman*'s classic "The Physics of High Pressure" was practically the only monograph on basic high pressure research. Since 1960, however, at least twenty specialized works on high pressure have been published, and a series entitled "Advances in High Pressure Research" has now been started. The editor has already been very successful with a two-volume monograph on "High Pressure Physics and Chemistry" published in 1963 by the same publishers. Since high pressure research is mainly defined by the application of certain experimental techniques, contributions from very diverse fields will be expected in such a progress report. This is found even in the first volume, which contains six chapters of some seventy pages each. The authors of these chapters have become well known through their own work in the fields that they describe.

In the first section ("Construction and operation of ultrahigh pressure equipment"), *J. Lees* describes the construction and operation of the "tetrahedral arrangements"; the production and calibration of high pressures is critically discussed.

In the second article, *S. D. Hamann* describes the effects of intense shock waves. A particularly interesting part of this article is the section on the possibility of achieving pressures of millions of atmospheres with the aid of reflected and converging shock waves. In connection with the article by *E. Whalley* on the refractive and the dielectric properties of solids and liquids under pressure, special mention should be made of the discussion of the modifications of ice. *R. C. Newton* describes the state and future of geophysical research with high static pressures. Even the outsider will find the detailed description of the present knowledge of the earth's crust, mantle, and core interesting. "The stability of solids under pressure" is discussed by *M. Tosi* and *A. Arai*. Special mention should be made of the section on the transition from the nonmetallic to the metallic state. The last article, by *L. S. Whatley* and *A. van Valkenburg*, is on high pressure optics. It is mainly confined to the description of the elegant and versatile diamond piston arrangement jointly developed by the authors in the Bureau of Standards for high pressure experiments on a microscopic scale.

The volume can be recommended both to those who are experimenting with high pressures and to those who are interested in recent information on highly compacted matter.

E. U. Franck [NB 591 IE]

The Peptides. Vol. I. By *E. Schröder* and *K. Lübke*. Translated from the German by *E. Gross*. Academic Press, Inc., New York-London. Methods of Peptide Synthesis. 1st Edit. 1965, xvii, 481 pages, several figures, $ 20.00.

All chemists interested in the synthesis of peptides will certainly welcome the publication of this book. The authors, who are known to all experts in this field by virtue of their numerous publications, work in the main laboratory of *Schering AG.*, Berlin. It is therefore only natural that the present volume is intended for the preparative chemist. The references, which are 2719 in number and cover the literature from 1950 to the end of 1964, permit a rapid and almost complete assessment of the methods available to date for the synthesis of peptides.

After a comprehensive discussion of the various protective groups and the methods of coupling peptide bonds, a detailed treatment is given of the behavior of individual amino acids – including some of the rarer ones – in preparative chemistry. The tabular presentation of the most important derivatives of amino acids containing side-chain functional groups deserves special mention.

Shorter sections are devoted to the synthesis of cyclic peptides, depsipeptides, and peptoids. The plastein reaction, solid-phase peptide synthesis, and the problem of racemization are also discussed. A most significant part of the book, 155 pages, contains a bibliography and an index. The occasional misprint in these sections is something that can hardly be avoided. On the other hand, the failure of the authors to adopt the nomenclature recommended by the European Peptide Symposium in 1962 is rather surprising.

Up-to-date tables of synthesized peptides, such as those that *Greenstein* and *Winitz* were able to include in their "Chemistry of the Amino Acids" in 1961, can no longer be expected; such an inclusion would render the book unwieldy. In accord with the subtitle of this first volume, no problems – such as desalting, purification, and analysis – are touched upon which are not directly concerned with the synthesis of peptides.

Printing and presentation of the book are excellent. The volume will, without doubt, soon be found in every peptide and protein laboratory, where it will fill a long-standing gap.

However, the practice of the publishers is regrettable – the book was not available in Germany until the spring of 1966 although it appeared in America on September 30th, 1965.

H. Zahn [Nb 596a]

The Peptides. Vol. II. By *E. Schröder* and *K. Lübke*. Translated from the German by *E. Gross*. Academic Press, Inc., New York-London. Synthesis, Occurrence, and Action of Biologically Active Polypeptides. 1st Edit., 1966, xxvii, 632 pages, several figures, $ 30.00.

A 90-page bibliography with about 2800 entries and a 60-page index mark this volume at first sight as an encyclopedia of biologically active peptides and polypeptides. The literature is almost completely covered up to mid-1965.

The subdivision of the material into linear, heterode cyclic and homode cyclic peptides corresponds to the point of view of the chemist working in synthetic chemistry, for whom this book is primarily intended. The inclusion of biochemical and pharmacological facts is useful, since the biological properties of the peptides discussed are generally the reason for their synthesis in the laboratory.

In the biological parts of the book, the authors can only sum up the relevant literature. However, in the description of syntheses, they offer a critical evaluation based on wide experience. This is particularly useful in the discussion of hormones of which numerous analogues have been synthesized. A number of characteristic synthetic routes are shown in each case, usually with reaction schemes; similar syntheses can then be described simply by reference to changes in the details of the method. Biological activities are generally compared in tables.

While the first volume of the work lacked an introduction to the isolation and purification of peptides, the description of the syntheses in the present volume also include the processes for the purification of many intermediate and final products. This is useful, since these operations are strongly dependent on the nature of the peptide, and cannot be generalized.

The ten chapters of the book cover a wide area of the polypeptide field. From glutathione to insulin and from antibiotics to enzyme sequences, nearly every polypeptide that has a characteristic biological action and whose synthesis could be of some interest is discussed. The reviewer would like to have seen a chapter on polyamino acids and "sequential polypeptides", though the biological actions of these substances lie mainly in the field of immunochemistry. It is naturally difficult to fit in substances whose structures are not yet known. However, these are not ignored, as is so often the case in the literature, but included according to source and pharmacological properties of known substances.

The various chapters of the book are more or less self-contained, and are well written throughout. A book suitable for reading from start to finish cannot be expected, in view of the heterogeneous nature of the subject matter. The second volume of "Peptides" is intended for a specialist readership, to whom it will prove an indispensable aid. The print and presentation are of the same high quality as in the first volume. Each volume is provided with an index and notes on nomenclature, so that the two can be used independently.

H. Zahn [NB 596b IE]

Theory of Elementary Gas Reaction Rates. By *D. L. Bunker*. The International Encyclopedia of Physical Chemistry and Chemical Physics, Topic 19, Vol. 1. Edited by *E. A. Guggenheim, J. E. Mayer*, and *F. C. Tompkins*. Pergamon Press, Oxford-London-Edinburgh-New York-Toronto-Paris-Braunschweig 1966. 1st Edit., xii, 115 pages, 18 figures, 9 tables, 35s.

After a short introduction, the book deals with three simple types of gas reactions: bimolecular exchanges, monomolecular reactions, and dissociation and recombination reactions. An effort is made to interpret the rates of these reactions with the aid of classical mechanics, quantum mechanics, and statistical mechanics. The mathematical treatment has been kept simple, but a study of the book will not be possible without a certain knowledge of theoretical physics. The discussion shows that we are still far from a general understanding of even the simplest reactions. However, it also shows that the introduction of new experimental methods (*e.g.* shock waves, molecular beams) has led to new information that brings us closer to an understanding of the reactions.

In looking through the references, the reviewer experiences a certain sadness, since only four of the 300 references, nearly all of which are very recent, are in German. Has the German language and German science really become so unimportant?

U. Schindewolf [NB 597 IE]

The Proteins: Composition, Structure, and Function. Edited by *H. Neurath*. Vol. IV. Academic Press, New York-London 1966. 2nd Edit., xviii, 508 pages, numerous figures, 35 tables, $ 20.00.

The fourth volume of "The Proteins"[*] contains three chapters. The first chapter, "Genetic Control of Protein Structure" by *Helinski* and *Yanofsky*, deals not only with the genetic control of the primary structure and the influence of mutations on the structure and activity of proteins, but also with the formation of the native conformation and the association of polypeptide chains to form the multimeric enzyme molecule. In the second chapter ("The Basic Structure of Glycoproteins"), *Gottschalk* and *Graham* discuss mainly orosomucoid, ovalbumin, and the submaxillary gland glycoprotein. Two thirds of the volume (303 Pages) are devoted to a description of "The Structure Proteins" by *Seifter* and *Gallop*. This field has recently become rather involved, partly because of the numerous widely scattered and difficultly obtainable publications. The authors have divided the material very clearly, and by examination of more than 1100 publications, they have collected all the important facts. This survey will be welcomed by anyone who wishes to learn more about structure proteins.

The literature is largely covered up to 1965, so that the volume represents the latest situation. The authors, who are well known for their experimental work have maintained the high standard set by the previous volumes.

H. Sund [NB 600 IE]

[*] Cf. Angew. Chem. *78*, 343 (1966); Angew. Chem. internat. Edit. *5*, 327 (1966).

Comprehensive Biochemistry. Vol. 14: Biological Oxidations. Edited by *M. Florkin* and *E. H. Stotz*. Elsevier Publishing Company, Amsterdam-London-New York 1966. 1st Edit., xvi, 512 pp., numerous figures and tables, Dfl. 70.–. / 140s., subsc. Dfl. 56.–. / 112s.

This volume of "Comprehensive Biochemistry"[1] is really gigantic. Ten chapters covering more than 500 pages (this time on thicker and coarser paper than before) deal with electron-transfer processes. The sections were systematically chosen from the vast field of biochemical reaction mechanisms and placed in the hands of specialists who had already proved themselves several times in the writing of such reviews. One consequence of this is that the reviews that have now appeared in numerous handbooks are very similar.

It is the more surprising, therefore, that this volume has taken so long to appear. On closer examination, it is found that a few of the ten chapters were late in being submitted, with the result that the more conscientious contributors are now likely to be blamed for submitting outdated and inadequately checked articles (e.g. photophosphorylation, mitochondrial electron transport system). Other authors had evidently planned the work differently from the outset, and so produced articles that could hardly become outdated in any case (oxy-

genases, catalases). However, as a result of careful selection and concise presentation of the material, these articles are also interesting and informative. The literature is generally fully covered up to 1964, and a few references from 1965 are also included.

The content of the volume ranges from the substrate to oxygen, and even a list of the author's names is enough to show the authority behind the discussions and to assure one that the quality of even the shortest contribution is very high. *S. P. Colowick*, *J. van Eys*, and *J. H. Park* deal at length with the dehydrogenases, with special emphasis on the chemistry, bonding, and mode of reaction of the prosthetic group. This is followed by a discussion of the lipoic acid enzymes (*L. J. Reed*) and their chemistry, function, and structure in the multienzyme complex of the α-ketoacid oxidases. In dealing with the flavoprotein dehydrogenases of the respiratory chain, *T. P. Singer* discusses the diphosphopyridine nucleotide and succinate dehydrogenases, and compares the modes of action of enzymes from different sources. The functional complexes of mitochondrial electron transport (*Y. Hatefi*) include oxidoreductions involving coenzyme Q. *K. Okunuki* describes in detail the isolation and crystallization of cytochromes and cytochrome oxidases from various sources. The functional complex of the mitochondrial electron transport system is described by *D. E. Green*, who concentrates on the function of the mitochondrial membrane, the subunits obtained from it, and their recombination.

The chapter by *E. C. Slater* on oxidative phosphorylation contains less personal color, but is more informative. On the basis of the phenomenon of different P/O ratios, the author discusses the possibility of formation of high-energy bonds, for which neither high-energy carriers nor phosphate intermediates have so far been isolated. Special emphasis is therefore placed on the chemiosmotic theory, which does not depend on such intermediates, and the formation of the pyrophosphate linkage as a result of a pH gradient transverse to the membrane is discussed.

Photosynthetic phosphorylation (*A. W. Frenkel* and *K. Cost*) is to some extent a reversal of oxidative phosphorylation, but the two processes are by no means identical. This electron transfer involves the conversion of light energy into thermochemical pyrophosphate energy. Though the process has been substantially broken down indirectly into unit steps, the intermediates have not yet been identified as chemical species. In all these reactions oxygen is only an indirect substrate; on the other hand, it is directly utilized in the enzymatic activation of oxygen, which is discussed by *L. L. Ingraham*. However this concise article takes into account very little of the work that has been published since 1960. The recent literature is also practically ignored in the article by *A. S. Brill* on the peroxidases and catalases.

Apart from these faults, the book is again a useful broad introduction to an extremely topical sector of biochemistry, and rounds off excellently Section III of the work. The presentation, as usual, is good. However, art paper has been used for the half-tone illustrations, and even the very small diagrams would have been much clearer and easier to follow on smooth paper. It is to be hoped that the later volumes will be of equal quality, but will not take so long to appear.

L. Jaenicke [NB 588 IE]

[1] Cf. Angew. Chem. *76*, 868 (1964).

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New Methods of Preparative Organic Chemistry IV

Syntheses of Isocyanide Dihalides[**]

BY E. KÜHLE, B. ANDERS, AND G. ZUMACH[*]

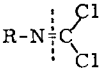
The methods for the preparation of isocyanide dihalides, and particularly of isocyanide dichlorides, are described. The scopes and courses of the various processes are critically discussed.

I. Introduction

In contrast to phosgene, thiophosgene, and the isocyanates and isothiocyanates derived from them, only a few of the structurally related isocyanide dihalides and their derivatives have been described in the literature until very recently. Even a recent standard work on organic chemistry [1] contains only a short discussion (without experimental details) of the syntheses of isocyanide dichlorides by the addition of chlorine to isocyanides and by chlorination of isothiocyanates. In recent years, various research groups have published numerous reports, which deal in particular with the chemistry of the isocyanide dichlorides and difluorides. The present article is intended as a review of the known methods for the preparation of isocyanide dihalides.

II. Nomenclature and Classification

The isocyanide dichlorides, which are sometimes also referred to as isonitrile dichlorides, carbylamine dichlorides, dichloromethyleneamines, carbonyl dichloride imide, or iminophosgene, are derivatives of carbonic acid. These special names become understandable on close examination of the isocyanide dichloride molecule.



The right-hand part of the formula shows the relationship with phosgene and thiophosgene, and so explains the name "iminophosgene". The analogy with phosgene and thiophosgene is further accentuated by the fact that the two geminal chlorine atoms can react selectively in succession.

The left-hand part of the above formula expresses the relationship of the isocyanide dichlorides with the isocyanates, isothiocyanates, and carbodiimides, and with certain limitations to the isonitriles. This is particularly emphasized by the fact that isonitriles can be prepared from isocyanide dichlorides; conversely, isocyanide dichlorides can be obtained from isocyanates, isothiocyanates, carbodiimides, and isonitriles.

III. Preparation of Aliphatic and Aromatic Isocyanide Dihalides

None of the many methods for the synthesis of isocyanide dihalides, and particularly of isocyanide dichlorides, is capable of general and unrestricted application. However, the methods are more or less mutually complementary.

[*] Dr. E. Kühle, Dr. B. Anders, and Dr. G. Zumach
Wissenschaftliches Hauptlaboratorium der
Farbenfabriken Bayer AG.
509 Leverkusen (Germany)

[**] The articles in this series have been published in five volumes by Verlag Chemie, Weinheim/Bergstr. An English edition has also been published. The present article will appear in Volume VI of the series.

[1] Houben-Weyl-Müller: Methoden der organischen Chemie. Georg Thieme Verlag, Stuttgart; see 4th Edit., Vol. VIII (1952), p. 354 or Vol. IX (1955), p. 882.

1. Chlorination of Isothiocyanates[2]

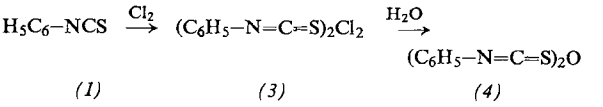
The oldest method for the production of isocyanide dichlorides is the chlorination of isothiocyanates[3], which was discovered almost 100 years ago. Chlorination of phenyl isothiocyanate *(1)* at low temperature in chloroform led to the elimination of sulfur dichloride and formation of phenyl isocyanide dichloride *(2)*.

This reaction, which was subsequently carried out on the industrial scale[4], generally gives yields of more than 90%[5] when the solvent is chloroform, carbon tetrachloride, or carbon disulfide. It can also be carried out in the absence of solvent, but the sulfur dichloride formed must then be removed under mild conditions, *e.g.* by distillation under reduced pressure.

Nef[6] was able to show that the phenyl isocyanide dichloride obtained by *Sell* and *Zierold*[3] also contained a nuclear chlorination product. More recently, *Murphy*[7] obtained 4-chlorophenyl isocyanide dichloride in 61% yield by introduction of an excess of chlorine into a solution of phenyl isothiocyanate. No nuclear chlorination takes place when carbon tetrachloride is used as the solvent.

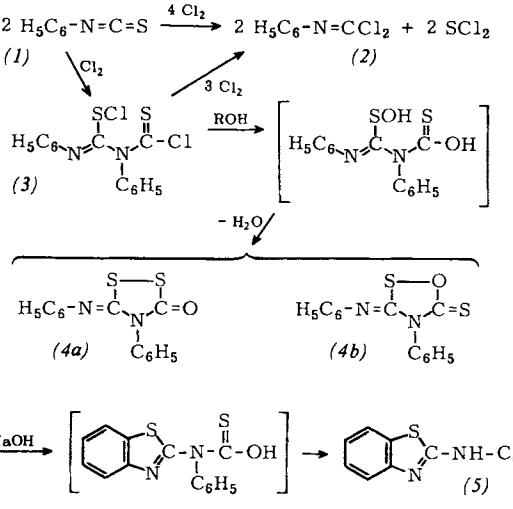
A few years ago, the chlorination of isothiocyanates was extended to the aliphatic and cycloaliphatic series[8], while individual alkyl isocyanide dichlorides had already been synthesized[9]. Yields of 70 to 95% are obtained when the reaction solutions are treated with sodium sulfite/sodium carbonate solution after chlorination, in order to remove interfering by-products containing chlorine and sulfur.

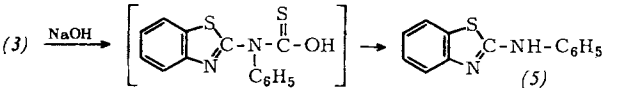
The structure of the intermediates occurring in the chlorination of isothiocyanates was investigated even by early workers. Thus *Sell*[10] isolated from the chlorination products of ethyl isothiocyanate in ether an unstable substance ("chloroethyl isothiocyanate"), which is converted by alkaline hydrolysis into an ethyl isothiocyanate oxide $(C_2H_5NCS)_2O$ having m.p. 42 °C. *Helmers*[11] later investigated the products obtained on partial chlorination of phenyl isothiocyanate *(1)*, and isolated a difficultly soluble, unstable substance *(3)* ("phenyl isothiocyanate monochloride") having m.p. 150–160 °C (decomp.). Treatment of *(3)* with alcohol or warm water gave a compound containing no chlorine and having a m.p. 118 °C, which was mentioned in the literature as "phenyl isothiocyanate oxide" *(4)*[12].



(1) *(3)* *(4)*

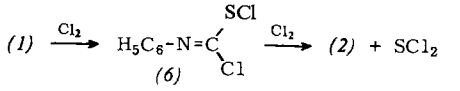
Dyson and *Harrington*[13] re-examined problems associated with the chlorination of phenyl isothiocyanate and proposed the following reaction scheme:



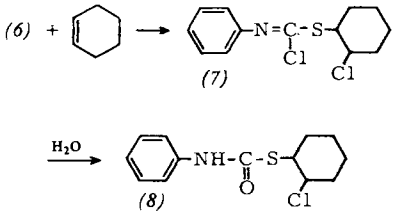


We repeated these chlorination experiments, since the constitution given for compound *(3)* seemed very unlikely in view of its poor solubility; furthermore, contrary to the report by *Dyson* and *Harrington*[13], the compound *(3)* could not be further chlorinated to form phenyl isocyanide dichloride *(2)*.

We found that the chlorination of phenyl isothiocyanate *(1)* yields first the primary chlorine adduct *(6)*[14] in a strongly exothermic reaction; further chlorination of *(6)* then leads to the elimination of sulfur dichloride and formation of phenyl isocyanide dichloride *(2)* with no appreciable evolution of heat.



N-(Chloro-chlorothiomethylene)phenylamine *(6)* can be isolated from the products of chlorination below 0 °C, can be destilled under vacuum (b.p. 84–86 °C/0.15 mm Hg), and can be stored for about 8 days under nitrogen. Addition to cyclohexene and hydrolysis of the adduct *(7)* gave *S*-(2-chlorocyclohexyl)-*N*-phenylmonothiocarbamate *(8)*, m.p. 105–106 °C, thus showing that *(6)* is a sulfenyl chloride.



(7) *(8)*

[2] The bromination of phenyl isothiocyanate leads only to bromine adducts, cf. *M. Freund*, Liebigs Ann. Chem. *285*, 154 (1895).

[3] *E. Sell* and *G. Zierold*, Ber. dtsch. chem. Ges. *7*, 1228 (1874).

[4] *J. Meyer*: Der Gaskampf und die chemischen Kampfstoffe. 3rd Edit., Hirzel-Verlag, Leipzig 1938.

[5] *R. S. Bly, G. A. Perkins*, and *W. L. Lewis*, J. Amer. chem. Soc. *44*, 2896 (1922).

[6] *U. Nef*, Liebigs Ann. Chem. *270*, 267 (1892).

[7] *D. B. Murphy*, J. org. Chemistry *29*, 1613 (1964).

[8] *E. Schmidt* and *K. Thulke*, Liebigs Ann. Chem. *663*, 46 (1963).

[9a] *H. Brintzinger, K. Pfannstiel*, and *H. Koddebusch*, Chem. Ber. *82*, 389 (1949).

[9b] *K. A. Petrov* and *A. A. Neimyseva*, Ž. obšč. Chim. *29*, 2165 (1959).

[9c] *N. N. Yarovenko, S. P. Motornyj*, and *L. I. Kirenskaya*, Ž. obšč. Chim. *29*, 3789 (1959).

[10] *E. Sell*, Ber. dtsch. chem. Ges. *6*, 322 (1873).

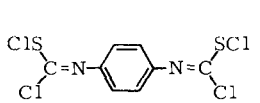
[11] *O. Helmers*, Ber. dtsch. chem. Ges. *20*, 786 (1887).

[12] *E. Fromm* and *R. Heyder*, Ber. dtsch. chem. Ges. *42*, 3800 (1909).

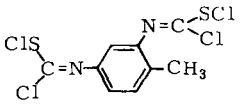
[13] *G. M. Dyson* and *T. Harrington*, J. chem. Soc. (London) *1942*, 150

[14] The formation of a chlorine adduct on chlorination of 2,2-difluoroethyl isothiocyanate was first reported by *N. N. Yarovenko et al.* [9c].

The same conclusion was reached by *Ottmann* and *Hooks jr.*[15], who also isolated *(6)* (yellow oil; $n_D^{24} = 1.6291$) as an intermediate in the chlorination of *(1)*; these authors also characterized the compounds *(6a)* and *(6b)*, m.p. 82–83 °C and 75–75.5 °C, respectively.

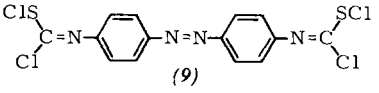


(6a)

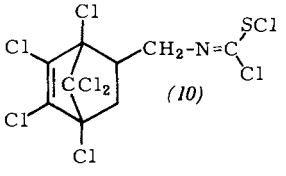


(6b)

Depending on the isothiocyanate used, chlorination under normal conditions does not proceed beyond the chlorine adduct stage. For example, chlorination of 4,4'-bis(isothiocyanato)azobenzene or of hexachlorinated bicyclo[2.2.1]-hept-2-enylmethyl isothiocyanate leads to good yields of the chlorine adducts *(9)* (m.p. 158–160 °C) and *(10)* (undistillable oil), respectively[16].



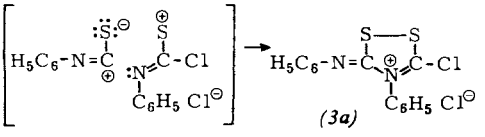
(9)



(10)

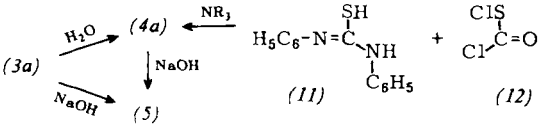
When phenyl isothiocyanate *(1)* in chloroform is added to an equimolar quantity of *N*-(chloro-chlorothiomethylene)phenylamine *(6)*, a difficulty soluble precipitate separates out after a short time. This precipitate is identical in its physical and chemical properties with "phenyl isothiocyanate monochloride" *(3)*, and cannot be further chlorinated. This shows that the difficultly soluble substance is not an intermediate, but a by-product of the chlorination of isothiocyanates; the extent to which it is formed is determined by the reaction conditions. On the basis of its unusual properties (*e.g.* poor solubility in organic solvents) and the results of an independent synthesis carried out by us, we suggest the polar structure *(3a)*[16a].

(1) + *(6)* ⟷



(3a)

The formation of 3-oxo-4-phenyl-5-phenylimino-1,2,4-dithiazolidine *(4a)* on hydrolysis of *(3a)* and the formation of 2-anilinobenzothiazole *(5)*, probably *via (4a)*, on alkaline saponification are now readily explained. The structure *(4a)*[17] has also been confirmed by synthesis from *N,N'*-diphenylthiourea and chlorocarbonylsulfenyl chloride *(12)*[18] in the presence of a tertiary amine.

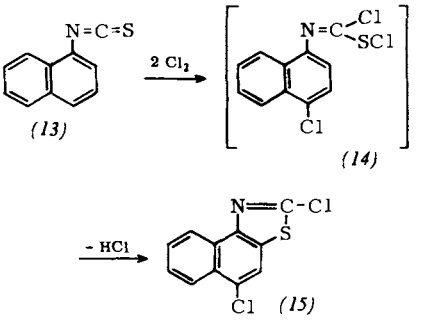


(3a) *(4a)* *(5)* *(11)* *(12)*

Similar results were obtained in the chlorination of methyl isothiocyanate.

The chlorination of isothiocyanates is not generally applicable for the synthesis of isocyanide dichlorides. Thus 2-nitrophenyl isocyanide dichloride cannot be prepared from 2-nitrophenyl isothiocyanate, since the reaction product decomposes explosively after removal of the solvent (water bath!)[19]. Products containing sulfur are sometimes obtained in the case of ring-chlorinated phenyl isothiocyanates[20].

In the chlorination of 1-naphthyl isothiocyanate *(13)*[21], the chloroadduct *(14)* loses hydrogen chloride with cyclization to form 2,5-dichloronaphtho-[1,2-*d*]thiazole *(15)*. Even "overchlorination" leads, not to the isocyanide dichloride, but to a more highly chlorinated naphthothiazole $C_{11}H_2Cl_5NS$, m.p. 235 °C.



(13) *(14)* *(15)*

On the other hand, isothiocyanates having an ether linkage at the α-position with respect to the nitrogen atom can be chlorinated smoothly and without chlorination in the side chain, *e.g.*

$$CH_3O{-}CH_2{-}NCS \xrightarrow{2\,Cl_2} CH_3O{-}CH_2{-}NCCl_2 + SCl_2\ [8,22].$$

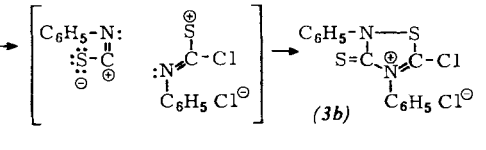
A special case of the chlorination of isothiocyanates was described by *Holtschmidt et al.*[23], who found that the chlorination of benzyl isothiocyanate leads *via* benzyl isocyanide dichloride *(17)*, by side-chain

[15] *G. Ottmann* and *H. Hooks jr.*, Angew. Chem. *77*, 427 (1965); Angew. Chem. internat. Edit. *4*, 432 (1965).

[16] *B. Anders*, unpublished.

[16a] A compound *(3b)* isomeric with *(3a)* would also be possible as follows:

(1) + *(6)* →



(3b)

[17] *(4a)* undergoes ring cleavage with aniline to form *N,N',N''*-triphenylmonothiobiuret.

[18] Chlorocarbonyl sulfenylchloride is formed on hydrolysis of trichloromethylsulfenyl chloride with sulfuric acid. Belg. Pat. 672167 (Nov. 11, 1964), Farbenfabriken Bayer AG, Inv.: *W. Weiss.*

[19] *G. M. Dyson* and *T. Harrington*, J. chem. Soc. (London) *1940*, 191.

[20] *E. Kühle*, unpublished.

[21] *G. M. Dyson* and *T. Harrington*, J. chem. Soc. (London) *1942*, 374.

[22] Belg. Pat. 682684 (June, 17, 1966), Farbenfabriken Bayer AG, Inv.: *G. Zumach* and *E. Kühle.*

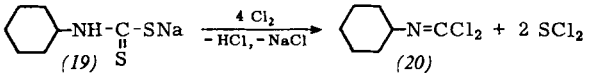
[23] German Pat. 1163803 (Dec. 14, 1962), Farbenfabriken Bayer AG, Inv.: *E. Degener, H. Holtschmidt*, and *H.-G. Schmelzer.*

chlorination at 150 to 180 °C in the presence of UV radiation, to 1,1,3,3-tetrachloro-3-phenyl-2-azapropene *(18)* [24].

$$H_5C_6{-}CH_2{-}N{=}CS \xrightarrow[-SCl_2]{2\,Cl_2} H_5C_6{-}CH_2{-}N{=}CCl_2 \xrightarrow[-2\,HCl]{2\,Cl_2} H_5C_6{-}CCl_2{-}N{=}CCl_2$$

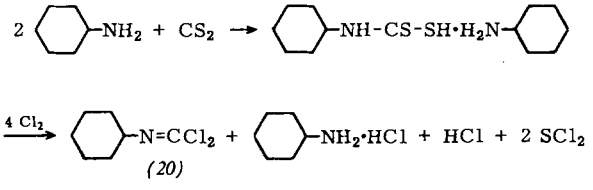
(16) *(17)* *(18)*

The fact that isothiocyanates are very readily obtainable by oxidation of *N*-monosubstituted dithiocarbamates with phosgene, iodine, or sodium hypochlorite, enabled us to obtain isocyanide dichlorides by single-step oxidation with chlorine and chlorination of dithiocarbamates, *e.g. (19)* [25]:



(19) *(20)*

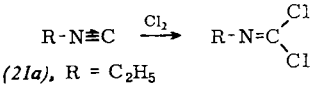
In a further simplification of this process, isocyanide dichlorides are prepared directly in a single vessel from 2 moles of a primary amine, 1 mole of carbon disulfide, and 4 moles of chlorine. In the case of cyclohexyl isocyanide dichloride *(20)*, the yield was 79% based on the amine used.



(20)

2. Addition of Halogen to Isocyanides

The addition of chlorine to isocyanides was first described in 1892 by *Nef* [26]; the starting compounds he used were ethyl isocyanide *(21a)* and phenyl isocyanide *(21b)*. The addition of bromine had already been reported by *Tscherniak* [27].



(21a), R = C_2H_5
(21b), R = C_6H_5

This straightforward process, which generally proceeds smoothly and almost quantitatively, subsequently attracted very little interest – possibly because of the limited availability of isocyanides. It was only as a result of the work of *Ugi et al.* [28] and other research groups that isocyanides became easily and economically obtainable by "dehydration" of *N*-monosubstituted formamides, *e.g.* with phosgene in the presence of a tertiary base.

The addition of chlorine or bromine to isocyanides takes place even in the cold or at room temperature. The isocyanide is dissolved in an inert organic solvent, one equivalent or a small excess of chlorine or bromine is added, and the reaction is allowed to proceed until the generally characteristic isocyanide odor has disappeared. The addition of chlorine to isocyanides is not a generally applicable process. Thus dodecyl isocyanide and its higher alkyl homologues [29] do not give isocyanide dichlorides on reaction with chlorine, since the principal reaction in these cases is side-chain chlorination.

In the preparation of isocyanates from isocyanides, the addition of halogen is to some extent a catalytic intermediate stage. Thus on addition of 5 mole-% of bromine to an equimolar mixture of isopropyl isocyanide *(23)* and dimethyl sulfoxide *(24)* in boiling chloroform, *Johnson jr.* and *Daughhetee jr.* [30] obtained isopropyl isocyanate *(25)* and dimethyl sulfide *(26)*; in this reaction, bromine is eliminated from the intermediate isocyanide dibromide and added on to free isonitrile. The reaction also proceeds in the presence of chlorine or iodine.

$$(CH_3)_2CH{-}N{\equiv}C + Br_2 + (CH_3)_2SO$$

(23)

$$\rightarrow [(CH_3)_2CH{-}N{=}CBr_2 + (CH_3)_2SO]$$

(24)

$$\rightarrow (CH_3)_2CH{-}N{=}CO + (CH_3)_2S + Br_2$$

(25) *(26)*

Isonitriles containing a tertiary amino group have also been converted into isocyanide dichlorides by the addition of chlorine [31]:

$(CH_3)_2N{-}CH_2{-}CH_2{-}CH_2{-}N{=}CCl_2$
m.p. 130.5–132 °C (hygroscopic), yield 62%

$(C_2H_5)_2N{-}CH_2{-}CH_2{-}CH_2{-}N{=}CCl_2$
m.p. 120–122 °C (hygroscopic), yield 64%

3. Chlorination of Monosubstituted Formanilides in the Presence of Thionyl Chloride

Bly, Perkins, and *Lewis* [5] observed that the chlorination of formanilide in chloroform in the presence of thionyl chloride leads to a mixture of phenyl, 4-chlorophenyl, and 2,4-dichlorophenyl isocyanide dichlorides as well as 2,4-dichloroformanilide. This observation formed the basis of our investigations of the preparation of aromatic isocyanide dichlorides. The results have already been reported in full [32], and we need only give the general reaction scheme here:

[24] This compound was recently also obtained by *R. Neidlein* and *W. Haussmann*, Chem. Ber. *99*, 239 (1966), by reaction of benzoyl isocyanide dichloride with phosphorus pentachloride in boiling chlorobenzene.

[25] DAS 1221213 (Aug. 23, 1963), Farbenfabriken Bayer AG, Inv.: *E. Kühle* and *B. Anders*.

[26] *U. Nef*, Liebigs Ann. Chem. *270*, 267 (1892); *280*, 291 (1894).

[27] *M. Tscherniak*, Bull. [2], *30*, 185 (1878); cf. also *H. Guillemard*, Ann. Chimie [8], *14*, 324 (1908).

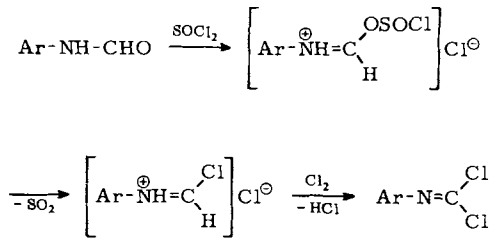
[28] *I. Ugi et al.*, Angew. Chem. *77*, 492 (1965); Angew. Chem. internat. Edit. *4*, 492 (1965).

[29] *E. Jungermann* and *F. W. Smith*, J. Amer. Oil Chemists' Soc. *36*, 388 (1959).

[30] *H. W. Johnson jr.* and *P. H. Daughhetee jr.*, J. org. Chemistry *29*, 246 (1964).

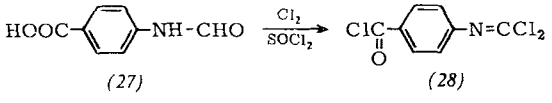
[31] *P. A. S. Smith* and *N. W. Kalenda*, J. org. Chemistry *23*, 1599 (1958).

[32] *E. Kühle*, Angew. Chem. *74*, 861 (1962); Angew. Chem. internat. Edit. *1*, 647 (1962).



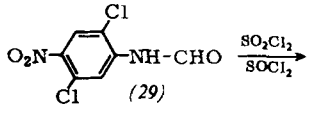
Contrary to the information given in the literature [5], we use thionyl chloride as the reaction solvent. Not only does this give better yields, but the separation of thionyl chloride from chloroform by distillation, which is particularly troublesome on the industrial scale, becomes unnecessary.

We had already pointed out that very good yields of isocyanide dichloride are always obtained when the aromatic ring can no longer be readily chlorinated, because of substituents (halogen, nitro, carboxyl, aryl residues, *etc.*) already present. Many substituents react with thionyl chloride; thus 4-formylaminobenzoic acid *(27)* gives 4-chlorocarbonylphenyl isocyanide dichloride *(28)*.

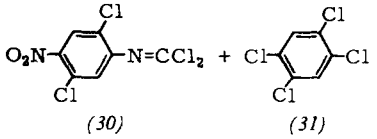


(27) *(28)*

If the aromatic nucleus carries substituents that facilitate aromatic substitution, cyanogen chloride is readily eliminated from the isocyanide dichloride grouping. For example, the reaction of 2,5-dichloro-4-nitroformanilide *(29)* with thionyl chloride/sulfuryl chloride yields not only the desired isocyanide dichloride *(30)*, but also considerable quantities of 1,2,4,5-tetrachlorobenzene *(31)*.



(29)

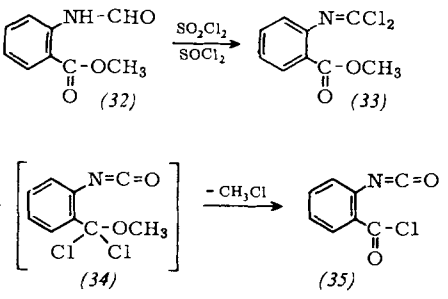


(30) *(31)*

In one case, we observed intramolecular chlorine/oxygen exchange [33]. Thus when methyl 2-formylaminobenzoate *(32)* reacts with sulfuryl chloride in thionyl chloride, the corresponding isocyanide dichloride *(33)* is obtained as a crude product when the excess thionyl chloride is evaporated off. During the distillation of the crude product, secondary reaction leads to elimination of methyl chloride and chlorine/oxygen exchange, probably *via* the intermediate *(34)*, with formation of 2-chlorocarbonylphenyl isocyanate *(35)* [34].

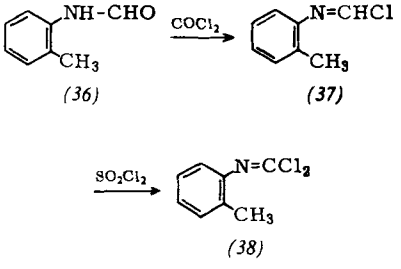
[33] *E. Kühle* and *E. Klauke*, German Pat. Appl. F 48971 IVb/12 o (April 20, 1966), Farbenfabriken Bayer AG.

[34] This isocyanate cannot be obtained by phosgenation of anthranilic acid, since isatoic anhydride is formed.



(32) *(33)* *(34)* *(35)*

The chlorination of monosubstituted aromatic formamides can, in principle, also be carried out in phosphorus oxide trichloride, phosgene, or oxalyl chloride instead of in thionyl chloride, but the yields of isocyanide dichloride are then much lower. Thus *Sayigh* and *Ulrich* [35] have described the chlorination of 2-tolylformamide *(36)* with phosgene and sulfuryl chloride in dichloroethane, which leads to 2-tolyl isocyanide dichloride *(38)* probably *via* the intermediate *(37)*.



(36) *(37)* *(38)*

We had observed earlier [32] that the use of this process with aliphatic and cycloaliphatic formamides generally leads to isocyanates [36]. However, when *N*-cyclohexylformamide in an excess of thionyl chloride is heated at 40 °C until the evolution of sulfur dioxide stops, the subsequent addition of sulfuryl chloride yields cyclohexyl isocyanide dichloride as the main product in yields of up to about 50%.

In attempts to prepare aromatic isocyanide dibromides from the corresponding formanilides with bromine in thionyl chloride, hydrogen bromide is split off and only the isocyanide dichlorides are obtained. Similar experiments with bromine in thionyl bromide led only to resinification products.

4. Chlorination of Isocyanates with Phosphorus Pentachloride [37]

In contrast to the chlorination of isothiocyanates, isocyanide dichlorides were only recently obtained from isocyanates.

Gumpert [38] had already treated boiling phenyl isocyanate with phosphorus pentachloride but, apart from phosphorus oxide trichloride, only resinous products were isolated from the reaction mixture.

[35] *A. A. R. Sayigh* and *H. Ulrich*, J. chem. Soc. (London) *1963*, 3146.

[36] German Pat. 1090197 (Aug. 19, 1959), Farbenfabriken Bayer AG, Inv.: *E. Kühle*.

[37] The chlorination of phenyl isothiocyanate with phosphorus pentachloride, which leads to phenyl isocyanide dichloride, was carried out by *A. W. Hofmann*, Ber. dtsch. chem. Ges. *12*, 1126 (1879).

[38] *F. Gumpert*, J. prakt. Chem. *31*, 119 (1885).

When an isocyanate is allowed to react with an equimolar quantity of phosphorus pentachloride at 20 to 50 °C in a chlorine-resistant solvent such as chlorobenzene, or in the phosphorus oxide trichloride formed in the reaction, an isocyanide dichloride is obtained in accordance with the following equation:

$$R{-}N{=}C{=}O + PCl_5 \rightarrow RN{=}CCl_2 + POCl_3.$$

This reaction gives moderate to good yields in the lower aliphatic and cycloaliphatic series [39,40], but side-chain chlorination must be expected with long-chain aliphatic isocyanates.

Aromatic isocyanates react with phosphorus pentachloride only above about 100 °C, with elimination of phosgene. Isocyanide dichlorides are formed only in small quantities. According to *Ulrich* and *Sayigh* [41], the main products are carbodiimides, which cannot be detected in the aliphatic and cycloaliphatic series. Thus the reaction of aromatic isocyanates with phosphorus pentachloride probably proceeds in accordance with the following reaction scheme:

$$Ar{-}N{=}C{=}O + PCl_5 \longrightarrow Ar{-}N{=}CCl_2 + POCl_3$$

$$Ar{-}N{=}CCl_2 + POCl_3 \longrightarrow Ar{-}N{=}PCl_3 + COCl_2$$

$$Ar{-}N{=}C{=}O + Ar{-}N{=}PCl_3 \longrightarrow Ar{-}N{=}C(-O{-}Ar){-}N{-}PCl_3$$

$$\longrightarrow Ar{-}N{=}C{=}N{-}Ar + POCl_3$$

5. High-temperature Chlorination of Tertiary Amines and Acyl Derivatives of Secondary Amines

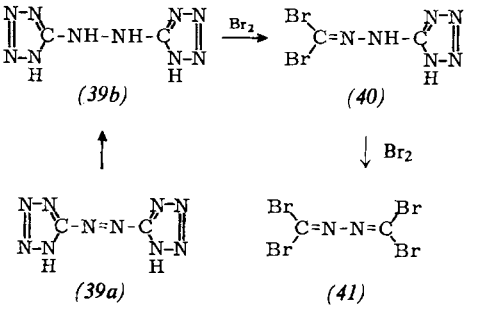
The high-temperature chlorination of tertiary amines, which is accompanied by dealkylation, and the high-temperature chlorination of acyl derivatives of secondary amines, which is accompanied by deacylation, have been described by *Holtschmidt* [42].

6. Special Methods for the Preparation of Individual Isocyanide Dihalides [42a]

The literature contains occasional references to compounds having the isocyanide dihalide structure, but which cannot be prepared by any of the methods described above. Moreover, special methods have recently been reported for the preparation of isocyanide dichlorides. These will be discussed below in chronological order.

a) Diisocyanogen Tetrabromide (Tetrabromoformalazine)

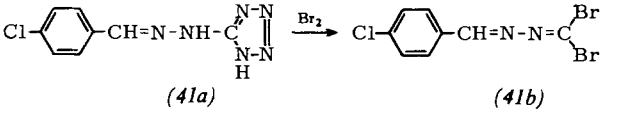
On bromination of hydrazotetrazole *(39b)*, which can be obtained by the reduction of the sodium salt of azotetrazole *(39a)*, *Thiele* [43] obtained diisocyanogen tetrabromide *(41)* [43b] (m.p. 42 °C), which is formed *via* the isolable *N'*-tetrazol-5-yldibromoformaldehyde hydrazone *(40)* (m.p. 177 °C), but which decomposes on storage.



(39b) *(40)* *(39a)* *(41)*

Similarly, the arylidene derivatives of 5-tetrazolylhydrazine react with bromine in aqueous acetic acid to form dibromomethylene compounds [43a].

Thus the 4-chlorobenzylidene derivative *(41a)* gives the dibromomethylene derivative *(41b)* in 80% yield.



(41a) *(41b)*

b) Trichloromethyl Isocyanide Dichloride

Trichloromethyl isocyanide dichloride *(43)* was first prepared by *Prandtl* and *Sennewald* [44] from trichloronitrosomethane *(42)* [45]. Trichloronitrosomethane decomposes on storage, or more rapidly when heated, to form trichloromethyl isocyanide dichloride *(43)*, chloropicrin *(44)*, and nitrosyl chloride in accordance with the following equation:

$$\underset{(42}{3\ Cl_3C{-}NO} \rightarrow \underset{(43)}{Cl_3C{-}N{=}CCl_2} + \underset{(44)}{Cl_3C{-}NO_2} + NOCl$$

[39] The yields are strongly dependent on the quality of the phosphorus pentachloride.

[40] German Pat. 1126371 (Sept. 17, 1959), Farbenfabriken Bayer AG, Inv.: *E. Kühle* and *R. Wegler*; US-Pat. 3267144 (Oct. 28, 1963), Olin Mathieson Chem. Corp., Inv.: *G. F. Ottmann* and *H. Hooks jr.*

[41] *H. Ulrich* and *A. A. R. Sayigh*, J. chem. Soc. (London) *1963*, 5558.

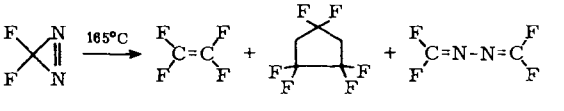
[42] *H. Holtschmidt*, Angew. Chem. *74*, 848 (1962); Angew. Chem. internat. Edit. *1*, 632 (1962).

[42a] The "unsubstituted isocyanide dichloride" (*N*-dichloromethyleneamine) which is formed by the addition of hydrogen chloride to cyanogen chloride, was obtained in the form of a salt by *E. Allenstein* and *A. Schmidt*, Chem. Ber. *97*, 1286 (1964).

[43] *J. Thiele*, Ber. dtsch. chem. Ges. *26*, 2645 (1893); Liebigs Ann. Chem. *303*, 57 (1898).

[43a] *F. L. Scott* and *D. A. Cronin*, Chem. and Ind. *1964*, 1757.

[43b] The analogous diisocyanogen tetrafluoride has recently been obtained by *R. A. Mitsch*, J. Heterocyclic Chem. *1*, 59 (1964), together with other products by pyrolysis of difluorodiazirine above 165 °C.



[44] *W. Prandtl* and *K. Sennewald*, Ber. dtsch. chem. Ges. *62*, 1754 (1929).

[45] According to *Holtschmidt* [42], this compound is formed in good yield in the high-temperature chlorination of *N,N*-dimethylcarbamyl chloride.

c) Dichloroformaldoxime (Phosgene Oxime)

Prandtl and *Sennewald*[44] obtained dichloroformaldoxime *(45)* in 44 to 50% yield by reduction of trichloronitrosomethane *(42)* with hydrogen sulfide or aluminum amalgam; the yield could be increased to 70% by the use of a different reducing agent[46]. Dichloroformaldoxime (m.p. 39–40 °C; b.p. 47 °C/18 mm Hg) cannot be stored for long periods; it has a pungent odor and attacks mucous membranes[47].

$$\underset{(42)}{Cl_3C{-}NO} + H_2S \rightarrow \underset{(45)}{Cl_2C{=}NOH} + HCl + S$$

Dichloroformaldoxime and its bromine and iodine analogues, *(46a)* and *(46b)*, can be obtained in yields of 65 to 85% from mercuric or sodium fulminate[48].



(46a) M.p. 68–69 °C; B.p. 73–75 °C/14 mm

(46b) m.p. 69 °C

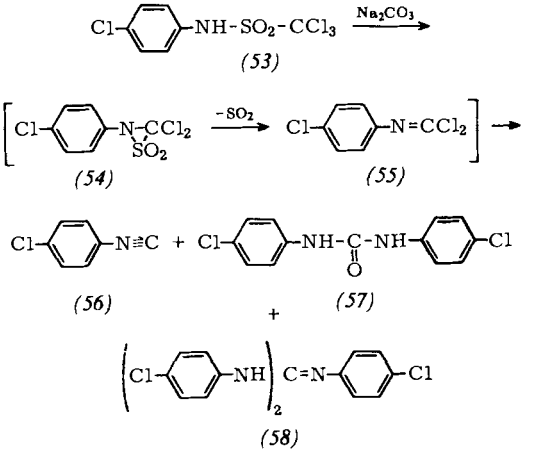
Dichloroformaldoxime can also be prepared by electrolytic reduction of trichloronitromethane in acidic media[49], chlorination of 1-chloro-1-hydroxyiminoacetone (from acetone, nitric acid, and hydrochloric acid)[50], and treatment of chloronitroacetyl chloride with hydrochloric acid[51].

d) Trifluoromethyl Isocyanide Dichloride

Barr, Haszeldine, and *Willis*[52] obtained a mixture of a 1,2-oxazetidine *(49)* and a 1:1 copolymer *(50)* from trifluoronitrosomethane *(47)* and 1,1-dichloro-2,2-difluoroethylene *(48)*; the copolymer decomposes at 550 °C into trifluoromethyl isocyanide dichloride *(51)*[53] and carbonyl difluoride *(52)*, while pyrolysis of the 1,2-oxazetidine (≈ 550 °C) yields trifluoromethyl isocyanide difluoride *(74)* (cf. Section III.7).

e) Alkaline Decomposition of *N*-Trichloromethanesulfonyl-4-chloroaniline

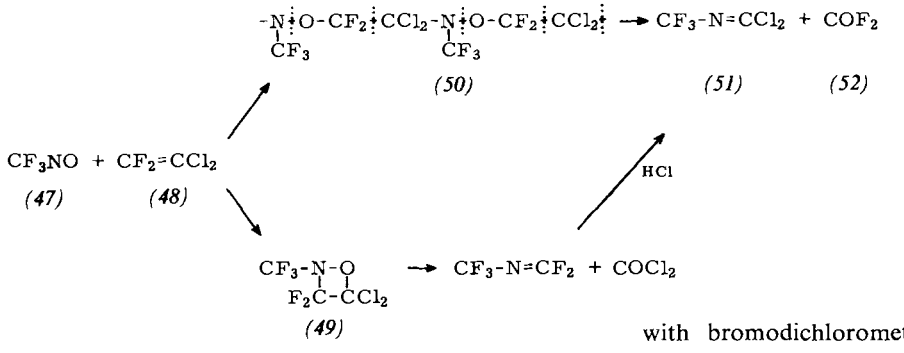
The alkaline hydrolysis (Na_2CO_3 solution) of *N*-trichloromethanesulfonyl-4-chloroaniline *(53)* probably proceeds *via* the three-membered heterocyclic compound *(54)* and 4-chlorophenyl isocyanide dichloride *(55)*, since the isocyanide *(56)*, the urea *(57)*, and the guanidine *(58)*, as well as 4-chloroaniline, could be isolated as reaction products[54].



(53) *(54)* *(55)* *(56)* *(57)* *(58)*

f) Cleavage of Carbodiimides by Dichlorocarbene

A recent publication describes the cleavage of carbodiimides with bromodichloromethylphenylmercury[55]. Thus the reaction of diisopropylcarbodiimide *(59)* with bromodichloromethylphenylmercury *(60)* in a molar ratio of 1:2 in chlorobenzene at 80 °C leads to isopropyl isocyanide dichloride *(61)* in 92% yield.



(47) *(48)* *(49)* *(50)* *(51)* *(52)*

$$\underset{(59)}{(CH_3)_2CH{-}N{=}C{=}N{-}CH(CH_3)_2} + \underset{(60)}{C_6H_5{-}Hg{-}CCl_2Br} \rightarrow \underset{(61)}{(CH_3)_2CH{-}N{=}CCl_2} + C_6H_5HgBr + (CH_3)_2CH{-}N{\equiv}C$$

[46] *W. Prandtl* and *W. Dollfus*, Ber. dtsch. chem. Ges. *65*, 754 (1932).

[47] Gas masks and rubber gloves must be worn when handling this compound.

[48] *L. Birckenbach* and *K. Sennewald*, Liebigs Ann. Chem. *489*, 7 (1931); *G. Endres*, Ber. dtsch. chem. Ges. *65*, 65 (1932).

[49] *E. Gryzskiewicz-Trochimowski, K. Dymowski,* and *E. Schmidt*, Bull. Soc. chim. France *1948*, 597; *H. Brintzinger, H. W. Ziegler,* and *E. Schneider*, Z. Elektrochem. angew. physik. Chem. *53*, 109 (1949).

[50] US-Pat. 2299742 (Nov. 24, 1941), Ansul Chem. Corp., Inv.: *P. J. Ehman* and *W. O. Walker*.

[51] *I. V. Martynov* and *Y. L. Krugljak*, Ž. obšč. Chim. *35*, 248 (1965).

[52] *D. A. Barr, R. N. Haszeldine,* and *C. J. Willis*, J. chem. Soc. (London) *1961*, 1351.

[53] This compound is also formed on prolonged heating of bis-(trifluoromethyl)amine with phosphorus trichloride, cf. *J. A. Young, S. N. Tsoukalas,* and *R. D. Dresdner*, J. Amer. chem. Soc. *80*, 3604 (1958).

[54] *W. V. Farrar*, J. chem. Soc. (London) *1960*, 3058.

[55] *D. Seyferth* and *R. Damrauer*, Tetrahedron Letters *1966*, 189.

g) Isocyanide Dichlorides by Friedel-Crafts Reaction

In special cases, isocyanide dichlorides can be obtained from chlorinated isocyanide dichlorides by Friedel-Crafts reactions in the presence of aluminum chloride. Thus the reaction of chloromethyl isocyanide dichloride *(62)* in boiling benzene in the presence of aluminum chloride yields benzyl isocyanide dichloride *(63)* [56].

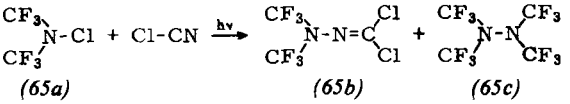
$$\underset{(62)}{ClCH_2-N{=}CCl_2} \xrightarrow[AlCl_3]{C_6H_6} \underset{(63)}{H_5C_6-CH_2-N{=}CCl_2}$$

Trichloromethyl isocyanide dichloride *(43)* reacts with benzene in the presence of aluminum chloride to form triphenylchloromethane *(65)*, probably by elimination of cyanogen chloride from the intermediate triphenylmethyl isocyanide dichloride *(64)*, which cannot be isolated [57].

$$(43) \xrightarrow[AlCl_3]{C_6H_6} \underset{(64)}{[(C_6H_5)_3C-N{=}CCl_2]} \xrightarrow{-ClCN} \underset{(65)}{(C_6H_5)_3CCl}$$

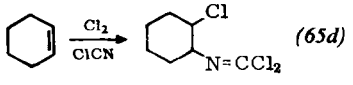
h) Reactions with Cyanogen Chloride

When a mixture of *N*-chlorobis(trifluoromethyl)amine *(65a)* and cyanogen chloride is irradiated, bis(trifluoromethyl)aminocarbylamine dichloride *(65b)* is formed in a yield of more than 40%, together with tetrakis(trifluoromethyl)hydrazine *(65c)* [57a].



(65a) *(65b)* *(65c)*

Arlt [57b] recently obtained α-chlorinated aliphatic and cycloaliphatic isocyanide dichlorides by the addition of chlorine to olefins in the presence of cyanogen chloride. For example, the chlorination of a solution of cyanogen chloride in cyclohexene at 0–10 °C gives 2-chlorocyclohexyl isocyanide dichloride *(65d)* in a yield of about 50% (b.p. 85 °C/0.8 mm Hg).



(65d)

[56] *H. W. v. Brachel*, unpublished.

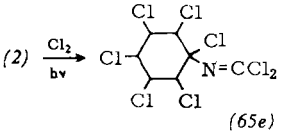
[57] *E. Kühle*, unpublished.

[57a] *R. C. Dobbie* and *H. J. Emeléus*, J. chem. Soc. (London) *A 1966*, 933.

[57b] *D. Arlt*, German Pat. Appl. F 52056 IV b / 12o (April 7, 1967) Farbenfabriken Bayer AG.

i) Hexachlorohexyl Isocyanide Dichloride

The radiation-induced addition of chlorine to phenyl isocyanide dichloride *(2)* leads to hexachlorocyclohexyl isocyanide dichloride *(65e)* [57c].



(65e)

7. Isocyanide Difluorides

Isocyanide difluorides cannot be prepared by the methods described so far. A special isothiocyanate fluorination process [61] has recently been developed but, apart from a few highly fluorinated aliphatic isocyanide difluorides, this class of compounds can generally be obtained only *via* the corresponding isocyanide dichlorides.

a) According to *Petrov* and *Neimyseva* [58], isocyanide dichlorides react with anhydrous hydrogen fluoride in an alternating addition-elimination reaction to form *N*-trifluoromethylamines *(66)*, which yield the isocyanide difluorides *(67)* on treatment with potassium fluoride at 140 to 150 °C in the absence of solvent.

$$\underset{}{R-N{=}CCl_2} \xrightarrow{HF} \underset{(66)}{RNH-CF_3} \xrightarrow{KF} \underset{(67)}{R-N{=}CF_2}$$

b) Aromatic isocyanide dichlorides react with an excess of an alkali-metal fluoride at 150 to 350 °C in a high-boiling inert solvent such as tetramethylene sulfone to form the corresponding isocyanide difluoride, sometimes in very good yields [60,61], *e.g.*

$$H_5C_6-N{=}CCl_2 \xrightarrow[\text{tetramethylene sulfone}]{NaF/200-240\,^\circ C} H_5C_6-N{=}CF_2$$

c) Whereas hydrogen fluoride is not eliminated from *N*-trifluoromethylaniline on reaction with quinoline [59],

$$\underset{(66)}{RNH-CF_3} + ClCO-R' \xrightarrow{N(C_2H_5)_3} \begin{cases} \not\rightarrow\ CF_3-RN-CO-R' & (68) \\ \rightarrow\ (67) + FCO-R' + (C_2H_5)_3N\cdot HCl \end{cases}$$

other *N*-trifluoromethylamines react, even at room temperature, with acyl chlorides in the presence of a strongly basic tertiary amine such as triethylamine.

[57c] US-Pat. 3254105 (Feb. 26, 1963), Diamond Alkali Comp., Inv.: *I. Rosen*.

[58] *K. A. Petrov* and *A. A. Neimyseva*, Ž. obšč. Chim. *29*, 2169 (1959); *D. A. Barr* and *R. N. Haszeldine*, J. chem. Soc. (London) 1955, 2532.

[59] *K. A. Petrov* and *A. A. Neimyseva*, Ž. obšč. Chim. *29*, 2695 (1959).

[60] *E. Klauke* and *E. Kühle*, DAS 1235291 (July 29, 1965), Farbenfabriken Bayer AG.

[61] According to *W. A. Sheppard*, J. Amer. chem. Soc. *87*, 4338 (1965), this reaction proceeds best with silver fluoride.

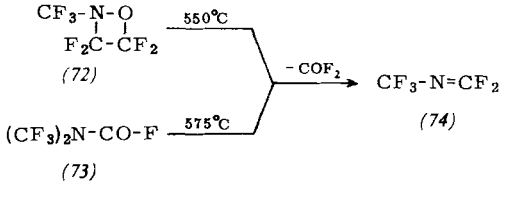
Instead of the expected acylation product *(68)* [62], the reaction yields the corresponding isocyanide difluoride together with the acyl fluoride [63]. Thus, under these conditions, the trifluoromethylamines act as fluorinating agents. As a by-product, this reaction sometimes gives a dimeric isocyanide difluoride, which can also be obtained from pure isocyanide difluoride with a trace of triethylamine, and which is assigned the structure *(69)* on the basis of its reactions [64].

$$2\ (67) \longrightarrow \underset{\underset{F}{|}}{\overset{\overset{|}{}}{R\text{-}N{=}C\text{-}N\text{-}R}}\ \underset{CF_3}{|} \quad (69)$$

d) According to *Sheppard* [61], the reaction of mercuric fluoride with aliphatic and aromatic isothiocyanates is a general method for the preparation of isocyanide difluorides. Whereas the reaction of aryl isothiocyanates leads not only to the desired isocyanide difluoride (yield in the case of phenyl isothiocyanate: 17%) but also to *N*-trifluoromethylaniline and the dimeric isocyanide difluoride, these by-products are not formed in the reaction of alkyl isothiocyanates. Thus ethyl isocyanide difluoride *(71)* is obtained in 37% yield from ethyl isothiocyanate *(70)*.

$$\underset{(70)}{C_2H_5\text{-}N{=}C{=}S} + HgF_2 \rightarrow \underset{(71)}{C_2H_5\text{-}N{=}CF_2} + HgS$$

e) Highly fluorinated lower aliphatic isocyanide difluorides have been obtained by various methods in recent years, generally by pyrolysis reactions. The simplest compound in this series, trifluoromethyl isocyanide difluoride (perfluoro-2-azapropene) *(74)* (b.p. −33.7 °C), is formed quantitatively on pyrolysis of 2-trifluoromethylperfluoro-1,2-oxazetidine *(72)* [65] or of bis(*N*-trifluoromethyl)carbamyl fluoride *(73)* [66] at 550 to 575 °C by elimination of carbonyl difluoride. According to the results of other pyrolysis experiments, *(74)* is obtained only in moderate yields or as a by-product [67].



Compound *(74)* can also be obtained under very mild conditions from bis(*N*-trifluoromethyl)halogenoamines *(75)* (Hal = Cl, Br) and pentacarbonyliron [68].

$$\underset{(75)}{(CF_3)_2NHal} \xrightarrow{Fe(CO)_5} (74)$$

The higher perfluoroalkyl isocyanide difluorides are obtained by pyrolysis of suitable perfluorinated tertiary amines [69], *e.g.*:

$$(C_2F_5)_3N \rightarrow CF_3\text{-}CF_2\text{-}N{=}CF_2;\ \text{b.p. } -18 \text{ to } -13\ ^\circ C$$

IV. Preparation of Acyl Isocyanide Dichlorides

Acyl isocyanide dichlorides are most easily and most smoothly obtained by chlorination of acyl isothiocyanates or their percursors (*e.g.* acylated dithiocarbamates).

The isothiocyanates of carboxylic acids [70] and of phosphorus acids [71] can be readily obtained by treatment of the acid chlorides with lead or alkali metal thiocyanates. An elegant process that proceeds in the homogeneous phase and gives consistently higher yields was described by *Anders* and *Malz* [72]. This process involves the reaction of silyl isothiocyanates [73] with acyl and carbamyl chlorides, esters of chlorocarbonic acid, or any compound of chlorine and phosphorus. In the simplest case, trimethylsilyl isothiocyanate *(77)*, which is readily obtainable from trimethylchlorosilane *(76)* and alkali metal thiocyanate, reacts with an acyl chloride to form the acyl isothiocyanate *(78)*, with regeneration of *(76)*.

$$\underset{(76)}{(CH_3)_3SiCl} \xrightarrow{KSCN} \underset{(77)}{(CH_3)_3Si\text{-}N{=}CS} \xrightarrow{RCOCl} R\text{-}CO\text{-}N{=}CS + \underset{(78)}{(76)}$$

Sulfonyl isothiocyanides cannot be prepared from sulfonyl chlorides, but are readily obtainable from the salts of *N*-sulfonyliminodithiocarbonic acid [74].

The sulfenyl isothiocyanates are as yet unknown, since sulfenyl chlorides react with metal thiocyanates to form sulfenyl thiocyanates [75].

1. Chlorination of Isothiocyanates of Carboxylic Acids

Acyl isothiocyanates *(79)* can generally be readily chlorinated, either in the absence of a solvent or in chloroform or carbon tetrachloride at 0 to 50 °C, in

[62] *N*-Trifluoromethylamides of carboxylic acids can be obtained from *N*-trifluoromethylamines *via* the thiobis-*N*-trifluoromethylamines. *T. E. Stevens*, J. org. Chemistry *26*, 3451 (1961).

[63] *E. Kühle* and *E. Klauke*, German Pat. Appl. F 49695 IVb/12 o (July 15, 1966), Farbenfabriken Bayer AG.

[64] *F. S. Fawcett, C. W. Tullock*, and *D. D. Coffman*, J. chem. Engng. Data *10*, 398 (1965), obtained the monomer in 84% yield from the dimeric trifluoromethyl isocyanide difluoride $(CF_3)_2N\text{-}CF{=}N\text{-}CF_3$ with sodium fluoride at 525 °C.

[65] *D. A. Barr* and *R. N. Haszeldine*, J. chem. Soc. (London) *1955*, 1881.

[66] *J. A. Young, T. C. Simmons*, and *F. W. Hoffmann*, J. Amer. chem. Soc. *78*, 5637 (1956).

[67] *J. A. Young, S. N. Tsoukalas*, and *R. D. Dresdner*, J. Amer. chem. Soc. *82*, 396 (1960); *R. D. Dresdner, F. N. Tlumac*, and *J. A. Young, ibid. 82*, 5831 (1960); *J. A. Young* and *R. D. Dresdner*, J. org. Chemistry *28*, 833 (1963).

[68] *M. Green* and *A. E. Tipping*, J. chem. Soc. (London) *1965*, 5774.

[69] US-Pat. 2643267 (Jan. 28, 1950), Minnesota Mining and Manufacturing Co., Inv.: *W. A. Pearlson* and *L. J. Hals*.

[70] *Houben-Weyl*: Methoden der organischen Chemie. 4th Edit. Georg Thieme Verlag, Stuttgart *1955*, Vol. IX, p. 878.

[71] Houben-Weyl: Methoden der organischen Chemie. 4th Edit. Georg Thieme Verlag, Stuttgart 1964, Vol. XII/2, p. 507.

[72] DAS 1215144 (Nov. 14, 1964), Farbenfabriken Bayer AG, Inv.: *B. Anders* and *H. Malz*.

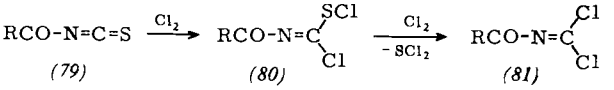
[73] *J. Goubeau* and *J. Reyhing*, Z. anorg. allg. Chem. *294*, 96 (1958).

[74] *K. Dickore* and *E. Kühle*, Angew. Chem. *77*, 429 (1965); Angew. Chem. internat. Edit. *4*, 430 (1965); *K. Hartke*, Arch. Pharmaz. *299*, 174 (1966).

[75] Houben-Weyl: Methoden der organischen Chemie. 4th Edit. Georg Thieme Verlag, Stuttgart 1955, Vol. IX, p. 280.

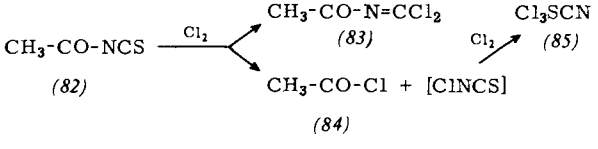
the same way as the aliphatic or aromatic isothiocyanates. $AlCl_3$ or $TiCl_4$ may be used as catalysts [76c].

As with normal isothiocyanates, the reaction proceeds in two steps. An *N*-(chloro-chlorothiomethylene)-carbonamide *(80)* is first formed by addition of chlorine [77]; further chlorination and elimination of sulfur dichloride then yields the acyl isocyanide dichloride



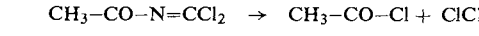
(79) *(80)* *(81)*

(81). In most cases the chlorination proceeds very smoothly; the yield of acyl isocyanide dichloride is about 50 to 95%. Even bisacyl isothiocyanates such as terephthaloyl diisothiocyanate can be converted directly into the bisacyl isocyanide dichlorides. Only the lower aliphatic acyl isothiocyanates give unwanted by-products on chlorination. Thus the chlorination of acetyl isothiocyanate *(82)* gives only a low yield of the desired acetyl isocyanide dichloride *(83)*, the principal products being acetyl chloride *(84)* and thiocyanogen trichloride *(85)*.



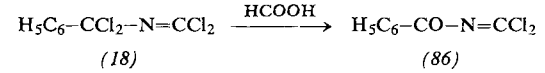
(82) *(83)* *(85)* *(84)*

The lower aliphatic acyl isocyanide dichlorides decompose into acyl chlorides and cyanogen chloride on prolonged standing, *e.g.*



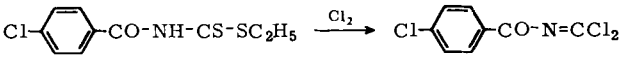
However, acyl isocyanide dichlorides containing longer chains (more than 6 C atoms) or a negative residue (*e.g.* chlorine or chlorophenoxy) are readily obtainable.

Structural evidence of the acyl isocyanide dichloride grouping was obtained by partial hydrolysis of the 1,1,3,3-tetrachloro-3-phenyl-2-azapropene *(18)*, which is formed on further chlorination of benzyl isothiocyanate. Benzoyl isocyanide dichloride *(86)* can be obtained by partial hydrolysis of *(18)* with formic acid [78].



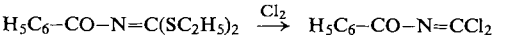
(18) *(86)*

The chlorination of *N*-acylated dithiocarbamates [79] [*e.g. (87)*] was re-examined in a recent study [76e]. In methylene chloride at room temperature, this reaction gives acyl isocyanide dichlorides [*e.g. (88)*] in yields of more than 80%. The same article contains a report on the chlorination of diethyl benzoyliminodithio-



(87) *(88)*

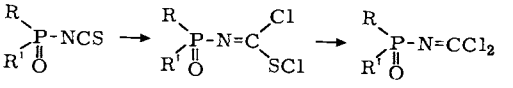
carbonate *(89)* in carbon tetrachloride at 60 °C, which leads to benzoyl isocyanide dichloride *(90)* in 69% yield.



(89) *(90)*

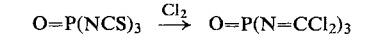
2. Chlorination of Phosphoryl Isothiocyanates

The chlorination of diorganylphosphoryl isothiocyanates *(91)* leads *via* the chlorine adduct [80] *(92)* to the phosphoryl isocyanide dichloride *(93)* [81].



(91) *(92)* *(93)*

This process is very versatile, since the residues R and R′ can be varied, and since phosphoryl compounds containing several chlorine atoms can be converted *via* the phosphoryl di- and tri-isothiocyanates into the corresponding phosphoryl di- and tri-isocyanide dichlorides. Thus phosphoryl tris(isocyanide dichloride) *(95)* (b.p. 83–85 °C/0.08–0.07 mm Hg) is obtained from phosphorus oxide trichloride *via* phosphoryl triisothiocyanate *(94)*.



(94) *(95)*

Alimov and *Levkova* [81b] described dichlorophosphoryl isocyanide dichloride *(97)* (b.p. 83–86 °C/25 mm Hg), which is formed by the reaction of diethoxyphosphoryl isocyanide dichloride *(96)* with phosphorus pentachloride.



(96) *(97)*

3. Sulfonyl Isocyanide Dichlorides by Chlorination of:

a) Sulfonyl Isothiocyanates

The chlorination of sulfonyl isothiocyanates does not proceed as smoothly as that of the isothiocyanates discussed so far. The reaction does not take place at temperatures below 40 to 60 °C; the elimination of sulfur dichloride is also very slow [82]. The intermediate

[76] a) *T. B. Johnson* and *L. H. Chernoff*, J. Amer. chem. Soc. *34*, 164 (1912); b) *T. B. Johnson* and *G. A. Menge*, Amer. chem. J. *32*, 371 (1904); c) DAS 1178422 (March 8, 1963), Farbenfabriken Bayer AG, Inv.: *B. Anders* and *E. Kühle*; d) *R. Neidlein* and *W. Haussmann*, Angew. Chem. *77*, 733 (1965); Angew. Chem. internat. Edit. *4*, 708 (1965); e) Chem. Ber. *99*, 239 (1966).

[77] *Z. M. Ivanova*, *N. A. Kirsanova*, and *G. I. Derkač*, Ž. org. Chim. *1*, 2186 (1965); *Z. M. Ivanova*, *G. I. Derkač*, and *N. A. Kirsanova*, Ž. obšč. Chim. *34*, 3516 (1964).

[78] *H. Holtschmidt*, *E. Degener*, and *H.-G. Schmelzer*, Liebigs Ann. Chem. *701*, 107 (1957).

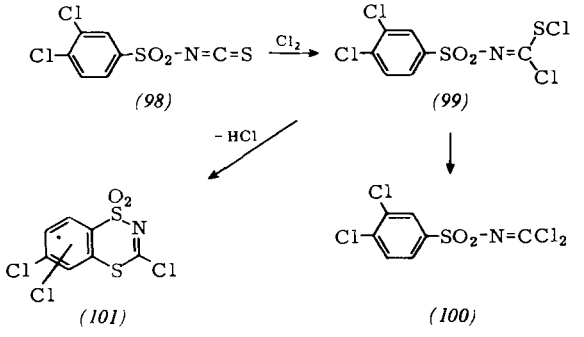
[79] *I. B. Douglass* and *T. B. Johnson*, J. Amer. chem. Soc. *60*, 1486 (1938).

[80] *B. Anders*, unpublished.

[81] a) DAS 1173469 (Dec. 22, 1962), Farbenfabriken Bayer AG, Inv.: *B. Anders*, *E. Kühle*, and *H. Malz*; b) *P. I. Alimov* and *L. N. Levkova*, Izv. Akad. SSSR *1964*, 189, 933; c) *A. V. Kirsanov*, *G. I. Derkač*, and *N. J. Liptuga*, Ž. obšč. Chim. *34*, 2812 (1964); d) cf. also *E. S. Kozlov* and *B. S. Drač*, *ibid. 36*, 760 (1966).

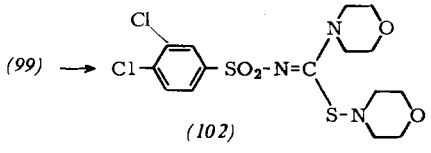
[82] Belg. Pat. 656843 (Dec. 11, 1963), Farbenfabriken Bayer AG, Inv.: *B. Anders*, *E. Kühle*, and *K. Dickoré*.

chlorine adduct sometimes escapes further chlorination in the aromatic ring by cyclization. Thus in the chlorination of 3,4-dichlorobenzenesulfonyl isothiocyanate *(98)*, the compounds *(99)* and *(101)* are formed as intermediates, but only *(99)* can be further chlorinated to form the desired 3,4-dichlorobenzenesulfonyl isocyanide dichloride *(100)*.

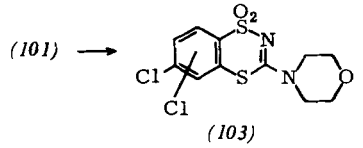


(98) *(99)* *(101)* *(100)*

The constitutions of *(99)* and *(101)* were established by reaction with morpholine; *(99)* reacts with 2 moles and *(101)* with only one mole of the amine to give *N*-(morpholinomorpholinothiomethylene)-3,4-dichlorobenzenesulfonamide *(102)*, m.p. 139 °C, and 3-morpholino-6,?-dichlorobenzo[1,4,2]-dithiazine 1,1-dioxide *(103)*, m.p. 165–167 °C (decomp.), respectively.

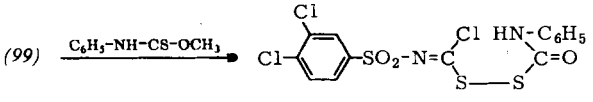


(102)

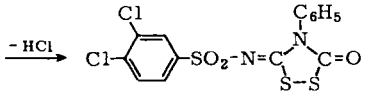


(103)

The compound *(99)* also reacts as a sulfenyl chloride with methyl *N*-phenylthiocarbamate, *via* the disulfide *(104)*, to give 3-(3,4-dichlorobenzenesulfonylimino)-5-oxo-4-phenyl-1,2,4-dithiazolidine *(105)* (m.p. 268 to 269 °C).



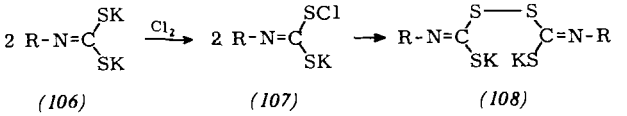
(104)



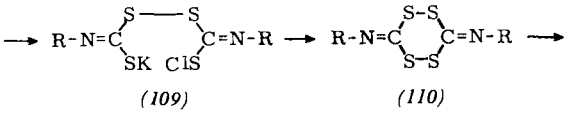
(105)

b) Salts and Esters of Sulfonyliminodithiocarbonic Acids

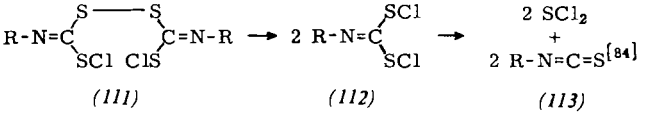
The chlorination of alkali metal salts of sulfonyliminodithiocarbonates *e.g.* in suspension in CCl_4 proceeds much more readily and at lower temperatures than that of the compounds mentioned in Section IV.3.a, with formation of sulfonyl isocyanide dichlorides [82]; furthermore, the number of steps required is one less [83]. Despite the good yields, the reaction appears to be much more complex than the chlorination of isothiocyanates. Thus in the chlorination of potassium dimethylaminosulfonyliminodithiocarbonate *(106)*, we were able to isolate a series of intermediates that suggest the following reaction course.



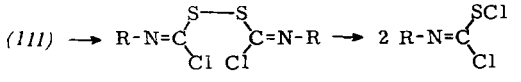
(106) *(107)* *(108)*



(109) *(110)*

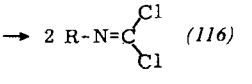


(111) *(112)* *(113)*



(114) *(115)*

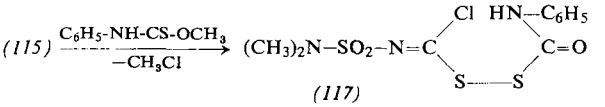
M.p. 127–130 °C B.p. 104–105 °C/0.075 mm
R = $(CH_3)_2N-SO_2-$



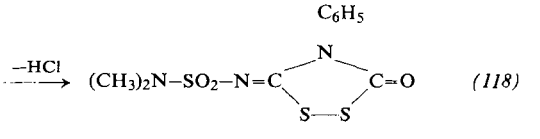
(116)

M.p. 64 °C

Compound *(115)* reacts as a sulfenyl chloride with methyl *N*-phenylthiocarbamate; elimination of methyl chloride takes place resulting in formation of the disulfide *(117)*, which cyclizes with loss of HCl to give 3-(dimethylaminosulfonylimino)-5-oxo-4-phenyl-1,2,4-dithiazolidine *(118)* (m.p. 189 °C).



(117)



(118)

The dimethyl esters *(119)* obtained by methylation of the sulfonyliminodithiocarbonates give good yields of the sulfonyl isocyanide dichlorides *(120)* on chlorination in boiling carbon tetrachloride [85].

[83] Isothiocyanates can be obtained from the *N*-sulfonyliminodithiocarbonates.

[84] B.p. 47–55 °C/0.09–0.06 mm; cf. *K. Hartke* [74]: B.p. 55–56 °C/0.01 mm.

[85] *R. Neidlein* and *W. Haussmann*, Tetrahedron Letters *1965*, 1753.

$$R-SO_2-N=C(SCH_3)_2 \xrightarrow[-CH_3SCl]{Cl_2} R-SO_2-N=CCl_2$$
(119) *(120)*

Reaction with sulfuryl chloride under the same conditions yields the *N*-sulfonyliminothiocarbonate chloride *(121)* [86].

$$(119) \xrightarrow{SO_2Cl_2} R-SO_2-N=C(SCH_3)(Cl) \quad (121)$$

4. Special Acyl Isocyanide Dichlorides

a) Thiocyanogen Trichloride

Thiocyanogen trichloride was synthesized by *Kaufmann* and *Liepe* [87] (in 1924) by chlorination of dithiocyanogen in ethyl bromide. This compound was subsequently examined by several groups of workers, who attempted to establish its constitution.

$$(SCN)_2 \xrightarrow{Cl_2} Cl_3SCN$$

(122a): $ClS-C(Cl)=N-Cl$

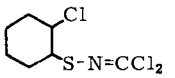
(122b): $ClS-N=C(Cl)_2$

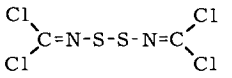
According to *Fehér* and *Weber* [88], thiocyanogen trichloride is a 1,2,3-trichlorothiocyanogen *(122a)*. This conclusion was based on the Raman spectrum and on chemical reactions, which, however, involved the sulfur chloride grouping only.

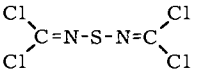
Bacon et al. [89,90] proposed the same structure *(122a)* on the basis of IR measurements and chemical reactions, but pointed out in a footnote (in [90]) that the isomeric *N*-chlorosulfenyl isocyanide dichloride form *(122b)* could not be ruled out. Chemical proof of the structure of thiocyanogen trichloride is difficult to obtain, since the thermally stable compound (b.p. 154–155 °C) splits off cyanogen chloride in most reactions and reacts as sulfur dichloride.

We have also studied thiocyanogen trichloride and, on the basis of its IR spectrum, we favor the structure *(122b)*, since such a structure would account for the characteristic isocyanide dichloride bands at about 900 and 1600 cm^{-1} (cf. also Section V.).

We also investigated the IR spectra of the compounds *(123)* and *(124)*, which are described in the literature and which are obtained from thiocyanogen trichloride [89], as well as the compound *(125)*, which is obtained from thiocyanogen trichloride and cyanogen chloride in the presence of dimethylformamide [91].

(123): 

(124): 

(125): 

The characteristic isocyanide dichloride bands were present in every case [92].

Finally, mention should be made of an elegant process for the production of thiocyanogen trichloride. On chlorination of trimethylsilyl isothiocyanate *(77)*, the weak silicon-nitrogen bond is immediately broken with formation of trimethylchlorosilane *(76)* and chloroisothiocyanate, which cannot be isolated, but which immediately adds on chlorine and rearranges to give chlorosulfenyl isocyanide dichloride *(122b)* [93].

$$(CH_3)_3Si-N=CS \xrightarrow{Cl_2} (CH_3)_3SiCl + [ClN=CS]$$
(77) *(76)*

$$[ClN=CS] \xrightarrow{Cl_2} ClS-CCl=NCl \longrightarrow ClS-N=CCl_2$$
(122a) *(122b)*

b) Addition of Cyanogen Chloride to Acyl Chlorides

Bacon et al. [89] were able to synthesize thiocyanogen trichloride in moderate yields by the addition of cyanogen chloride to sulfur dichloride. A recent Ameri-

$$ClSCl \xrightarrow{ClCN} ClS-N=CCl_2$$
(122b)

can patent [94] describes the addition of cyanogen chloride to sulfur chloride pentafluoride *(126)* on UV irradiation of a mixture of these compounds. Sulfur pentafluoride isocyanide dichloride *(127)* (b.p. 86 to 88 °C) is formed in 38% yield.

$$SF_5Cl \xrightarrow{ClCN} SF_5-N=CCl_2$$
(126) *(127)*

Pawellek [95] recently converted various acyl chlorides into the corresponding acyl isocyanide dichlorides by treatment with cyanogen chloride. Thus the reaction of chloroacetyl chloride *(128)* with cyanogen chloride in a molar ratio of 1:3 at 50 °C gives chloroacetyl isocyanide dichloride *(129)* in a yield of more than 60%.

$$ClCH_2-CO-Cl \xrightarrow{ClCN} ClCH_2-CO-N=CCl_2$$
(128) *(129)*

[86] *R. Neidlein* and *W. Haussmann*, Angew. Chem. *77*, 549 (1965); Angew. Chem. internat. Edit. *4*, 521 (1965).

[87] *H. P. Kaufmann* and *J. Liepe*, Ber. dtsch. chem. Ges. *57*, 923 (1924).

[88] *F. Fehér* and *H. Weber*, Chem. Ber. *91*, 2523 (1958); cf. also Z. Naturforsch. *11b*, 426 (1956).

[89] *R. G. R. Bacon*, *R. S. Irwin*, *J. M. Pollock*, and *A. D. E. Pullin*, J. chem. Soc. (London) *1958*, 764.

[90] *R. G. R. Bacon* and *R. S. Irwin*, J. chem. Soc. (London) *1960*, 5079.

[91] *E. Kühle*, unpublished.

[92] None of the compounds having the formula R–N=C(Cl)–SCl gives a band at 900 cm^{-1}.

[93] *B. Anders*, unpublished.

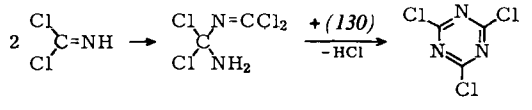
[94] US-Pat. 3228981 (June 27, 1962), Du Pont, Inv.: *C. W. Tullock*.

[95] *D. Pawellek*, Angew. Chem. *78*, 908 (1966); Angew. Chem. internat. Edit. *5*, 845 (1966).

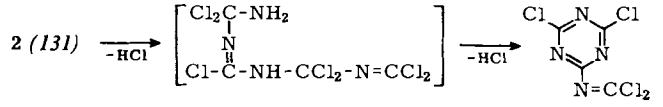
c) Tetrameric Cyanogen Chloride

Tetrameric cyanogen chloride may be regarded as a special case of the addition of cyanogen chloride. The residue left on distillation of cyanuryl chloride, which is formed by trimerization of cyanogen chloride, contains a compound having the same empirical formula, ClCN; this product is the tetramer. The compound was identified a few years ago as 4,6-dichloro-2-triazinyl isocyanide dichloride *(134)* [96,97]. The tetramerization of cyanogen chloride is best carried out in the presence of hydrogen chloride and dimethylformamide [98].

Japanese workers [99] were able to show that tetrameric cyanogen chloride is not formed from cyanuryl chloride. They therefore proposed a reaction mechanism, in which the first step is the addition of hydrogen chloride to cyanogen chloride to form *(130)*, which dimerizes to give dichloroaminomethyl isocyanide dichloride *(131)*. In the principal reaction, *(131)* reacts with *(130)*, with elimination of HCl, to form cyanuryl chloride *(132)*. Compound *(131)* can also enter into a side reaction in which HCl is split off *via (133)* to yield tetrameric cyanogen chloride *(134)*:



(130) *(131)* *(132)*



(133) *(134)*

d) Chlorocarbonyl Isocyanide Dichloride

According to *Holtschmidt* [42] α-chlorinated isocyanates react as acid chlorides. An interesting special case is that of trichloromethyl isocyanate *(135)*, which is obtained by chlorination of methyl isocyanate, and whose chemical behavior [99a] and IR spectrum (CO band at 1770 cm^{-1}; $N{=}CCl_2$: at 1650 and 925 cm^{-1}) correspond to the structure of *N*-chlorocarbonyl isocyanide dichloride *(136)*.

$$CH_3N{=}CO \xrightarrow{Cl_2} (Cl_3C{-}N{=}CO) \longrightarrow Cl_2C{=}N{-}COCl$$

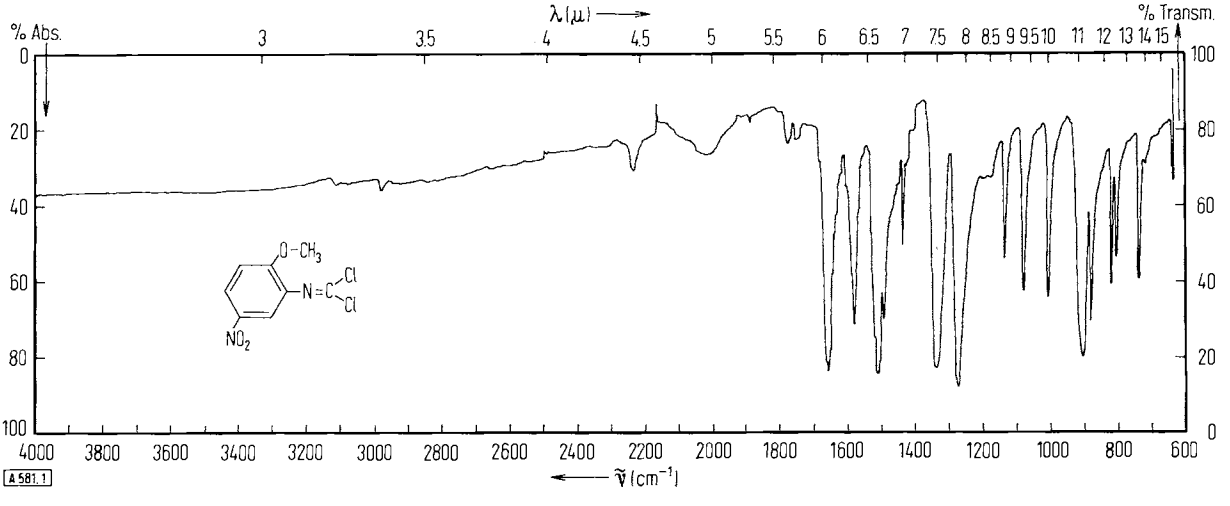
(135) *(136)*

V. Spectroscopy [100]

In IR spectra of the aliphatic, cycloaliphatic, and aromatic isocyanide dichlorides, the band corresponding to the NC double bond appears at 1645 to 1660 cm^{-1}, while the stretching vibrations of the CCl bonds occur at 850 to 910 cm^{-1}. The NC band for the isocyanide dibromides is situated at 1650 to 1680 cm^{-1}.

Owing to the strong electronegativity of fluorine, the bands for the isocyanide difluorides are displaced to much shorter wavelengths, the NC bands appearing at 1789 to 1790 cm^{-1} and the FC stretching bands at 1260 to 1275 cm^{-1} and 1220 to 1237 cm^{-1}; all the bands are very strong.

The bands for the NC double bond vary considerably between different acyl isocyanide dichlorides, and in the case of the phosphoryl isocyanide dichlorides these bands are actually split.



[96] This compound was identified independently by chemists at J. R. Geigy AG and at Farbenfabriken Bayer AG.

[97] According to *H. Holtschmidt*, tetrameric cyanogen chloride is also very readily obtainable by high-temperature chlorination of 2,4-dichloro-6-dimethylaminotriazine.

[98] DAS 1132559 (Jan. 19, 1960), J. R. Geigy AG, Inv.: *J. Riethman* and *H. Wegmüller*.

[99] *Y. Kodama, T. Sebika*, and *T. Ito*, J. Soc. org. synth. Chem., Japan *22*, 567 (1964).

[99a] German Pat. 1167848 (June 5, 1962), Farbenfabriken Bayer AG, Inv.: *E. Degener, H. Holtschmidt*, and *K. Swincicki*.

[100] Co-author: Dr. *Dorothea Lauerer*, Farbenfabriken Bayer AG, Wiss. Hauptlabor.

1) Acyl isocyanide dichlorides of

a) aliphatic carboxylic acids:

C=O double bond: 1735 to 1750 cm^{-1}
N=C double bond: 1635 to 1650 cm^{-1}
Cl–C bond: 890 to 930 cm^{-1}

b) aromatic carboxylic acids:

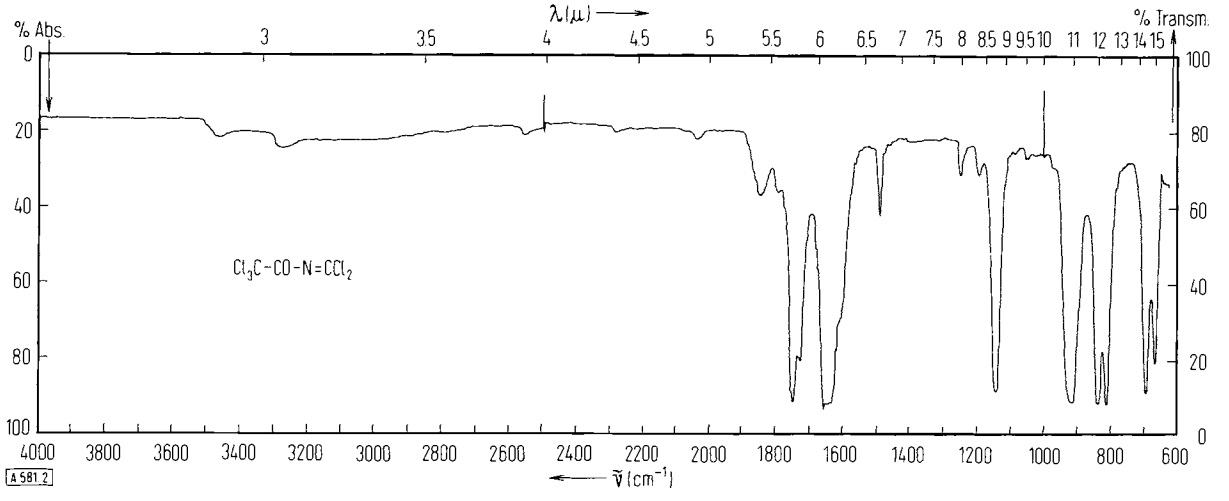
C=O double bond: 1705 to 1722 cm^{-1}
N=C double bond: 1630 to 1640 cm^{-1}
Cl–C bond: 890 to 915 cm^{-1}

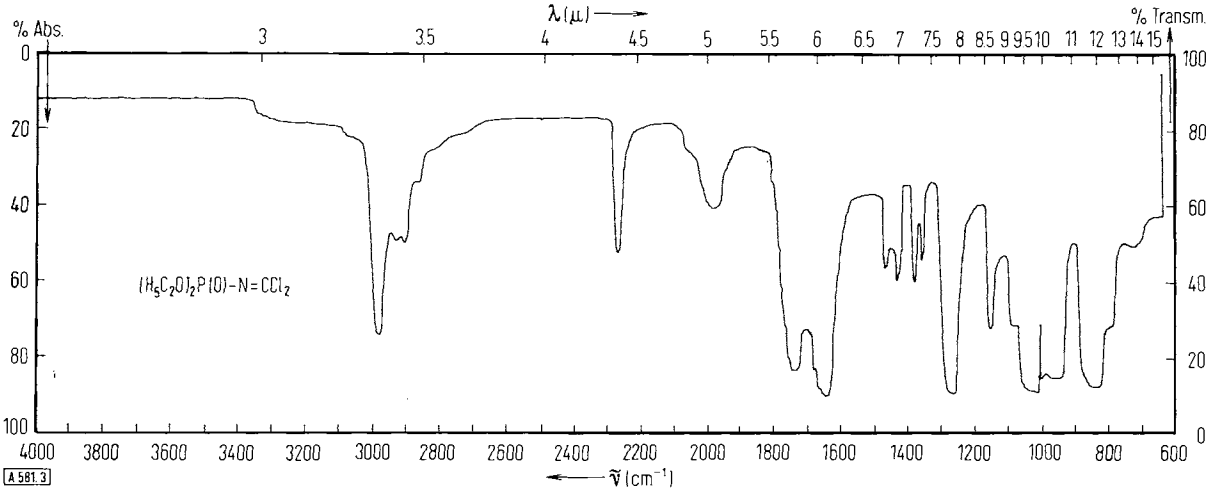
2) Phosphoryl isocyanide dichlorides

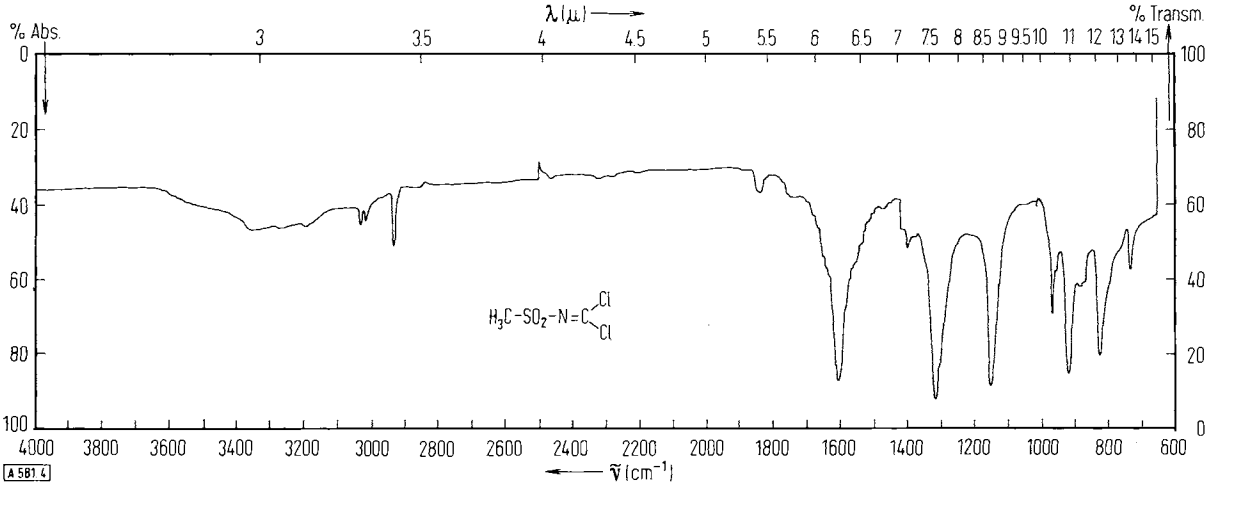
N=C double bond: 1735 to 1770 cm^{-1} (m);
1640 to 1645 cm^{-1} (s)
Cl–C bond: 840 to 885 cm^{-1}

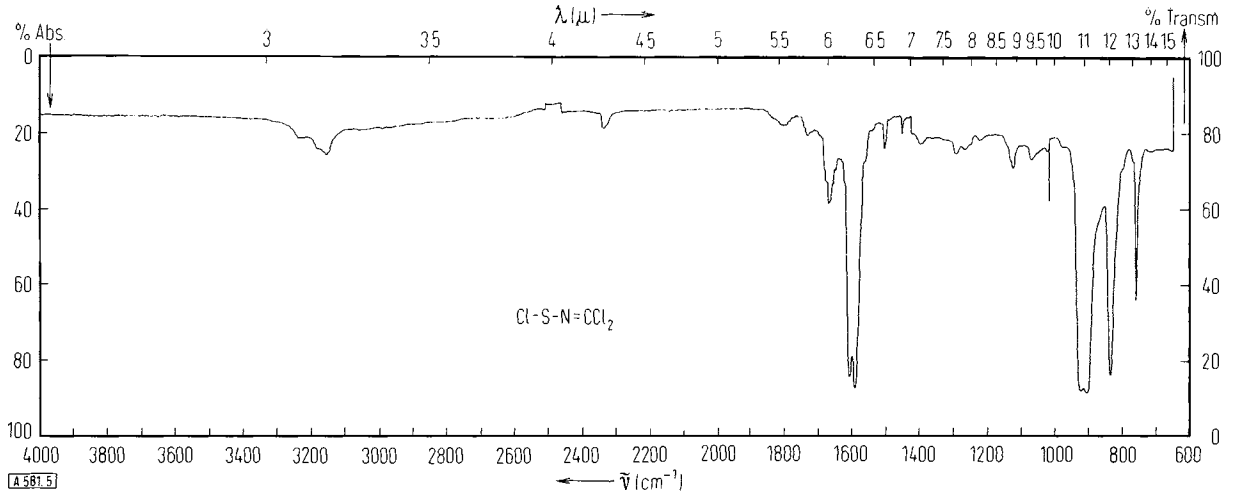
3) Sulfonyl isocyanide dichlorides

N=C double bond: 1580 to 1610 cm^{-1}
SO_2 group: 1317 to 1360 cm^{-1}
and 1145 to 1175 cm^{-1}
Cl–C bond: 860 to 915 cm^{-1}









4) Sulfenyl isocyanide dichlorides having the structure $-SN=CCl_2$

N=C double bond: 1578–1592 cm^{-1}

Cl–C bond: 895– 915 cm^{-1}

VI. Procedures

1. *Phenyl Isocyanide Dichloride by Chlorination of Phenyl Isothiocyanate*

A solution of 2905 g of phenyl isothiocyanate in 5 l of carbon tetrachloride is introduced into a 10 l three-neck flask fitted with a stirrer, a reflux condenser, a thermometer, and inlet and outlet tubes. The solution is cooled with ice, and 3075 g of chlorine are passed in at 5 to 15 °C. Stirring is continued for one hour; most of the solvent and the sulfur dichloride formed in the reaction are distilled off on a water bath at constant pressure, and the remainder of the solvent is removed under vacuum. The residue is then distilled on an oil bath (bath temperature 120–130 °C) under vacuum. 3622 g (96%) of phenyl isocyanide dichloride, b. p. 83–85 °C/11 mm Hg, is obtained.

Table 1. Isocyanide dichlorides (R–N = CCl_2) by chlorination of isothiocyanates.

R	B.p. (°C/mm)	n_D^{20}	Yield (%)	Ref.
Methyl	77.5–78/760		85.7	[9b]
2-Chloroethyl-	62/16			[9a]
2,2-Difluoroethyl-	63/100	n_D^{17}: 1.4235		[9c]
Methoxymethyl-	30–32/12			[22]
Ethoxymethyl-	51–53/14		77	[22]
Propoxymethyl-	57–59/10	1.4554	72	[8]
1-Butoxypropyl-	99–102/10	1.4578	85	[8]
$Cl_3C-CH_2OCH_2OCH_2$-	70–72/0.2		57	[22]
Cyclohexyloxymethyl-	70–75/10		32	[22]
Benzoxymethyl-	87–89/0.2		41	[22]
2,4-Dichlorophenoxymethyl-	134–138/0.5			[22]
1,1,3,3-Tetramethylbutyl-	78–79/10	1.4651	88	[8]
Dodecyl-	107/0.002	1.4642	95	[8]
Tetradecyl-	140–141/0.01	1.4656	95	[8]
Hexadecyl-	164–166/0.02	1.4662	95	[8]
Octadecyl-	159–161/0.03	1.4670	91	[8]
2-Isocamphanyl-	73–75/0.01	1.5091	91	[8]
Cyclohexyl-	76–77/10	1.4961	90	[8]
2-Tolyl-	125–130/15			[19]
3-Tolyl-	130/10			[19]
4-Tolyl-	121–124/20			[19]
4-Methoxyphenyl-	155–160/15			[19]
4-Bromphenyl-	122–124/15			[19]
3-Nitrophenyl-	165–170/15			[19]
4-Nitrophenyl-	127/0.35			[19]
1-Phenylethyl-	56.5–58.5/0.002	1.5408	92.3	[101]
Diphenylmethyl-	118–120/0.01	1.5940	93	[101]

[101] *W. Räuschl*, Dissertation, Universität München, 1961.

2. *Cyclohexyl Isocyanide Dichloride by Chlorination of Cyclohexylamine N-Cyclohexyldithiocarbamate*

198 g of cyclohexylamine is dissolved in 450 ml of carbon tetrachloride, and 90 g of carbon disulfide is added dropwise at 5 to 40 °C, with cooling. The mixture is stirred for 1 h. Stirring is then continued while the excess carbon disulfide is distilled off up to a distillation temperature of 75 °C (about 75 ml of distillate). The reaction mixture is cooled, and a total of 284 g of chlorine is passed in at 10 to 30 °C over a period of 4 hours. Heat is liberated strongly at first, but much less rapidly when evolution of HCl begins. The mixture is stirred for several hours, the precipitated cyclohexylamine hydrochloride is filtered off, and the carbon tetrachloride and sulfur dichloride are evaporated off from the filtrate. The cyclohexyl isocyanide dichloride is distilled under vacuum. Yield: 142 g (79% based on the amine used), b.p. 79–82 °C/13 mm Hg.

3. *t-Butyl Isocyanide Dichloride by Addition of Chlorine to t-Butyl Isocyanide*

15 g of chlorine (a 5% excess) is passed into a solution of 17 g of t-butyl isocyanide in 200 ml of chloroform at 0 to 5 °C, with cooling. When the strongly exothermic reaction is complete, the mixture is stirred for 10 minutes at room temperature, and the solvent is then distilled off. 16 g (52%) of t-butyl isocyanide dichloride, b.p. 129–131 °C, $n_D^{20} = 1.4520$, is obtained.

Table 2. Isocyanide dichlorides (R–N=CCl_2 and $Cl_2C=N-R'-N=CCl_2$) by addition of chlorine to isocyanides.

R, R'	B.p. (°C/mm) (m.p. (°C))	n_D^{20}
Cyclohexyl-	76–78/11	
Phenyl-	204–205/760	
2-Tolyl-	214–215/760	
4-Tolyl-	225–226/760	
Ethyl-	102/760	
2,6-Dimethylphenyl-	72–76/0.4	1.5496
1,4-Tetramethylene-	85–86/0.25	1.5053
1,4-Cyclohexylene-	(116–118)	
3,5,3',5'-Tetraethyldiphenylmethane-4,4'-diyl-	205–210/0.2	

Table 3. Isocyanide dichlorides (R—N=CCl_2, Cl_2C=N—R′—N=CCl_2) by chlorination of *N*-substituted aromatic formamides in thionyl chloride.

R, R′	Reaction temp. (°C)	Yield (%)	B.p. (°C/mm)	M.p. (°C)
Phenyl-	10—12	51	94—99/14	
2-Chlorophenyl-	10—15	86.7	104—106/10	
2,4-Dichlorophenyl-	15—20	85.5	126—132/10	
2,5-Dichlorophenyl-	15—20	78.4	128—135/15	
2,3-Dichlorophenyl-	15—20	73.5	142—149/14	
3,4-Dichlorophenyl-	20—25	80	141—148/13	
3,5-Dichlorophenyl-	20—25	53	147—155/13	
2,4,5-Trichlorophenyl-	35—40	88	156/14	
2-Methyl-4-chlorophenyl-	15—20	96.6	121—123/10	
2-Chloro-6-methylphenyl-	35—40	92.5	110—112/11	
2,4-Dichloro-5-methylphenyl-	20—25	84	143—146/10	
2-Methoxy-4-chlorophenyl-	20—25	37	161—166/11	81
2-Chloro-5-trifluoromethylphenyl-	20—25	75	101—102/12	
2-Trifluoromethyl-4-chlorophenyl-	15—20	78.3	104—110/10	
2,6-Diethyl-4-methylphenyl-	20—25	55.6	151—161/10	
2,6-Diisopropylphenyl-	20—25	80.5	104—120/0.4	
4-Fluorophenyl-	25—30	71.5	82—87/11	
4-Bromophenyl-	20—25	72.5	131—137/12	
2,4-Dibromophenyl-	20—25	85.5	161—162/12	
4-Nitrophenyl-	60—70	88	127/0.35	78—82
3-Nitrophenyl-	20—25	83	120—125/0.5	69
2-Chloro-4-nitrophenyl-	55—60	22	131—133/0.1	
4-Chloro-3-nitrophenyl-	30—40	79.5	118/0.11	
2-Methyl-5-nitrophenyl-	40—50	94	119—120/0.15	59
4-Methyl-3-nitrophenyl-	20—25	82.5	166—168/13	
2-Methoxy-5-nitrophenyl-	50—60	82.5	140—141/0.17	
4-Methoxycarbonylphenyl-	20—25	88.5	157—159/12	96—98
4-Chlorocarbonylphenyl-	55—60	49	152—158/11	50—53
2,5-Dichloro-4-nitrophenyl-	40—50	20	136—138/0.15	83
1,4-Phenylene-	45—50	51.7	172—180/14	96—98
Azobenzyl-	50	31 (recryst.)		82—84
4,4′-Dichlorodiphenylether-2-yl-	20—25	81.7	172—180/0.25	46—48
Benzophenon-4-yl-	20—25	73.5	170—180/0.2	
Diphenylsulfon-2-yl-	50—60	39	210/0.3	
Biphenyl-2-yl-	20—25	72	172—177/12	
1-Naphthyl-	20—25	20	183—190/14	
3-Methyl-4-chlorophenyl-	20—30	58	95/0.25	
2-Methyl-3-nitrophenyl-	20—30	69	116/0.3	
2-Methyl-4-nitrophenyl-	20—30	66	130/0.4	68—72
3-Chloro-4-nitrophenyl-	20—30	59	140/0.5	61—63
2-Methyl-4-nitro-5-chlorophenyl-	20—30	69	150/0.4	55—58
3-Chlorocarbonylphenyl-	40—45	91	149—152/14	
3-Ethoxycarbonylphenyl-	20	89	164—168/13	
4-Ethoxycarbonylphenyl-	20	91	165—167/11	

4. *Phenyl Isocyanide Dibromide by Addition of Bromine to Phenyl Isocyanide*

32 g of bromine is added dropwise to an ice-cooled solution of 21 g of phenyl isocyanide in 150 ml of chloroform at 0 to 5 °C. The mixture is stirred for 10 minutes, the solvent is evaporated off under vacuum, and the residue is distilled. Yield: 40 g (76%) of phenyl isocyanide dibromide, b.p. 76.5—77.5 °C/0.15 mm Hg.

A similar method can be used for the preparation of cyclohexyl isocyanide dibromide, $n_D^{20} = 1.5494$, which decomposes on distillation or on prolonged standing.

5. *4-Chlorophenyl Isocyanide Dichloride by Chlorination of 4-Chloroformanilide in Thionyl Chloride*

67.5 g of sulfuryl chloride is dissolved in 150 ml of thionyl chloride in a 500 ml three-neck flask fitted with a stirrer, thermometer, reflux condenser, and gas outlet tube. 77.5 g of 4-chloroformanilide is added in portions at 15 to 20 °C. The solution is stirred for several hours at room temperature and heated slowly to an internal temperature of 80 °C, HCl and SO_2 escaping continuously. The excess of thionyl chloride, which can be used in further preparations, is distilled off, and the residue is fractionated under vacuum. 89 g (86%) of 4-chlorophenyl isocyanide dichloride is obtained as a pale yellow oil, b.p. 110—113 °C/10 mm Hg.

6. *n-Butyl Isocyanide Dichloride by Chlorination of n-Butyl Isocyanate with Phosphorus Pentachloride*

49 g of n-butyl isocyanate is added dropwise to a suspension of 104 g of phosphorus pentachloride in 80 ml of phosphorus oxide chloride at 55 °C. The mixture is stirred until it becomes clear, the phosphorus oxide chloride is distilled off under vacuum; further distillation yields 38 g (50%) of n-butyl isocyanide dichloride, b.p. 45—45.5 °C/14 mm Hg.

7. *Phenyl Isocyanide Difluoride by Reaction of N-Trifluoromethylaniline with Potassium Fluoride*

8 g of freshly distilled *N*-trifluoromethylaniline and 4.5 g of powdered potassium fluoride (150% excess) are stirred for 5 hours at 140 °C. The reaction product is separated at room temperature from the solid (4.9 g), which is then washed with ether. The washings are combined with the filtrate and distilled under vacuum after removal of the solvent. Redistillation yields phenyl isocyanide difluoride, b.p. 49 °C/12 mm Hg, $n_D^{21.5} = 1.4805$.

8. *Pentachlorophenyl Isocyanide Difluoride by Reaction of Pentachlorophenyl Isocyanide Dichloride with Potassium Fluoride*

A mixture of 143 g of pentachlorophenyl isocyanide dichloride and 174 g of well dried potassium fluoride is heated to 225 °C within 2 hours in a V2A steel vessel fitted with a stirrer and a small column with a descending condenser; in the course of a further hour, the mixture is heated to 320 °C while being stirred vigorously. Pentachlorophenyl isocyanide difluoride ($n_D^{20} = 1.5744$) distils over continuously and crystallizes in the receiver. Yield: 88 g, m.p. 54—58 °C.

Table 4. Isocyanide difluorides (R—N=CF_2) by reaction of aryl isocyanide dichlorides with potassium fluoride.

R	B.p. (°C/mm)	n_D^{20}
Phenyl-	74—78/50	1.4762
4-Tolyl-	72—74/14	1.4771
4-Chlorophenyl-	82—83/15	1.5035
2,5-Dichlorophenyl-	92—95/15	1.5071
2,4,6-Trichlorophenyl-	130—137/23	1.5205

9. *4-Chlorophenyl Isocyanide Difluoride by Reaction of N-Trifluoromethyl-4-chloroaniline with Acetyl Chloride in the Presence of Triethylamine*

195.5 g of *N*-trifluoromethyl-4-chloroaniline and 78 g of acetyl chloride are dissolved in 400 ml of benzene, and 102 g of triethylamine in 100 ml of benzene is added to the solution at 20 to 40 °C with cooling. The mixture is stirred for a time, the triethylamine hydrochloride is filtered off, and the filtrate is evaporated to dryness under vacuum. Double distillation yields 66 g of 4-chlorophenyl isocyanide difluoride, b.p. 62–68 °C/12 mm Hg.

10. *Ethyl Isocyanide Difluoride by Reaction of Ethyl Isothiocyanate with Mercuric Fluoride*

15 g of ethyl isothiocyanate is added dropwise to 96 g of mercuric fluoride that has been heated to 100 °C. The volatile distillate is condensed in a cold trap (dry ice). Distillation yields 4.3 g of ethyl isocyanide difluoride, b.p. 17–18 °C.

11. *Dichloroacetyl Isocyanide Dichloride by Chlorination of Dichloroacetyl Isothiocyanate*

2 ml of titanium tetrachloride is added to 724 g of dichloroacetyl isothiocyanate, and 800 g of chlorine is passed in below 20 °C, with cooling. Subsequent distillation gives, after the sulfur dichloride has been removed, 771 g of dichloroacetyl isocyanide dichloride, b.p. 80–82 °C/15 mm Hg.

Table 5. Acyl isocyanide dichlorides (Ac–N=CCl_2, Cl_2C=N–Ac'–N=CCl_2) by chlorination of acyl isothiocyanates.

Ac, Ac'	B.p. (°C/mm) (m.p. (°C))	Yield (%)	Ref.
Chloroacetyl-	78/18	54	[76c]
Trichloroacetyl-	76–78/12	76	[76c]
2-Chloropropionyl-	53–55/0.06	86.7	[76c]
1,1-Dichlorobutyryl-	93–95/14	82.2	[76c]
Octanoyl-	79.5–81/0.07	39	[76c]
Dodecanoyl-	125–130/0.06	54	[76c]
Benzoyl-	75–78/0.07	95	[76c]
2-Chlorobenzoyl-	160–162/20		[77]
4-Chlorobenzoyl-	96–99/0.04	93	[76c]
3,4-Dichlorobenzoyl-	113/0.09	85	[76c]
2,5-Dichlorobenzoyl-	118–121/0.07	94	[76c]
2,6-Dichlorobenzoyl-	120–123/0.1	37.2	[76c]
4-Nitrobenzoyl-	(62–66)	90	[76c]
3-Nitro-4-chlorobenzoyl-	(58–61)	91.5	[76c]
2,4-Dichlorophenoxyacetyl	140–141/0.09	87	[102]
2,4,5-Trichlorophenoxyacetyl-	non-destillable	94	[102]
Terephthaloyl-	(79–83)	60	[76c]
Phenoxycarbonyl-	127–130/11	85	[76c]
2,3-Dichloroquinoxaline-6-carbonyl-	(91–94)	77	[76c]

12. *Diisopropoxyphosphoryl Isocyanide Dichloride by Chlorination of Diisopropoxyphosphoryl Isothiocyanate*

310 g of chlorine is passed into 283 g of diisopropoxyphosphoryl isothiocyanate over 6 hours at 10–20 °C, with cooling. The low-boiling components are removed in a water-jet vacuum. The residue is then distilled under vacuum. 273.5 g of diisopropoxyphosphoryl isocyanide dichloride, b.p. 81–83 °C/1 mm Hg, is obtained.

Table 6. Phosphoryl isocyanide dichlorides ($(RO)_2PO$–N=CCl_2) by chlorination of phosphoryl isothiocyanates.

$(RO)_2PO$–	B.p. (°C/mm)	n_D^{20}	Yield (%)	Ref.
Diethoxyphosphoryl-	76–78/0.08	1.4642	89	[81a]
Dipropoxyphosphoryl-	94–96/1	1.4630	61	[81b]
Dibutoxyphosphoryl-	113–114/0.05	1.4607	85	[81a]
Diisobutoxyphosphoryl-	88/0.06	1.4595	87	[81a]
Diphenoxyphosphoryl-	157/0.05		70	[81c]

13. *Benzenesulfonyl Isocyanide Dichloride by Chlorination of Benzenesulfonyl Isothiocyanate*

57 g of chlorine is passed into 75 g of benzenesulfonyl isothiocyanate at 60 °C over a period of 4 days, and the sulfur dichloride is then removed under vacuum. Vacuum distillation of the oily residue yields 57 g of benzenesulfonyl isocyanide dichloride, b.p. 122–125 °C/0.1 mm Hg.

14. *4-Tosyl Isocyanide Dichloride by Chlorination of Dipotassium 4-Toluenesulfonyliminodithiocarbonate*

A slurry of 323 g of dipotassium 4-toluenesulfonyliminodithiocarbonate in 1 l of carbon tetrachloride is saturated with chlorine at room temperature. The potassium chloride that is formed is filtered off and the filtrate is freed from solvent. 251 g of 4-toluenesulfonyl isocyanide dichloride is obtained as a crystalline residue (m.p. 80–85 °C).

Table 7. Sulfonyl isocyanide dichlorides (R–SO_2–N=CCl_2) [82].

R–SO_2–	M.p. (%)
Methanesulfonyl-	76–78
4-Chlorobenzenesulfonyl-	75–77
3,4-Dichlorobenzenesulfonyl-	74–78
2-Toluenesulfonyl-	oil
Benzylsulfonyl-	83–87
Dimethylaminosulfonyl-	61–64

15. *Thiocyanogen Trichloride (Chlorosulfenyl Isocyanide Dichloride) by Chlorination of Trimethylsilyl Isothiocyanate*

760 g of chlorine is led into 700 g of trimethylsilyl isothiocyanate over 90 min at 0 to 10 °C, with cooling. The reaction mixture is distilled under vacuum (water-jet). 573 g of thiocyanogen trichloride (b.p. 43–46 °C/11 mm Hg) is obtained.

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Neighboring-Group Effects and Rearrangements in Reactions of Cyclopropylmethyl, Cyclobutyl, and Homoallyl Systems

BY M. HANACK AND H.-J. SCHNEIDER [*]

The neighboring-group effect produced by a double bond in the homoallyl position or by a cyclopropane or cyclobutane ring leads to interesting rearrangements, which are discussed in this paper mainly from the point of view of mechanism, but also from that of preparative work. The question of the postulated non-classical carbonium ions acquires a special significance in this connection.

Introduction

The unusual reactions of cyclopropylmethyl, cyclobutyl, and homoallyl compounds, which are frequently accompanied by rearrangement of one of these systems into another (homoallyl rearrangement), have attracted considerable attention in recent years. While the earlier literature contains only a few observations on these rearrangements [1a], the recent growth of interest in the mechanisms of the reactions of carbonium ions and in the bonding in small rings has led to numerous investigations in this field [1].

The cyclopropylmethyl, cyclobutyl, and homoallyl esters, which can form carbonium ions, are solvolysed 10 to 10^{14} times as rapidly as the open-chain or saturated compounds used for comparison. Moreover, the solvolysis is often accompanied by complete rearrangement. These reactions are therefore particularly good examples of neighboring-group effects. For example, the three-membered ring not only lowers the energy required, so increasing the reaction rate, but also causes modification of the structure by the formation of new bonds. The decrease in energy due to charge delocalization in ionic intermediates that are incapable of resonance led to the assumption that non-classical ions occur [1l,2]. Finally, these rearrangements are also becoming increasingly important in preparative work.

[*] Priv.-Doz. Dr. M. Hanack and Dipl.-Chem. H.-J. Schneider
Chemisches Institut der Universität
Wilhelmstr. 31, 74 Tübingen (Germany)

[1] For a detailed review, see: [a] *M. Hanack* and *H.-J. Schneider*, Fortschr. chem. Forsch., in press; for summaries of special topics, see: [b] *J. A. Berson* in *P. de Mayo*: Molecular Rearrangements. Interscience, New York. 1963, Vol. I, p. 111; [c] *R. Breslow, ibid.* Vol. I, p. 233; [d] *N. L. Wendler, ibid.* Vol. II, p. 1075; [e] *B. Capon*, Quart. Rev. *18*, 45 (1964); [f] *M. Y. Lukina*, Russ. Chem. Rev. *32*, 635 (1963); [g] *E. Vogel*, Angew. Chem. *72*, 4 (1960); [h] *E. Vogel*, Fortschr. chem. Forsch. *3*, 430 (1955); [i] *S. Winstein*, Experientia Suppl. II, 137 (1955); [k] *A. Streitwieser, jr.*: Solvolytic Displacement Reactions. McGraw-Hill, New York 1962; [l] cf. also *P. D. Bartlett*: Nonclassical Ions. Benjamin, New York 1965.

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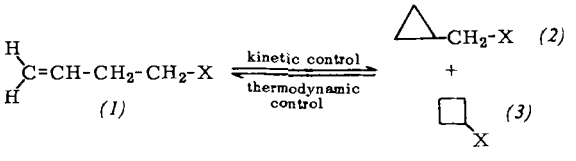
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Direction of Rearrangement and Reaction Conditions

The strong influence of the reaction conditions on the direction of the homoallyl rearrangement is due to the difference in the energies of the compounds concerned, which are appreciable in most cases.

In kinetically controlled reactions the ratio of the products depends on their rates of formation, and hence also on the stability and structure of the intermediates. Thus the solvolysis of homoallyl esters *(1)*, X = OSO_2R or Hal, generally leads to the isomeric cyclic systems *(2)* and *(3)*, X = OR', which are about 10 kcal/mole more strained in the ground state, but which are more stable than the open-chain systems as ionic intermediates.



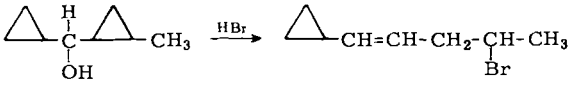
A necessary condition for the rearrangement is the production of a carbonium ion by an S_N1 reaction. For example, homoallyl *p*-toluenesulfonate *(1)*, X = OTs, which tends to undergo S_N2 reactions, gives the rearrangement products *(2)* and *(3)*, X = –O–CH=O, only in the weakly nucleophilic but strongly ionizing (ionizing power Y = 2.1 [1k]) formic acid [3]; for the same reason, less rearrangement is observed on alcoholysis than on acetolysis or hydrolysis [4].

The formation of a carbonium ion by an S_N1 reaction is also possible on deamination of homoallylamines *(1)*, X = NH_2. Nevertheless, the quantity of cyclization products obtained is generally very small; hydride shifts [4,5] take place in addition to retention of structure. As will be shown later, the double bond assists the release of the acid residue during solvolysis, so that the resulting carbonium ion already has the optimum conformation for the subsequent ring closure. On the other hand, the carbonium ion formed by the removal of nitrogen from a diazonium ion probably adopts the thermodynamically more stable extended conformation, which is unfavorable for the rearrangement, and as a "hot" carbonium ion, it can

readily provide the energy required for a hydride shift [6,7].

In thermodynamically controlled rearrangements, the initial products can react again until a reversible equilibrium has been established, as in the reaction if cyclic alcohols *(2)* and *(3)*, X = OH, with strong acids, zinc chloride, thionyl chloride, or phosphorus halides [8–10]. The conversion into the stable, predominantly *trans* homoallyl system is more or less complete, depending on the reaction conditions [11].

When the dicyclopropylcarbinol *(4)* is treated with HBr, the substituted ring is opened [12] to give the homoallyl system *(5)*, whose carbonium ion is particularly strongly stabilized by substituents [13].



(4) *(5)*

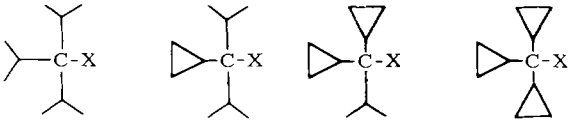
The acid-catalysed ring cleavage of cyclopropylcarbinols has been investigated by numerous Russian authors [1a, 14], and has been used in particular by *Julia et al.* in an elegant preparation of open-chain isoprenoids [15].

Kinetic Neighboring-Group Effects

The earliest and most important indication of the formation of non-classical cations from cyclopropylmethyl, cyclobutyl, and homoallyl compounds was given during the determination of the kinetic neighboring-group effect, which is defined as the ratio of the rate of solvolysis of a compound containing a neighboring group to that of a structurally similar compound with no neighboring group [16]. The magnitude of this ratio depends, not only on the substitution and stereochemistry of the system, but also on the solvents used. The neighboring-group effect of a homoallyl sulfonate can be less than 1 in ethanol [4], but about 10^2 in formic acid [7]. This is because the primary effect of the neighboring-group is frequently to displace the reaction mechanism from S_N2 toward S_N1 [17]. This effect can be determined *e.g.* by kinetic measurements in different solvents [18].

The ratio of rate constants $k_{unsaturated}/k_{saturated}$ for unsubstituted homoallyl *p*-toluenesulfonate *(1)*, X = OTs, in formic acid is only 3.7 [7], and so corresponds to an unusually small neighboring-group effect for a homoallyl compound. On the other hand, if there were no neighboring-group effect, the inductive effect of the double bond should slow the reaction by a factor of 10^2 to 10^3 [19].

For the same reason, the cyclopropyl group should have a retarding (not accelerating [20]) effect; however, cyclopropylmethyl *p*-toluenesulfonate is acetolysed $\sim 10^6$ times as rapidly as the comparable isobutyl *p*-toluenesulfonate [21]. The rate of hydrolysis of cyclopropylmethyl chloride *(2)*, X = Cl, is even 40 times as high as that of methylallyl chloride [8]. Even in the presence of sodium alkoxide, the alcoholysis of cyclopropylmethyl benzenesulfonate *(2)*, X = $OSO_2C_6H_5$, is first order, and proceeds without any additional increase in rate [22]. A second and third three-membered ring each make an additional contribution of the same magnitude to the stabilization of the carbonium ion, as was concluded by *Hart et al.* from the increase in the hydrolysis constants of the *p*-nitrobenzoates *(6)* to *(9)* [23].



(6) *(7)* *(8)* *(9)*

$k_{rel.}$ = 1 250 $23{,}5 \times 10^3$ ca. 25×10^6

The ratio of the rate constants for the acetolysis of cyclobutyl and cyclohexyl *p*-toluenesulfonates is 11 [24], and the ratio for the hydrolysis of the chlorides is 40 [25]. On the other hand, from the total strain energy (I strain), one would expect the formation of an sp^2 state with a C–C angle of 120° to be much more difficult for the four-membered than for the six-membered ring [26]. The particularly clear conflict between the reactivity of the cyclobutyl compound and the classical theory also led *H. C. Brown* to postulate a different structure for the carbonium ion in this case [24].

Non-Classical Carbonium Ions

According to classical views, ionic intermediates may be stabilized in two fundamentally different ways. Steric factors can increase the reaction rate, parti-

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[13] See, *e.g.*, *H. M. Walborsky* and *L. Plonsker*, J. Amer. chem. Soc. *83*, 2138 (1961); *H. M. Walborsky* and *J. F. Pendleton, ibid. 82*, 1405 (1960).

[14] *T. A. Favorskaya, K. A. Konopova*, and *M. I. Titov*, Ž. obšč. Chim. *29*, 2894 (1959), and earlier papers.

[15] For example, *M. Julia*, Ind. chim. belge *1961*, 995; further work cited in [1a].

[16] *W. Lwowski*, Angew. Chem. *70*, 483 (1958).

[17] *M. Hanack* and *H.-J. Schneider*, Tetrahedron *20*, 1863 (1964).

[18] *H. Schneider-Bernlöhr, H.-J. Schneider*, and *M. Hanack*, Tetrahedron Letters *1967*, 1425.

[19] Cf., *e.g.*, *S. Winstein, H. M. Walborsky*, and *K. Schreiber*, J. Amer. chem. Soc. *72*, 5795 (1950).

[20] *E. S. Gould*: Mechanismus und Struktur in den organischen Chemie. Verlag Chemie, Weinheim 1962, p. 706.

[21] *D. D. Roberts*, J. org. Chemistry *29*, 294 (1964); *30*, 23 (1965).

[22] *C. G. Bergstrom* and *S. Siegel*, J. Amer. chem. Soc. *74*, 145 (1952).

[23] *H. Hart* and *P. A. Law*, J. Amer. chem. Soc. *86*, 1957 (1964).

[24] *H. C. Brown* and *G. Ham*, J. Amer. chem. Soc. *78*, 2735 (1956).

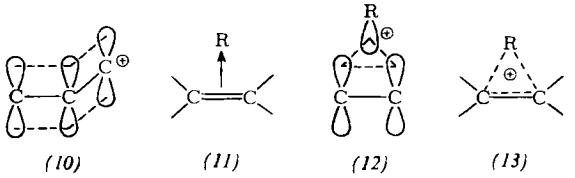
[25] *J. D. Roberts* and *V. C. Chambers*, J. Amer. chem. Soc. *73*, 5034 (1951).

[26] *H. C. Brown, R. S. Fletcher*, and *R. B. Johannesen*, J. Amer. chem. Soc. *73*, 212 (1951).

cularly of cyclic compounds, by allowing the total strain energy (I strain)[27] to become large in the ground state and small in the ionic state. The obvious idea of a gain in energy by relief of the high strain in the three-membered ring during the solvolysis of cyclopropylmethyl compounds is refuted, *inter alia*, by the fact that the three-membered ring is generally found to have remained intact in the reaction products[23]. The second classical means of stabilization of carbonium ions is distribution of the charge concentrated on the C atom with the aid of π electrons in the conjugation position. This resonance *(10)* which is characterized by a pure π overlap, is ideally achieved in allyl and benzyl cations and related systems.

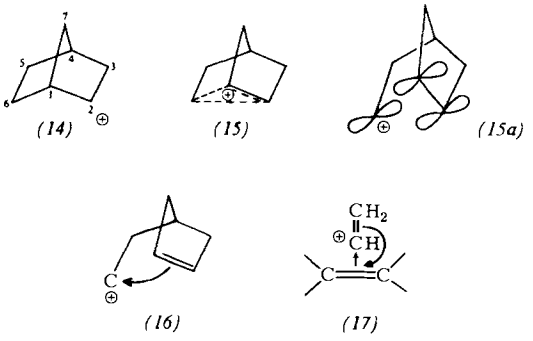
Non-classical ions, on the other hand, are relatively stable intermediates, which exhibit charge delocalization involving electron pairs having a high σ character[11] or more distant double bonds that cannot enter into resonance[2,28]. The bonds concerned are partially broken, so that the C atoms can accept part of the charge. This is indicated in the formulae by dotted bonds.

Non-classical carbonium ions have been postulated on the basis of various ideas. Electron acceptors such as protons or metal cations can form stable complexes, not only with lone pairs of electrons on suitable donors (*e.g.* NH_3), but also with the pairs of π electrons in olefins. The covalent bond in such π-complexes, which is distributed over three centers, was represented by *Dewar* as shown in formula *(11)*; the interaction of a carbonium ion with a double bond gives a typical electron-deficient compound, and is represented in a similar manner[29]. The bonding results from the overlap of the bonding π orbitals with the vacant acceptor orbital[30] [*(12)* and *(15a)*][31].



(10) *(11)* *(12)* *(13)*

Winstein and other authors[32] formulated bridged ions *(13)* without invoking double bonds *(13)*, an example being the norbornyl cation[11,21], *(14)* = *(15)*. Ions such as *(14)* can also be formulated as π complexes by formal cleavage at their weakest point to form a double bond suitable for complex formation [*e.g.* C(1)–C(6) in *(14)* → *(16)*]. According to this view, the cyclopropylmethyl, cyclobutyl, and homoallyl cations would contain a vinyl group *(17)* capable of accepting and simultaneously back-donating π electrons[29].



(14) *(15)* *(15a)* *(16)* *(17)*

Walsh has proposed an explanation of the three-center bond that does not involve extensive cleavage of the molecule. According to this explanation, an acceptor can be coordinately bound, not only by free pairs of electrons, but also by pairs of bonding electrons, though only on condition that the bond formed by these electrons is weak[33]. For example, the weak B–H bond interacts with the p orbital of a second boron atom to give a filled molecular orbital linking the three atoms B,H,B, in the boron hydrides[33]. Apart from the system involving π electrons, the non-classical ions described so far all have one or more weakened C–C bond close to the carbonium ion (cyclopropylmethyl, cyclobutyl, 2-norbornyl, and cyclobutylmethyl cations). These bonds can make their electrons available to the carbonium ion for the formation of a coordinate multicenter bond *(13)*. The non-classical ions would thus provide the connection observed in many systems between an increase in reaction rate and a tendency toward isomerization.

On the basis of the high rates of reaction and rearrangement in a number of Wagner-Meerwein rearrangements, *Ingold* and *Hughes* postulated the formation of a type of non-classical ion, which is described as a "synartetic" ion *(13)*[34]. This is a carbonium ion (which is isoelectronic with a boron atom) that is not stabilized in any other way than by entering into an energy-reducing interaction with the σ electrons of a C–C bond. This interaction removes the energy barrier between the classical ions and permits "resonance"[34,36] between them, as was also suggested by *Winstein*[35]. The concept of non-classical carbonium ions has been definitely rejected by some authors. The concepts developed by *H. C. Brown et al.*[28] are, in essence, opposed to the participation of σ bonds in the ionization. The rearrangements of systems having the structure *(14)* are explained by means of rapid equilibria between classical cations in which kinetics, and composition of product, are controlled by steric effects.

Homoallyl Resonance and Bicyclobutonium Ions

The i-steroid rearrangement[1d], which has been known for some time, is stereospecific in that only the 3β-cholesteryl derivatives *(18)* cyclize to give 6β-cyclocholestanyl derivatives *(19)*, while no 3α compounds[1d] are formed on solvolysis. *Winstein et al.* found that the cyclopropylmethyl system *(19)*, X = Cl, is solvolysed $10^{7.4}$ times as rapidly as the homoallyl system *(18)*, X = Cl; the hydrolysis of *(19)* is only about 10 times as fast as that of the stereoisomeric 6α product, despite the less favorable position of the

[27] *M. Hanack*: Conformation Theory. Academic Press, New York 1965, p. 167.

[28] Cf., however, *H. C. Brown, K. J. Morgan*, and *F. J. Chloupek*, J. Amer. chem. Soc. *87*, 2137 (1965), and further literature there; see also *H. C. Brown*: „The Transition State," Special Publ. No. 16, Chemical Society, London, 1962; cf. also *W. Hückel*, J. prakt. Chem. *28*, 27 (1965).

[29] *M. J. S. Dewar* and *A. P. Marchand*, Ann. Rev. Phys. Chem. *16*, 321 (1965).

[30] *M. J. S. Dewar*, Bull. Soc. chim. France *18*, C 71 (1951).

[31] *A. Streitwieser jr.*: Molecular Orbital Theory for Organic Chemists. Wiley, New York 1961.

[32] *S. Winstein, B. K. Morse, E. Grunwald, K. C. Schreiber*, and *J. Corse*, J. Amer. chem. Soc. *74*, 1113 (1952).

[33] *A. D. Walsh*, J. chem. Soc. (London) *1947*, 89.

[34] *C. K. Ingold*: Structure and Mechanism in Organic Chemistry. Cornell University Press, New York 1953, p. 511, 519.

[35] Cf. [32] as well as *S. Winstein* and *H. J. Lucas*, J. Amer. chem. Soc. *61*, 1576 (1939).

[36] *C. K. Ingold*, J. chem. Soc. (London) *1953*, 2845.

three-membered ring with respect to the leaving substituent in the latter case [37]. *Winstein* interprets the rearrangements and its kinetics on the basis of a common non-classical intermediate *(22)*, in which the charge is delocalized by "homoallyl resonance" *(20)* ↔ *(21)* [38].

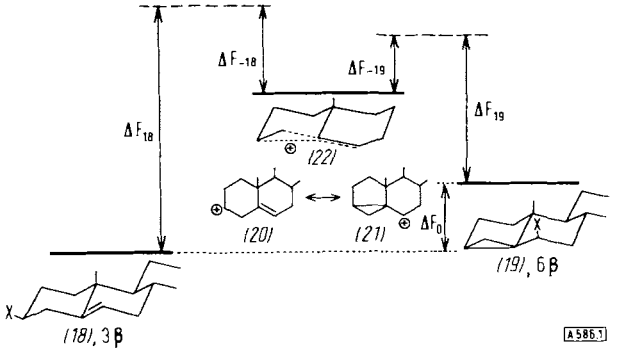


Fig. 1. Homoallyl resonance in the i-steroid rearrangement.

It can be deduced from Figure 1 that

$$\Delta F_0 = RT \ln K = (\Delta F_{18} - \Delta F_{19}) - (\Delta F_{-18} - \Delta F_{-19})$$

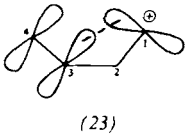
or

$$K = [(18), X = Cl]/[(19), X = Cl] = R \times P$$

where R is the ratio of the rate constants $k_{(18),\ X=Cl}/k_{(19),\ X=Cl}$ and P is the ratio of the products [*(19)*, X = OH]/[*(18)*, X = OH] after hydrolysis. (However, a similar relationship can be deduced if several ionic intermediates are postulated (see p. 670).) The calculated difference between the strain energies of *(19)* and of *(18)*, $\Delta F_0 = 9$ kcal/mole, shows the importance of the energy of the ground state in the kinetics and direction of homoallyl rearrangements [37].

According to *Winstein* and *Simonetta*, the mixed π, σ overlap [31] of the vacant p orbital with the first double-bond orbital in the homoallyl cation *(23)* should result in an energy gain of 6 kcal/mole [38a]. The principle of such calculations involves the estimation of the delocalization energies (DE) and strain energies (SE) for several positions of the atoms by an LCAO–MO procedure. The arrangement in which the difference (DE–SE) is greatest is the most probable arrangement; the greatest difference (DE–SE) is thus the most probable energy gain.

However, *Dewar* and *Coulson* [29] have pointed out that since the different repulsive forces between electrons and between nuclei are disregarded, a single MO calculation of geometrically different systems is practically impossible.



(23)

Nevertheless, mention should be made of the recalculation of the homoallyl cation *(23)* by the same method by *Roberts* and *Howden*. This calculation gave a (DE–SE) value of only 2.8 kcal/mole for simple 1,3 overlap, but 11.4 kcal/mole when a 1,4 interaction was also taken into account. The optimum geometry of the cation is shown in Fig. 2 [38b].

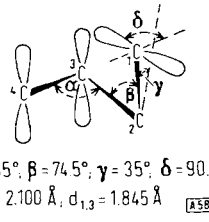
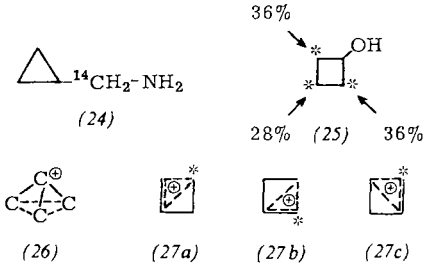


Fig. 2. Geometry of the bicyclobutonium ion [38b].

A structure in which both a 1,3 and a 1,4 interaction are assumed is the bicyclobutonium ion postulated by *Roberts*. On solvolysis and deamination of simple homoallyl, cyclopropylmethyl, and cyclobutyl derivatives, the reaction products were repeatedly found to occur in the same ratio [8]. This observation together with the fact that the reaction of labeled compounds resulted in substantial migration of the isotope [39], led to the assumption that all the isomers give the same ionic intermediate. The reaction of [α-^{14}C]-cyclopropylmethylamine *(24)* gave a non-uniform distribution of the ^{14}C, see *(25)* [40]; this rules out the possibility of the fully symmetrical intermediate *(26)* (tricyclobutonium ion) [39]. On the other hand, this ^{14}C distribution and many substituent effects would be compatible with the existence of three pyramidal bicyclobutonium ions *(27a)* to *(27c)*, which are converted rapidly, but at different rates, into one another [40]. Each bicyclobutonium ion yields cyclopropylmethyl, cyclobutyl, and homoallyl products, which differ only in the position of the ^{14}C atom.



Bisected Cyclopropylmethyl Ions and Isomeric Carbonium Ions

While the kinetic behavior of the compounds discussed gives a clear indication of the formation of non-classical ions, the structure and number of these intermediates can be deduced only from a series of further observations, some of which contradict the bicyclobutonium ion model.

In non-classical structures such as *(13)* and *(27)*, substitution can take place only from the unbridged side, and will therefore be stereospecific. However, the rearrangement of cyclic homoallyl compounds does not yield sterically uniform products [17,41]. The racemization that accompanies the

[37] *S. Winstein* and *E. M. Kosower*, J. Amer. chem. Soc. *81*, 4399 (1959).

[38] [a] *S. Winstein* and *M. Simonetta*, J. Amer. chem. Soc. *76*, 18 (1954); [b] see also *M. E. H. Howden* and *J. D. Roberts*, Tetrahedron *19*, Suppl. 2, 423 (1963).

[39] *J. D. Roberts* and *R. H. Mazur*, J. Amer. chem. Soc. *73*, 3542 (1951).

[40] *R. H. Mazur*, *W. N. White*, *D. A. Semenow*, *C. C. Lee*, *M. S. Silver*, and *J. D. Roberts*, J. Amer. chem. Soc. *81*, 4390 (1959).

[41] *M. Hanack* and *W. Keberle*, Chem. Ber. *96*, 2937 (1963).

solvolysis of optically active cyclopropylmethyl derivatives [42] and the fact that the rates of racemization and of solvolysis are the same [43] show that the solvent can attack from both sides of the cyclopropylmethyl cation.

A product expected on the basis of a common bridged intermediate may not be formed if a carbonium ion corresponding to the product is particularly unstable [17].

Methyl groups on cyclopropylmethyl *p*-nitrobenzoates increase the rate of hydrolysis, even when they are attached to the C atom that is uncharged in the bicyclobutonium ions *(27a)* to *(27c)*. This means that the charge must in fact be delocalized over all the C atoms [44].

According to the models discussed so far, the dissociation products of the homoallyl, cyclopropylmethyl, and cyclobutyl compounds are identical; the common intermediate means, not only ease of isomerization, but also a decrease in the ionization energies of all the compounds involved, owing to the delocalization of the charge. However, many homoallyl compounds exhibit little or no kinetic neighboring-group effect, though they undergo substantial cyclization. Conversely, it is often found that the very systems that do not rearrange have very high rates of solvolysis.

Hanack and *Schneider* explained these observations by assuming separate but rapidly isomerizing carbonium ions [17]. Accordingly, for example, a homoallyl ester dissociates relatively slowly to give the homoallyl cation, in which there is generally little delocalization. Owing to its high energy content, this cation quickly isomerizes into the cyclopropylmethyl and cyclobutyl cations, which experience greater non-classical stabilization.

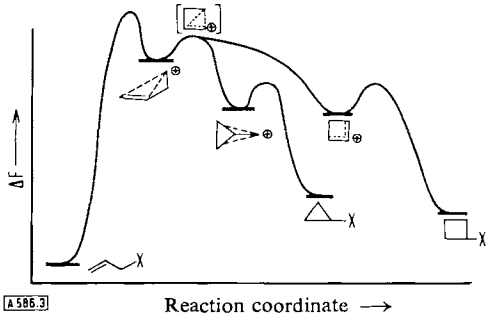
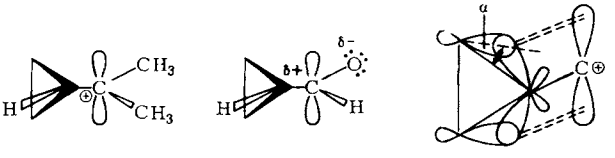


Fig. 3. Energy relationships in the solvolysis of homoallyl esters.

Thus in the solvolysis of homoallyl esters, the composition of the product depends on the relative stabilities of the isomeric ions; however, it also depends on the rates of substitution of the ions by the solvent and on the ratio of the isomerization energy to the substitution energy (Fig. 3). The rearrangement of an ion, the rate of which depends on the energy of the non-classically stabilized transition state (bicyclobutonium ion), competes with substitution by the solvent. The various activation energies can also be deduced mathematically. The relationship obtained is similar to that presented on p. 669 [17, 45].

The elucidation of the structure of cyclopropylmethyl carbonium ions was aided in particular by the direct investigation of the ionic intermediates obtained, according to *Olah* [46,47] and *Deno* [48], by reaction of the alcohols with strong acids in solution at low temperatures. The tricyclopropylcarbinyl cation corresponding to *(9)* is even formed in weaker acid than is required for the triphenylcarbinyl cation [49], which has been known for some time. The UV spectra of the tricyclopropylcarbinyl and cyclopropyldimethylcarbinyl cations show conjugation with the three-membered ring (λ_{max} = 270 mμ, ε = 22000 [49] or λ_{max} = 289 mμ, ε = 10800 [47]), whereas the t-butyl cation shows practically no absorption above 200 mμ [50].

The NMR spectra of cyclopropylmethyl cations impressively demonstrate the delocalization of the positive charge over all the C atoms: the 2 to 3 ppm shift of the α-proton signal of the three-membered ring toward lower fields could, in certain circumstances, be due to the inductive effect of the positive charge, but this could not explain the larger shift of the β-proton signals [46,47,51]. The position of the $C^{\oplus}$–H signal is displaced by the positive charge to τ = −3.5 in the isopropyl cation, to τ = 0.2 in the diphenylmethyl cation, but only to τ = 1.9 in the dicyclopropyl cation, since the charge in the last case is distributed over other atoms [47]. The signal due to the methyl protons in the cyclopropyldimethylcarbinyl cation *(28)* differ by 0.54 ppm, indicating [47] that the methyl groups occupy different positions in a fixed bisected form *(28)* [48].



(28) *(29)* *(30)*

The fact that a bisected form is a necessary condition for conjugation is also clear, *inter alia*, from the NMR [47] and UV spectra [1f,52,53] of cyclopropyl ketones *(29)*, olefins, and nitriles, as well as from the kinetics of the solvolysis of *p*-cyclopropylbenzyl systems [54].

The homoallyl carbonium salts obtained by reaction of 1-butenyl or 2-pentenyl bromides with $AgBF_4$ in nitromethane or methylene chloride rearrange immediately, even at low temperatures, to give the three-

[42] *M. Vogel* and *J. D. Roberts*, J. Amer. chem. Soc. *88*, 2262 (1966).

[43] *H. G. Richey* and *J. M. Richey*, J. Amer. chem. Soc. *88*, 4971 (1966).

[44] [a] *P. v. R. Schleyer* and *G. W. Van Dine*, J. Amer. chem. Soc. *88*, 2321 (1966); [b] cf., however, [21] and *D. D. Roberts*, J. org. Chemistry *31*, 2000 (1966).

[45] *M. Hanack* and *H.-J. Schneider*, unpublished.

[46] *C. U. Pittman jr.* and *G. A. Olah*, J. Amer. chem. Soc. *87*, 2998 (1965).

[47] *C. U. Pittman jr.* and *G. A. Olah*, J. Amer. chem. Soc. *87*, 5123 (1965).

[48] *N. C. Deno*, Progr. physical org. Chem. *2*, 148 (1964).

[49] *N. C. Deno, H. G. Richey jr., J. S. Liu, D. N. Lincoln*, and *J. O. Turner*, J. Amer. chem. Soc. *87*, 4533 (1965).

[50] *G. A. Olah, E. B. Baker, J. C. Evans, W. S. Tolgyesi, J. S. McIntyre*, and *I. J. Bastien*, J. Amer. chem. Soc. *86*, 1360 (1964).

[51] *N. C. Deno, H. G. Richey jr., J. S. Liu, J. D. Hodge, J. J. Houser*, and *M. J. Wisotaky*, J. Amer. chem. Soc. *84*, 2016 (1962).

[52] [a] *C. A. Grob* and *J. Hostynek*, Helv. chim. Acta *46*, 1676 (1963); [b] *G. L. Kloss* and *H. B. Klinger*, J. Amer. chem. Soc. *86*, 3265 (1965); cf. also *A. L. Goodman* and *R. H. Eastman, ibid. 86*, 908 (1964).

[53] [a] *N. H. Cromwell* and *G. V. Hudson*, J. Amer. chem. Soc. *75*, 872 (1953); [b] *E. M. Kosower* and *M. Ito*, Proc. chem. Soc. (London) *1962*, 25.

[54] *H. C. Brown* and *J. D. Cleveland*, J. Amer. chem. Soc. *88*, 2051 (1966); *L. B. Jones* and *V. K. Jones*, Tetrahedron Letters *1966*, 1493.

and four-membered ring systems. The more stable cyclopropylmethyl and cyclobutyl cations, on the other hand, isomerize much more slowly, as can be seen by hydrolysis of the carbonium salts after various times [55].

The non-classical interaction in cyclopropylmethyl carbonium ions depends on the fact that the vacant $C^{\oplus}$ orbital is parallel to the plane of the three-membered ring [1f]. The published theoretical studies on cyclopropane, in which a wide range of methods was used, all agree that the C–C bonds have a considerable p component in the plane of the ring. *Walsh* formulated cyclopropane as a combination of three trigonal sp^2-hybridized C atoms in which the 2p orbitals are situated parallel to one another in one plane [56]. *Coulson* carried out complicated VB calculations [57] and simpler calculations using the principle of maximum overlap [58], according to which cyclopropane is most stable when the atomic orbitals that form the C–C bonds are $\alpha = 22$ to 24° outside the C–C axis, cf. *(30)*. The hybridization parameters show a particularly small amount of s character. Calculation of the C–C bonds in cyclopropane by the MO method gave an angle of $\alpha = 21$ to 25°, and a higher p component for the atomic orbitals of the carbon [59].

The charge delocalization in the cyclobutyl cation is probably also due to the ring strain. Both VB [57] and MO calculations [59] indicate that the C–C orbitals are situated 5 to 10° outside the ring, and that they have a p character intermediate between that of the three-membered ring and that of the strain-free bonds.

Simple Substituted Homoallyl, Cyclopropylmethyl, and Cyclobutyl Compounds

The composition of the solvolysis products and the kinetic neighboring-group effect of the double bond have been particularly intensively studied for aliphatic homoallyl compounds. It can be seen from Table 1 that the neighboring-group effect $k_{unsaturated}/k_{saturated}$ (see p. 667) is influenced not only by the solvent used, but also by the substituent on the double bond. Whereas the ratio $k_{unsaturated}/k_{saturated}$ for ethanolysis is smaller than, or only slightly greater than 1, considerably higher rates of solvolysis are found for the homoallyl compounds in less nucleophilic solvents (acetic acid, formic acid) [4,7]. The neighboring-group effect increases with the number of substituents on the double bond (Table 1).

Table 1. Kinetic neighboring-group effects in the solvolysis of homoallyl sulfonates.

	$k_{unsaturated}/k_{saturated}$		
	Ethanolysis [4] [a]	Acetolysis [4] [a]	Formolysis [7] [b]
$CH_2{=}CH{-}(CH_2)_2{-}X$	0.55		3.7
trans-$H_3C{-}CH{=}CH{-}(CH_2)_2{-}X$	0.76	25.8	*ca.* 770
cis-$H_3C{-}CH{=}CH{-}(CH_2)_2{-}X$	0.57		*ca.* 165
trans-$H_5C_6{-}CH{=}CH{-}(CH_2)_2{-}X$	0.88	12.5	*ca.* 350
$(H_3C)_2C{=}CH{-}(CH_2)_2{-}X$	47.5	350 [c]	*ca.* 16×10^3
trans-cyclopropyl-$CH{=}CH{-}(CH_2)_2{-}X$	3.9	72.0	

[a] For β-naphthylsulfonates.

[b] For *p*-toluenesulfonates.

[c] Cf. also *J. B. Rogan*, J. org. Chemistry *27*, 3910 (1962).

The UV spectra of alkyl-substituted olefins show that the strength of the electrostatic bonding of the π electrons decreases with the number of alkyl groups [60] (red shift). As can be seen from Fig. 4, an approximately linear relationship exists between the ionization energies of olefins [61], found spectroscopically and by electron or photon impact methods, and the logarithm of the solvolysis constants (which are proportional to the activation energy) of corresponding homoallyl compounds in S_N1 reactions [62].

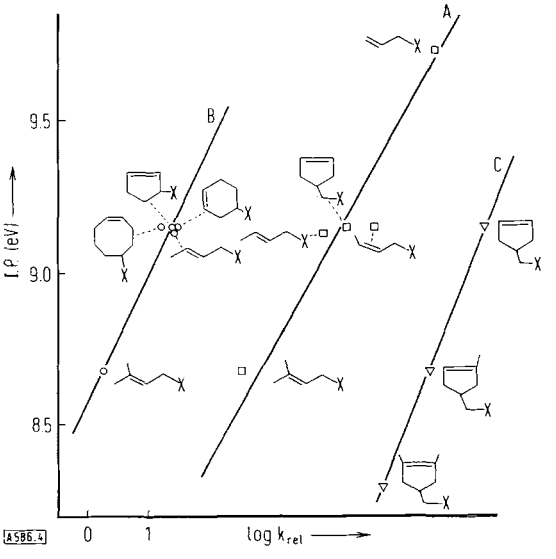


Fig. 4. Relationship between rate of solvolysis (k_{rel}) and the spectroscopically determined ionization potential (IP).

A: formolyses, X = OTs (after [7]); B: acetolyses, X = OTs (after [1a]); C: acetolyses, X = *p*-$NO_2C_6H_4SO_3$ – [k_{rel} calculated from data given by *P. D. Bartlett* and *G. D. Sargent*, J. Amer. chem. Soc. *87*, 1297 (1965)].

A similar relationship is found for cyclic homoallyl compounds and other compounds which solvolyse with participation of a double bond (B and C in Fig. 4.).

Under the conditions of a kinetically controlled S_N1 reaction, the substituted homoallyl systems listed in Table 1 are solvolysed exclusively to cyclopropyl derivatives formed from more stable carbonium ions [4]. Special mention should again be made of the difference in the compositions of the solvolysis products and of the products formed on deamination of appropriate homoallylamines (see p. 666) [4,6].

If the alkyl group is situated in position 3 on the double bond *(31)*, the reaction leads exclusively

[55] *M. Hanack* and *H.-J. Schneider*, Angew. Chem. *77*, 1023 (1965); Angew. Chem. internat. Edit. *4*, 976 (1965).

[56] *A. D. Walsh*, Trans. Farad. Soc. *45*, 179 (1949).

[57] *C. A. Coulson* and *W. E. Moffit*, Phil. Mag. *40*, 1 (1949).

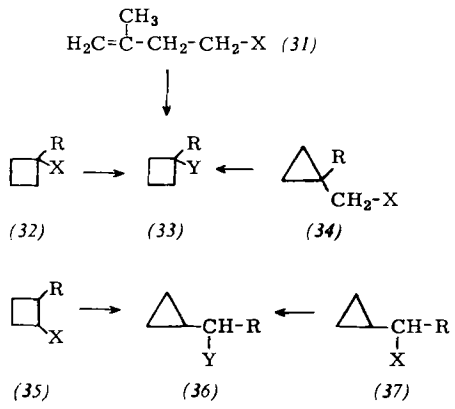
[58] *C. A. Coulson* and *T. M. Goodwin*, J. chem. Soc. (London) *1962*, 2851.

[59] *D. Peters*, Tetrahedron *19*, 1539 (1963).

[60] [a] *H. A. Staab*: Einführung in die theoretische organische Chemie. 3rd Edit., Verlag Chemie, Weinheim 1962, p. 307; [b] *F. A. Matsen* in *W. West*: Technique of Organic Chemistry. Interscience, New York 1956, Vol. VIII, p. 647f.

[61] *W. C. Price*, *R. Bralsford*, *P. V. Harris*, and *R. G. Ridley*, Spectrochim. Acta *14*, 45 (1959).

[62] *H.-J. Schneider*, Dissertation, Universität Tübingen, 1967.

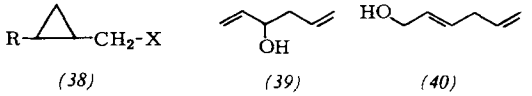


(31) (32) (33) (34) (35) (36) (37)

to rearrangement into the cyclobutane compound *(35)* [7,63].

In the solvolysis and in the deamination of simple substituted cyclopropylmethyl and cyclobutyl compounds, one isomer again predominates in the product. Compounds *(32)* and *(34)* [21] give *(33)*, whereas *(35)* and *(37)* give *(36)* [63,64]. An explanation for this [6,63] is that the positive charge in the bicyclobutonium ions [cf. *(27a)* to *(27c)*] is concentrated on the substituted C atom.

Cyclopropylmethyl compounds having the structure *(38)*, R = CH_3, X = NH_2, rearrange during deamination, mainly with formation of *(36)*, R = CH_3, Y = OH [6]. On the other hand, hydrolysis of 2-vinylcyclopropylmethyl *p*-toluenesulfonate *(38)*, R = $-CH=CH_2$, X = OTs is accompanied by a cleavage of the three-membered ring and formation of *(39)* and *(40)*. This ring cleavage, which has not been observed in any other kinetically controlled reactions, is explained by the high stability of the allyl cation corresponding to *(39)* and *(40)* [65].



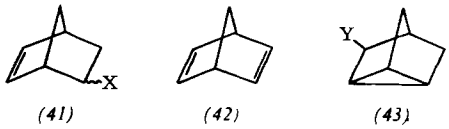
(38) (39) (40)

Cyclopropylmethyl derivatives having the structure *(37)*, R = CH_3 or C_6H_5, X = p-CO_2-C_6H_4-NO_2, as esters of secondary alcohols, are solvolysed particularly rapidly [66], whereas tertiary cyclobutyl esters *(32)* react at roughly the same rate as the corresponding t-butyl esters [63]. This indicates that the ionization of *(37)* proceeds *via* a non-classical intermediate, and that of *(32)* *via* a classical intermediate. The presence of the strongly electronegative CF_3 group in *(35)*, R = CF_3, X = OTs, and *(37)*, R = CF_3, X = OTs, directs the hydrolysis both toward *(35)*, R = CF_3, X = OH, and *(38)*, R = CF_3, X = OH, and toward the corresponding homoallyl alcohol (4-trifluoromethyl-3-buten-1-ol) [67].

The rearrangements of cyclic homoallyl compounds and of bicyclic cyclopropylmethyl and cyclobutyl compounds are particularly interesting, since they provide a further insight into the mechanism of the rearrangements. As can be deduced from considerations of models and from the rules of conformational analysis, the geometry of the compounds taking part in the rearrangements is partly fixed in such a way that the ability of the orbitals involved to overlap is considerably altered (see p. 669), with the result that both the direction of the rearrangement and the kinetics are affected. The same arguments apply to the carbonium ion formed during the rearrangement, whose tendency to be formed depends both on the possibility of delocalization of the positive charge and on the strain in the system formed (see p. 669). As was mentioned earlier, a stereochemically, uniform reaction course is of the utmost importance to the assumption that non-classical bridged ions are involved [1,2] (see p. 669). The stereochemistry of the homoallyl rearrangement has become known only by the study of cyclic compounds.

Rearrangements of Bicyclic Homoallyl Compounds

The influence of strain on the direction of rearrangement can be illustrated by the example of a bicyclic homoallyl compound. The solvolysis of 2-norbornenyl derivatives *(41)* leads to nortricyclyl derivatives *(43)* [11,68–70] not only under the conditions of a kinetically controlled reaction, but also (in contrast to the examples discussed so far) in thermodynamically controlled reactions. Thus the reaction of bicycloheptadienes [71–73] *(42)* or norborneols *(41)*, X = OH, with acids (HCl, $HCl/ZnCl_2$, HF) leads to rearrangement and formation of *(43)*, X = Cl or F [70,74]. *Schleyer* showed by the position of the equilibrium between norbornene and nortricyclene, that the cyclo-



(41) (42) (43)

[63] *E. F. Cox, M. C. Caserio, M. S. Silver*, and *J. D. Roberts*, J. Amer. chem. Soc. *83*, 2719 (1961).

[64] *J. W. Wilt* and *D. D. Roberts*, J. org. Chemistry *27*, 3430 (1962).

[65] *M. Hanack* and *P. Krause*, unpublished.

[66] *R. A. Sneen* and *A. L. Baron*, J. Amer. chem. Soc. *83*, 614 (1961).

[67] *M. Hanack* and *H. Meyer*, unpublished.

[68] *J. D. Roberts, W. Bennett*, and *R. Armstrong*, J. Amer. chem. Soc. *72*, 3329 (1950).

[69] *S. Winstein, M. Shatavsky, C. J. Norton*, and *R. B. Woodward*, J. Amer. chem. Soc. *72*, 5795 (1950).

[70] *M. Hanack* and *W. Kaiser*, Liebigs Ann. Chem. *657*, 12 (1962); cf. also *W. Treibs*, Naturwissenschaften *49*, 255 (1962).

[71] *S. Winstein* and *M. Shatavsky*, J. Amer. chem. Soc. *78*, 2819 (1956).

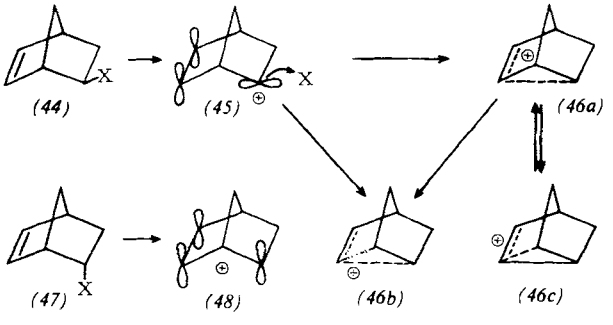
[72] *H. Krieger*, Suomen Kemistilehti *33B*, 183 (1960).

[73] *S. J. Cristol, W. K. Seifert, D. W. Johnson*, and *J. B. Jurale*, J. Amer. chem. Soc. *84*, 3918 (1962).

[74] *M. Hanack, H. Eggensperger*, and *R. Hähnle*, Liebigs Ann. Chem. *652*, 96 (1962).

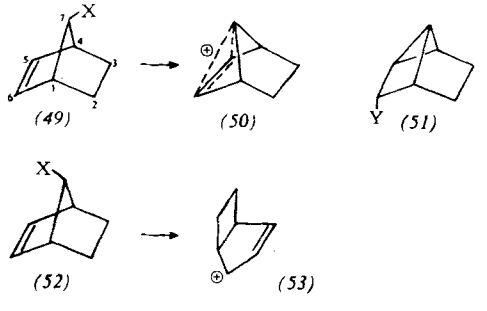
propane systems *(43)* are more stable than their homoallyl isomers *(41)*, both as the carbonium ions and as the final products, owing to their tricyclic structure [75].

Though both *exo*- *(44)* and *endo*-norbornyl derivatives *(47)* rearrange during solvolysis to give the nortricyclyl system *(43)* for the reasons given above [68, 69], a characteristic difference is found in the rates of solvolysis, owing to the different positions of the substituents in relation to the double bond. 2-*exo*-Norbornenyl *p*-toluenesulfonate *(44)*, X = OTs, acetolyses at almost the same rate as the saturated 2-*exo*-norbornyl *p*-toluenesulfonate [69, 76], since the arrangement of the orbitals of *(45)* favors overlap. On the other hand, the *endo*-compound *(47)*, X = OTs, reacts more slowly than the saturated comparison system, owing to the less favorable arrangement *(48)*.

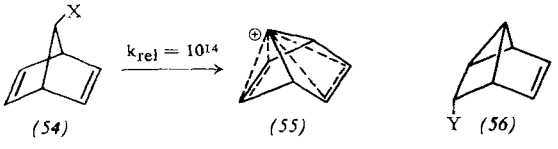


The higher rate of solvolysis of *(44)* and the distribution of ^{14}C between positions 2 and 3 in the products obtained on acetolysis of [2-^{14}C]- or [3-^{14}C]-2-norbornenyl sulfonates point to the formation of the non-classical cation *(46a)* [68]. Since the ^{14}C is also found in positions 1 and 7 after solvolysis with the weakly nucleophilic formic acid, secondary formation of the symmetrical ion *(46b)* from *(46a)* is assumed to take place [69, 76a]. On the other hand, the acetolysis of 3-*cis*-deuterio-2-*exo*-norbornenyl brosylate also yields 7-deuterated acetate, pointing to primary formation of *(46b)* or to the establishment of an equilibrium *(46a)* ⇌ *(46c)* [77].

The 7-*anti*-norbornenyl system satisfies the steric requirements for a substantial σ overlap (see p. 669). Consequently, 7-*anti*-norbornenyl derivatives *(49)*, X = OTs or Cl, are solvolysed 10^{11} times as rapidly as the corresponding 7-norbornyl compounds in acetic acid [78, 79]. NMR-spectroscopic investigation of the ion *(50)* showed that the charge is located mainly on C-5 and C-6, and less on C-7 [80, 81].



7-*syn*-Norbornenyl *p*-toluenesulfonate *(52)* is also solvolysed 10^4 times as rapidly as the saturated system. Since the position of the vacant orbital in relation to the double bond is unfavorable for overlap, the high rate of solvolysis is assumed to be due to the energetically favorable formation of the allyl cation *(53)* [82]. The introduction of a second double bond *(54)*, X = Cl, leads to a further increase in the rate of solvolysis [83, 84]. Ionization leads to *(55)*, which is assigned an asymmetric form on the basis of the NMR spectrum of a solution of 7-norbornadienyl tetrafluoroborate in liquid SO_2 [81, 85].



The systems *(49)* and *(54)*, which are particularly favorable for charge delocalization, do not rearrange into the tricyclic derivatives *(51)* and *(56)* on solvolysis under the conditions indicated. However, *(51)* and *(56)*, Y = H, can be obtained by reaction of *(49)*, X = OTs [86], or *(54)*, X = OTs or Cl [86, 87], with $NaBH_4$ or $LiAlH_4$. Methanolysis of *(49)*, X = OTs or Cl, and *(54)*, X = Cl, yields the tricyclic *endo*-methyl ethers *(51)*, Y = OCH_3, and *(56)*, Y = OCH_3, if the strongly nucleophilic sodium methoxide is used in excess [80, 88, 89].

Kinetic studies and analysis of the products have also revealed neighboring-group effects in other bicycloheptyl systems having a double bond in the homoallyl position with respect to the C atom carrying the functional group [1a]. The 7-isopropylidene-2-*endo*-norbornyl system *(57)* satisfies the stereoelectronic requirements for the formation of a non-classical ion *(58)*; the acetolysis rate constant is therefore much higher than that of *endo*-2-norbornyl *p*-toluenesulfonate, and the reaction proceeds with retention of configuration. The same is true of the 2-*exo* system *(59)*, since delocalization involving the second double bond is possible in this case with formation of *(60)*. In *(61)*, on the other hand, overlap with π-electron orbitals is geometrically impossible, so that the solvolysis of this compound is practically no faster than that of *exo*-2-

[75] *P. v. R. Schleyer*, J. Amer. chem. Soc. *80*, 1700 (1958).

[76] [a] *J. D. Roberts, C. C. Lee*, and *W. H. Saunders jr.*, J. Amer. chem. Soc. *77*, 3034 (1955); [b] *S. Winstein* and *M. Shatavsky, ibid. 78*, 592 (1956).

[77] *S. J. Cristol, T. C. Morril*, and *R. A. Sanchez*, J. Amer. chem. Soc. *88*, 3087 (1966).

[78] *S. Winstein, M. Shatavsky, C. Norton*, and *R. B. Woodward*, J. Amer. chem. Soc. *77*, 4183 (1955).

[79] *W. G. Woods, R. A. Carboni*, and *J. D. Roberts*, J. Amer. chem. Soc. *78*, 5653 (1956).

[80] *M. Brookhart, A. Diaz*, and *S. Winstein*, J. Amer. chem. Soc. *88*, 3135 (1966).

[81] *H. G. Richey jr.* and *R. K. Lustgarten*, J. Amer. chem. Soc. *88*, 3136 (1966).

[82] *S. Winstein* and *E. T. Stafford*, J. Amer. chem. Soc. *79*, 505 (1957).

[83] *S. Winstein* and *C. Ordronneau*, J. Amer. chem. Soc. *82*, 2084 (1960).

[84] *P. R. Story* and *M. Saunders*, J. Amer. chem. Soc. *82*, 6199 (1960).

[85] *P. R. Story, L. C. Snyder, D. C. Douglas, E. W. Anderson*, and *R. L. Kornegay*, J. Amer. chem. Soc. *85*, 3630 (1963).

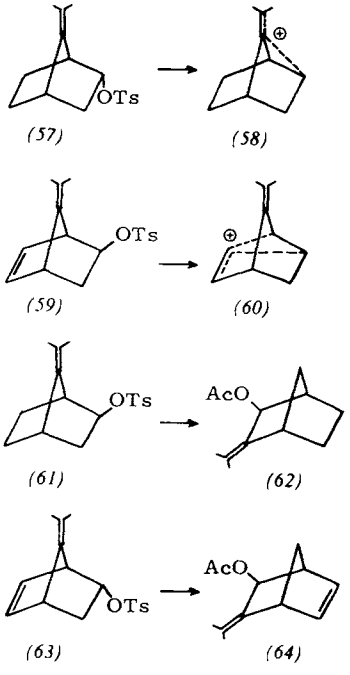
[86] *H. C. Brown* and *H. M. Bell*, J. Amer. chem. Soc. *85*, 2324 (1963).

[87] *P. R. Story*, J. Amer. chem. Soc. *83*, 3347 (1961).

[88] *H. Tanida, T. Tsuji*, and *T. Irie*, J. Amer. chem. Soc. *88*, 864 (1966).

[89] *A. Diaz, M. Brookhart*, and *S. Winstein*, J. Amer. chem. Soc. *88*, 3133 (1966).

norbornyl *p*-toluenesulfonate, and leads to the product *(62)* of a Wagner-Meerwein rearrangement, such as would be expected from a 2-norbornyl system; *(63)* reacts similarly to give *(64)* [90].



(57) *(58)* *(59)* *(60)* *(61)* *(62)* *(63)* *(64)*

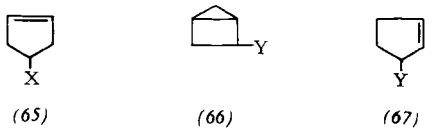
Kinetic neighboring-group effects and homoallyl rearrangements have also been observed with bicyclo[2.2.2]octenyl and bicyclo[3.2.1]octenyl compounds [1a]. The resulting tricyclic cyclopropane derivatives have a low thermodynamic stability. Reports on the other related systems have also been published [1a].

Rearrangements of Monocyclic Homoallyl Compounds

The dependence of the neighboring-group effect on stereochemistry and on the strain in the systems can be seen even in simple cyclic homoallyl compounds and in the cyclopropylmethyl and cyclobutyl derivatives obtained from them.

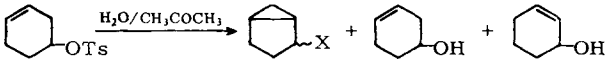
The lowest homologue of the 3-cycloalkene series, *i.e.* the 3-cyclopentene system *(65)*, does not undergo a homoallyl rearrangement to form the bicyclo[2.1.0]-pentyl system *(66)*. The absence of a neighboring-group effect of the double bond, which is due to the planar conformation of the cyclopentene ring, is also indicated by the low rate of solvolysis of *(65)*, X = Br or β-naphthylsulfonate (ONs), in comparison with corresponding cyclopentyl derivatives [62,91]. The investigation of various 3-cyclopentenyl derivatives *(65)*, X = Br, OTs, or ONs, showed that solvolysis leads mainly to 2-cyclopentenyl compounds *(67)* [62,92].

Since the position of the double bond in relation to the positive charge is unfavorable for overlap of the orbitals, the ion is stabilized by hydride shift. However, on solvolysis with complex anions, *e.g.* in the reaction of 3-cyclopentenyl *p*-toluenesulfonate *(65)*, X = OTs, with $LiAlH_4$ or $NaBH_4$, a small quantity of an unstable intermediate can also be intercepted in the form of bicyclopentane *(66)*, Y = H [92].



(65) *(66)* *(67)*

The 3-cyclohexenyl carbonium ion can assume a conformation close to the homoallyl resonance model (see p. 669), so that the rearrangement should be facilitated. *Hanack et al.* not only found that the rate of acetolysis of 3-cyclohexenyl *p*-toluenesulfonate *(68)* was higher than that of cyclohexyl *p*-toluenesulfonate, but also isolated the expected bicyclo[3.1.0]hexyl compounds *(69)* on acetolysis and hydrolysis [41,93].



(68) 7% cis + 8% trans *(69)* 70% *(70)* 15% *(71)*

The dependence of the three-membered ring-carbonium ion interaction on the spatial position of the three-membered ring is not very pronounced in the bicyclo[3.1.0]hexyl derivatives *(69)*. *cis*-Bicyclo[3.1.0]hex-2-yl *p*-nitrobenzoate *(69)*, X = *p*-NO_2–$C_6H_4CO_2$, is hydrolysed only 1.5 times as rapidly as the *trans* isomer [94], and both of these compounds also hydrolysed only slightly more slowly than methylcyclopropylcarbinyl *p*-nitrobenzoate *(37)*, R = CH_3, X = *p*-$NO_2C_6H_4CO_2$, which can assume the optimum conformation for a neighboring-group effect of the three-membered ring [66]. The hydrolysis of *(69)* is not stereospecific, but yields a mixture of *cis*- and *trans*-bicyclo[3.1.0]hexan-2-ol [94].

Because of their greater conformational mobility, 3-cycloheptenyl *(75)*, *n* = 3, and 3-cyclooctenyl derivatives *(75)*, *n* = 4, can attain almost completely the geometry required for homoallyl resonance (see p. 669). As was shown by *Cope et al.* [95], derivatives of these systems are solvolysed much more rapidly than corresponding cyclohexyl compounds, and the solvolysis is accompanied by extensive rearrangement into the *cis-trans*-isomeric bicyclic derivatives *(74)*.

2-Cycloalkenylmethyl compounds with small rings do not undergo the homoallyl rearrangement. Thus neither 2,3-diphenyl-2-cyclopropenylmethyl *(72)* [96] nor 2-cyclobutenylmethyl *p*-toluenesulfonate [97] *(73)*, *n* = 1, X = OTS, rearranges to give the corresponding bicyclic compound; the main products are those formed by ring expansion, as is shown *e.g.* by the formation of the isomeric cyclopentenols *(75)*, *n* = 1, Y = OH, and

[90] *C. H. DePuy, J. A. Ogawa*, and *J. C. McDaniel*, J. Amer. chem. Soc. *83*, 1668 (1961).

[91] *P. D. Bartlett* and *M. C. Rice*, J. org. Chemistry *28*, 3351 (1963).

[92] Cf. *M. Hanack*, Angew. Chem. *77*, 624 (1965); Angew. Chem. internat. Edit. *4*, 603 (1965).

[93] *M. Hanack* and *P. Ch. Krause*, unpublished.

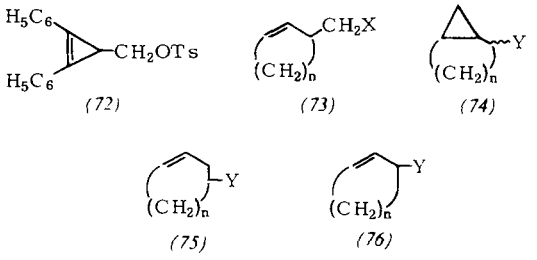
[94] *M. Hanack* and *H. Allmendinger*, unpublished.

[95] Summary: *A. C. Cope, M. M. Martin*, and *M. A. McKervey*, Quart. Rev. *20*, 119 (1966).

[96] *R. Breslow, J. Lockhart*, and *A. Small*, J. Amer. chem. Soc. *84*, 2793 (1962).

[97] *M. Hanack* and *K. Riedlinger*, Chem. Ber. *100*, 2107 (1967).

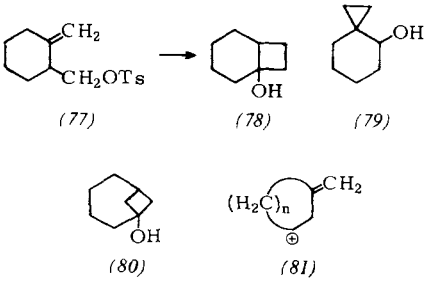
(76), $n = 1$, Y = OH, on hydrolysis of *(73)*, $n = 1$, X = OTs. The rate of acetolysis of cyclobutenylmethyl *p*-toluenesulfonate, which is lower by a factor of 3 than that of cyclobutylmethyl *p*-toluenesulfonate [97], can again be explained by the unfavorable position of the C atom carrying the functional group in relation to the double bond.



(72) *(73)* *(74)* *(75)* *(76)*

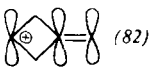
A further increase in ring size in the 2-cycloalkenylmethyl system *(73)* allows the homoallyl rearrangement to predominate over ring expansion. 2-Cyclopentenylmethyl derivatives *(73)*, $n = 2$, X = OTs or NH_2, rearrange on solvolysis or deamination into the stereoisomeric bicyclo[3.1.0]hexyl compounds *(74)*, $n = 2$. The 3-cyclohexenyl derivatives are obtained – particularly in weakly nucleophilic solvents [17]. The neighboring-group effect of the double bond in the more mobile systems *(73)*, with $n = 2$, is also reflected in the kinetics; *(73)*, $n = 2$, X = ONs, is acetolysed 10 times as rapidly as the saturated cyclopentylmethyl naphthylsulfonate [17].

In methylenecyclohexylcarbinyl *p*-toluenesulfonate *(77)*, the C atom carrying the functional group can assume the axial position, so that the steric requirements for a homoallyl rearrangement are satisfied. The hydrolysis of *(77)* leads not only to *(78)* but also to *(79)*, which is formed from the bicyclo[4.2.0]octyl cation corresponding to *(78)* by isomerization into the spirooctyl cation corresponding to *(79)* [18]. Another product is assigned the structure *(80)*. To explain the formation of this product, it is assumed that the homoallyl rearrangement is accompanied by ring expansion to form the ion *(81)*, which then rearranges into the bicyclo[4.1.1.] system *(80)*.



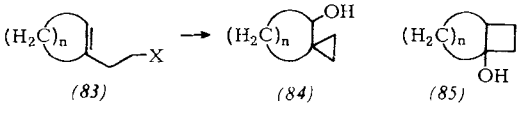
(77) *(78)* *(79)* *(80)* *(81)*

3-Methylenecycloalkyl derivatives, which lead directly to the carbonium ion *(81)*, have not so far been studied very extensively. It can be seen particularly clearly in the case of the 3-methylenecyclobutyl cation *(82)* that the reactivity of a homoallyl compound is determined by the positions of the p orbitals of the double bond and of the vacant orbital of the carbonium ion. Since these are parallel in *(82)*, σ overlap is impossible. Accordingly, the solvolysis of 3-methylenecyclobutyl bromide is slower by a factor of 160 than that of 3-butenyl bromide, and the deamination of 3-methylenecyclobutylamine proceeds without rearrangement [98].



(82)

The 1-cycloalkenylethyl derivatives *(83)*, which are influenced only slightly by steric effects, are examples of the few cases in which cyclopropane and cyclobutane compounds are formed simultaneously. As was shown by *Hanack* and *Schneider* [99], it is possible in this way to obtain both spirocyclopropane derivatives *(84)* and condensed cyclobutane derivatives *(85)* in good yields. The rearrangement of homoallyl compounds, which has so far been studied mainly from the point of view of mechanism, is also of preparative importance in this case. The hydrolysis of 1-cyclohexenylethyl *p*-toluenesulfonate *(83)*, $n = 4$, X = OTs, gives spiro[2.4]octan-1-ol *(84)*, $n = 4$, in 50 % yield, and deamination of *(83)*, $n = 4$, X = NH_2, leads by acid-catalysed secondary rearrangement of *(84)*, $n = 4$, to a 50 % yield of bicyclo[4.2.0]octan-1-ol *(85)*, $n = 4$.



(83) *(84)* *(85)*

In addition to 1-cyclopentenylethyl derivatives [99, 100], corresponding medium-sized rings were also subjected to this rearrangement; spiro compounds and bicyclic compounds containing four-membered rings, some of which had previously been known only as hydrocarbons, were obtained [101].

Condensed Cyclopropylmethyl and Cyclobutyl Compounds

These systems, which have been studied mainly by *Wiberg* and his co-workers, show particularly clearly that the formation of a non-classical cation is dependent on certain structural and steric conditions. Acetolysis of *exo*-bicyclo[2.2.0]hex-2-yl *p*-toluenesulfonate *(86)*, $n = 2$, does not lead to rearrangement into the cyclopropylmethyl system, as is expected of a cyclobutyl compound; on the contrary, the main products isolated are *exo*-bicyclo[2.1.1]hexyl derivatives *(87)*, X = OTs or OAc [102, 103]. The rigid planar

[98] *E. F. Kiefer* and *J. D. Roberts*, J. Amer. chem. Soc. *84*, 784 (1962).

[99] *M. Hanack* and *H.-J. Schneider*, Liebigs Ann. Chem. *686*, 8 (1965).

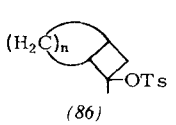
[100] *W. D. Closson* and *G. T. Kwiatkowski*, Tetrahedron *21*, 2779 (1965).

[101] *H. Schneider-Bernlöhr*, *R. Hüttinger*, *H.-J. Schneider*, and *M. Hanack*, unpublished.

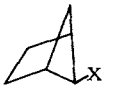
[102] [a] *K. B. Wiberg* and *A. J. Ashe III*, Tetrahedron Letters *1965*, 4245; [b] *R. N. McDonald* and *C. E. Reineke*, J. Amer. chem. Soc. *87*, 3020 (1965).

[103] [a] *K. B. Wiberg* and *A. J. Ashe III*, Tetrahedron Letters *1965*, 1553; [b] *F. Th. Bond* and *L. Scerbo*, Tetrahedron Letters *1965*, 4255.

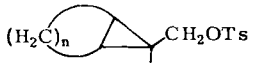
fusion of the two four-membered rings prevents the formation of a bicyclobutonium ion. Similarly, the isomeric compound *(88)*, $n = 2$, which is acetolysed to *(89)* without rearrangement, cannot react *via* this ion. The slightly higher rate of solvolysis of *(88)* in comparison with cyclopropylmethyl *p*-toluenesulfonate leads to the conclusion that stabilization of the carbonium ion by the cyclopropane ring is also possible in this system.



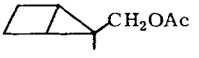
(86)



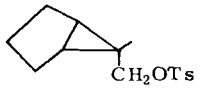
(87)



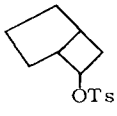
(88)



(89)



(90)

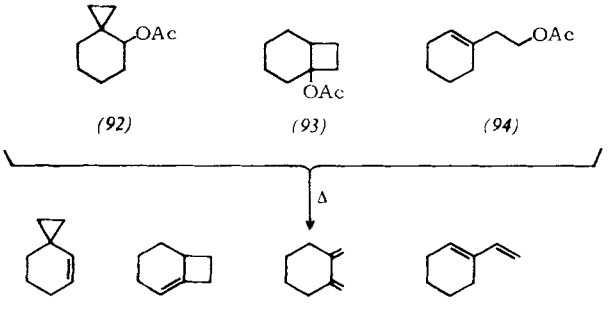


(91)

exo- and *endo*-Bicyclo[3.1.0]hex-6-ylmethyl *p*-toluenesulfonate *(88)*, $n = 3$, and *(90)* are acetolysed at approximately the same rate, but give different products [103]. While the *exo-p*-toluenesulfonate *(88)*, $n = 3$, gives the same products as the *exo-p*-toluenesulfonate *(86)*, $n = 3$ [104], the *endo* isomer *(90)* cannot form the same bicyclobutonium ion as *(91)*. Consequently, acetolysis of *(90)* and of *(91)* leads to different products.

Rearrangements during Pyrolysis

The rearrangements of cyclopropylmethyl, cyclobutyl, and homoallyl systems into one another have so far been considered only in connection with typical carbonium ion reactions such as solvolysis or deamination. However, they have recently also been observed



(92) *(93)* *(94)*

in the pyrolysis of esters having the structures *(92)*, *(93)*, and *(94)* [105], which give not only the olefins of the same structure, but also isomeric hydrocarbons.

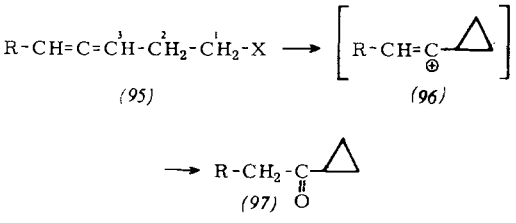
These products, as well as the pyrolysis kinetics [105], show that the pyrolysis of esters can also proceed *via* an ionic mechanism if the formation of a carbonium ion is facilitated by neighboring-group effect or by steric effects *(e.g.* in tertiary esters). The strong temperature-dependence of the composition of the products indicates that several parallel reactions are involved [105].

[104] *F. F. Nelson*, Ph.D. Thesis, University of Wisconsin, 1960.

[105] *M. Hanack, H. Schneider-Bernlöhr*, and *H..J. Schneider*, Tetrahedron, *23*, 2195 (1967).

Allene Derivatives

The allene derivatives *(95)*, which are similar to the homoallyl compounds, can also cyclize to give cyclopropane derivatives, though a vinyl cation *(96)* is involved as an intermediate in this case [106]. Solvolysis of *(95)*, R = H or alkyl, X = ONs, leads mainly to the cyclopropyl ketones *(97)*; cyclobutyl compounds have also been obtained from 1- or 3-substituted allenes [107].

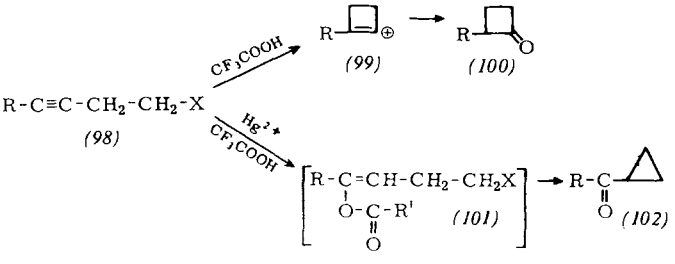


(95) *(96)* *(97)*

The direct participation of an allene double bond in the carbonium ion reaction has been detected by kinetic studies [106, 108].

Acetylene Derivatives

An interesting and useful cyclization reaction is exhibited by acetylene derivatives having the structure *(98)*, R = CH_3, C_2H_5, i-C_3H_7, X = *m*-SO_3–$C_6H_4NO_2$. Solvolysis with a solvent having a low nucleophilic strength and a high ionizing power leads to practically quantitative rearrangement into α-alkylcyclobutanones *(100)* [109, 110].



(99) *(100)* *(98)* *(101)* *(102)*

The solvolysis of phenyl-3-butynyl sulfonates *(98)*, R=C_6H_5, X = OSO_2R, leads mainly to phenyl cyclopropyl ketone, though other products are also formed. Ethoxy-3-butynyl *p*-toluenesulfonate *(98)*, R=C_2H_5O, X = OTs, partly rearranges on hydrolysis to give ethyl cyclopropanecarboxylate [111]. The cyclization of *(98)*

[106] *M. Hanack* and *J. Häffner*, Tetrahedron Letters *1964*, 2191; *M. Hanack* and *J. Häffner*, Chem. Ber. *99*, 1077 (1966).

[107] *M. Bertrand*, and *M. Santelli*, C. R. hebd. Séances Acad. Sci. *259*, 2251 (1964).

[108] *A. R. Ballentine, R. S. Bly*, and *S. U. Koock*, Abstracts 152nd Meeting Amer. chem. Soc., New York, Sept. 1966, Section S.

[109] *M. Hanack, J. Häffner*, and *I. Heterich*, Tetrahedron Letters *1965*, 875.

[110] *M. Hanack* and *I. Herterich*, Tetrahedron Letters *1966*, 3847.

[111] *M. Hanack* and *W. Kaiser*, unpublished.

(R = alkyl) presumably involves the direct participation of the triple bond, and, as with the allene derivatives, proceeds *via* a vinyl cation *(99)*. This is supported by the fact that, despite the strong inductive effect of the triple bond, the rates of solvolysis of the acetylene derivatives *(98)*, R = alkyl, are only slightly lower than those of the corresponding saturated compounds. The formation of the cyclobutanones *(100)* could also be explained by addition of the solvent to the triple bond and subsequent homoallyl rearrangement. In the presence of Hg^{2+} salts, which are known to catalyse the addition to the triple bond, solvolysis of *(98)*, R = alkyl, leads mainly *via (101)*, R = alkyl, to cyclopropyl ketones *(102)*, R = alkyl. This indicates that the uncatalysed solvolysis of *(98)*, R = alkyl, proceeds *via* a direct participation of the triple bond [112].

Conclusion

The present survey of the reactions of cyclopropylmethyl, cyclobutyl, and homoallyl compounds has had to be confined to selected typical examples. The large number of articles published even very recently shows that this field is not yet closed. The present article has been concerned only with cationic reactions. No mention has been made of numerous publications *e.g.* from the steroid field, or of the interesting rearrangements of carbanions, free radicals, and carbenes [1a]. Finally, it should be pointed out that cyclizations involving a double bond have been observed, not only with homoallyl compounds, but also with other unsaturated systems [8c, 113].

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German version: Angew. Chem. *79*, 709 (1966)
Translated by Express Translation Service, London

[112] *M. Hanack, I. Herterich*, and *V. Vött*, unpublished.
[113] *P. D. Bartlett*, Liebigs Ann. Chem. *653*, 45 (1962).

Formation and Properties of Carbosilanes [1]

BY G. FRITZ [*]

The present paper describes the formation of silicon-carbon compounds (carbosilanes), the molecular skeletons of which consist of alternate Si and C atoms, and which can be obtained by thermal decomposition of $Si(CH_3)_4$, CH_3SiCl_3, $(CH_3)_2SiCl_2$, and $(CH_3)_3SiCl$. The description of the formation of carbosilanes is followed by a discussion of the reactions of polychlorinated carbosilanes with organometallic compounds.

1. Synthesis of Carbosilanes by Pyrolysis

Carbosilanes are compounds with alternate Si and C atoms in their molecular skeleton [2]. They may be open-chain or cyclic compounds, *e.g.* $(Cl_3Si\text{-}CH_2)_2SiCl_2$ (1,1,1,3,3,5,5,5 - octachloro - 1,3,5 - trisilapentane) or $(SiCl_2\text{–}CH_2)_3$ (1,1,3,3,5,5-hexachloro-1,3,5-trisilacyclohexane). The work described in this article arose from experiments in which compounds containing SiH were pyrolysed and made to react with hydrogen compounds of other elements [3]. Such reactions can in fact be carried out once H atoms and silyl radicals have been produced, as is shown by the formation of numerous organosilicon compounds on reaction of SiH_4 with ethylene [4] and with vinyl chloride [5] above 400 °C, as well as by the reaction of SiH_4 with PH_3 to form $H_3Si\text{–}PH_2$ and other silylphosphines [6]. Since these and other observations on silicon chemistry pointed to the possibility of obtaining complicated silicon compounds from simple compounds by free-radical reactions, we tried to utilize the thermal cleavage of Si–CH_3 and C–H groups for the synthesis of silicon-carbon compounds.

The Si–C bond in simple alkylsilanes is much more stable to heat than the Si–H bond [7]. The thermal

[*] Prof. Dr. G. Fritz
Institut für Anorganische Chemie der Technischen Hochschule
Englerstrasse 11
75 Karlsruhe (Germany)

[1] Lecture at the 151st National Meeting of the American Chemical Society in Pittsburg (USA) on March 28, 1966, on the occasion of the presentation of the ACS Frederic Stanley Kipping Award, 1966.

[2] *G. Fritz, J. Grobe*, and *D. Kummer*, Advances inorg. Chem. Radiochem. *7*, 349 (1965).

[3] *G. Fritz*, Fortschr. chem. Forsch. *4*, 459 (1963).

[4] *G. Fritz*, Z. Naturforsch. *7b*, 207 (1952).

[5] *G. Fritz*, Z. Naturforsch. *7b*, 379, 507 (1952).

[6] *G. Fritz*, Z. Naturforsch. *8b*, 776 (1953); Z. anorg. allg. Chem. *280*, 332 (1955).

[7] *G. Fritz*, Z. anorg. allg. Chem. *273*, 275 (1953).

decomposition of $Si(CH_3)_4$ or $Si(C_2H_5)_4$ can be readily followed only above 650 °C [8], whereas H_2 is split off from the Si–H groups at 400 °C. When the alkylsilanes are heated for several hours in the gaseous phase at about 700 °C, they are almost completely decomposed, with deposition of silicon, carbon, silicon carbide and similar products, while hydrogen and lower hydrocarbons (mainly methane) escape. However, if the pyrolysis mixture is removed from the reaction zone after a short time and cooled, the primary radicals produced in the gaseous phase can form a series of silicon compounds [9]. The products are mainly compounds having an Si–C–Si skeleton. The proportion of high molecular weight compounds in the reaction mixture increases with rising pyrolysis temperature and with increasing residence time in the reaction vessel.

To prepare these products in reasonable quantities we used a system consisting of a storage vessel containing tetramethylsilane or methylchlorosilanes, a rotary pump (to transport the evaporating starting material through the reaction vessel, which is heated in a furnace), and traps situated under the reaction vessel to collect the reaction products [9, 10]. Since the pressure in the reaction vessel very quickly reaches atmospheric pressure, owing to the relatively high vapor pressures of tetramethylsilane and of the methylchlorosilanes, the conditions remain constant so long as the storage vessel still contains liquid starting material.

2. Treatment of the Pyrolysis Mixture

The pyrolysis mixture was worked up by distillation followed by gas chromatography [10]. Approximately half of the pyrolysis mixture can be distilled off and resolved into more than 50 compounds, each of which accounts for between 0.01 and 10 % of the total pyrolysis product. The undistillable residue consists of higher silicon compounds. The liquid fraction also contains very small quantities of lower hydrocarbons (up to hexane). All the higher fractions contain silicon compounds having large molecules and with several Si atoms. The principal gaseous products are hydrogen and methane. The products containing more than two Si atoms per molecule are listed in Table 1.

The higher products (> 5 Si atoms per molecule) in the undistillable residue, which account for about 50 % of the reaction mixture in the pyrolysis of $Si(CH_3)_4$, are particularly interesting. Before being further investigated, the residue must be resolved into pure compounds. However, this cannot be achieved by distillation or by gas chromatography, particularly since further reactions take place when the pyrolysis mixture is heated above 280 °C. In order to isolate and investigate further the various compounds, and to study, firstly, the influence of the reaction conditions on the composition of the pyrolysis mixture and, secondly, the secondary changes of the pyrolysis products, it was necessary to develop new chromatographic methods for their separation. A considerable proportion of our work was devoted to the solution of these problems.

Table 1. Compounds formed on pyrolysis of $Si(CH_3)_4$ (700 °C, residence time in reaction vessel ~ 1 min).

	Compound	B.p. (°C/mm) (m.p. (°C))	Proportion of total pyrolysis product (vol.-%)
(1)	$(CH_3)_3Si-CH_2-SiH(CH_3)_2$	120/768	2.4
(2)	1,1,3,3-Tetramethyl-1,3-disilacyclobutane [11]	122.8/745	3.2
(3)	$(CH_3)_3Si-CH_2-Si(CH_3)_3$	135.5/750	6.9
(4)	1,1,3,3-Tetramethyl-1,3-disila-4-cyclopentene [12]	138.5/745	0.7
(5)	$C_6H_5Si(CH_3)_3$	172/745	5.6
(6)	1,1,3,3,5,5-Hexamethyl-1,3,5-trisilacyclohexane	205/745	7.5
(7)	1,1,3,3,5-Pentamethyl-1,3,5-trisilacyclohexane	201/767	7.5
(8)	$[(CH_3)_3Si-CH_2]_2Si(CH_3)_2$	206/760	7.5
(9)	1,3,5,7-Tetramethyl-1,3,5,7-tetrasilaadamantane	103/1 (m.p. 122)	10.1
(10)	$Si_5C_{13}H_{34}$	126–132/1	
(11)	$Si_6C_{14}H_{36}$	150–153/1	
(12)	$Si_7C_{18}H_{46}$ [13]	170–195/1	
(13)	$Si_8C_{20}H_{50}$	200–230/1	
(14)	$Si_8C_{24}H_{66}$	230–240/1	
(15)	$Si_9C_{27}H_{74}$	245–300/1	
(16)	$Si_7C_{16}H_{36}$		
(17)	$Si_9C_{19}H_{46}$		

Compound *(12)* consists of three six-membered rings with alternating Si and C atoms. The Si valences that are not involved in the skeleton are occupied by CH_3 groups or by an H atom, while the carbon valences are satisfied by hydrogen atoms. *(16)* and *(17)* consist of six-membered rings in a three-dimensional arrangement and joined by Si–C groups. The entire skeleton consists of alternate Si and C atoms. The Si valences that are not involved in the skeleton are occupied by CH_3 groups and the carbon valences by H atoms [14a].

2.1. Chromatographic Separation of the Pyrolysis Products

Preliminary experiments showed that after the distillable fractions have been removed, the higher-boiling products of the pyrolysis of $Si(CH_3)_4$ can be separated into three groups on alumina columns. The first group (A) is not adsorbed on the column from a solution of the reaction mixture in benzene. The second group (B) can be eluted with benzene, and the third group (C), which remains in the column on elution with benzene, can be washed out with benzene-methanol mixtures. Group C can be further resolved on the column by successive elution with benzene-methanol mixtures having increasing methanol contents [14] (cf. Fig. 1).

Group A can be further resolved on an alumina column with pentane. This group includes two crys-

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[9] *G. Fritz* and *B. Raabe*, Z. anorg. allg. Chem. *286*, 149 (1956); *299*, 232 (1959).

[10] *G. Fritz* and *J. Grobe*, Z. anorg. allg. Chem. *315*, 157 (1962).

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[12] *G. Fritz, D. Kummer*, and *G. Sonntag*, Z. anorg. allg. Chem. *342*, 114, 121 (1966).

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[14] *G. Fritz* and *D. Wick*, Z. anorg. allg. Chem. *342*, 130 (1966).

[14a] *G. Fritz, H. Köhler*, and *H. Scheer*, unpublished.

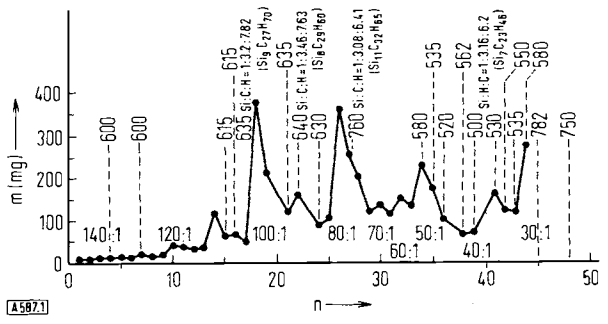


Fig. 1. Resolution of group C of the products from the pyrolysis of $Si(CH_3)_4$ (Al_2O_3 column neutral activity grade I, length 66 cm, diameter 3.5 cm) with benzene-methanol mixtures (140:1, 120:1, 100:1, 80:1, 70:1, 60:1, 50:1, 40:1, 30:1); volume of solvent per fraction: 5 l.
Ordinate: quantity m of substance eluted (mg);
Abscissa: number of fractions n.
The quantities of the various fractions were determined after the solvents had been distilled off. The molecular weights are given against the broken lines and the atomic ratios found by elemental analysis are given in many cases together with the empirical formulae. These empirical formulae are "averages" since it is not yet known whether the fractions were pure [14].

talline substances ($Si_7C_{16}H_{36}$ and $Si_9C_{19}H_{40}$, *(16)* and *(17)* in Table 1). The solid products formed on pyrolysis of $Si(CH_3)_4$ are deep brown, and fluoresce in organic solvents. The fluorescence of individual compounds and mixtures becomes more clearly visible on separation and further resolution of the groups, and can be used as a means of following the separation processes [14], particularly in the case of the compounds of group B.

2.2. Changes in the Pyrolysis Products on Distillative Separation

The development of the chromatographic separation method makes it possible to study the secondary changes that take place on distillation of the pyrolysis mixture. These changes can be represented as follows (see Table 2) [14, 15]:

The products formed when $Si(CH_3)_4$ was heated were distilled in a high vacuum to remove as much as possible of the more volatile products, the temperature of the pyrolysis mixture not being allowed to exceed 20 °C (Column 1). A second portion of the original pyrolysis mixture was then freed from all the components that distilled off up to 110 °C/1–2 mm Hg; to achieve this, it was necessary to heat the pyrolysis mixture to 200–260 °C (Column 2). Part of the residue was distilled further to remove all the components that distilled off up to 260 °C/1 mm Hg; this involved heating the pyrolysis mixture to 340–400 °C (Column 3). Part of this last residue was heated for 4 hours at 430 to 450 °C (Column 4), and part for 5 min at 600 °C (Column 5).

The composition of the pyrolysis mixture clearly becomes more complex with rising temperature on separation by distillation, since the quantities of high molecular-weight components increase rapidly. This is particularly true of the substances of groups D and E, which are initially almost entirely absent. The quantity of substances of group C also increases (but without formation of insoluble products) when the temperature in the distillation vessel is raised from 260 to 400 °C. Group B forms only a very small part of the mixture; this group appears to be formed only on heat treatment, and is destroyed again when heated further.

The investigation showed that the mixtures of higher molecular-weight compounds formed on pyrolysis of tetramethylsilane are simpler than was originally thought, and that complex chemical changes take place on distillation of the reaction mixtures.

To obtain an insight into the secondary changes that take place on distillation of the pyrolysis mixture, the thermal stabilities of a number of substances and groups of substances were studied. The temperature ranges in which changes begin were determined, and the changes were followed by means of molecular-weight determinations. The gases formed during the heat treatment were collected with a view to obtaining

[15] *G. Fritz* and *N. Götz*, unpublished.

Table 2. Composition of the pyrolysis products of $Si(CH_3)_4$ after being heated to various temperatures. After heat treatment the mixture was cooled and resolved by chromatography.

Group		Col. 1 Up to 20 °C	Col. 2 Heated for 10 h at 200–260 °C	Col. 3 Heated for 5 h at 340–400 °C	Col. 4 Heated for 4 h at 430–450 °C	Col. 5 Heated for 5 min at 600 °C
	Proportion of total pyrolysis product (vol.-%)	~ 40	48	11	6	1.4
A	Molecular weight	515	550	800		
	Si:C:H	1:2.8:5.0	1:3.6:5.4			
	Proportion of total pyrolysis product (vol.-%)	traces	0.56	0.2	–	–
B	Molecular weight		550			
	Proportion of total pyrolysis product (vol.-%)	~ 30	10	26.5	12	
C	Molecular weight	770	660	1370		
	Si:C:H	1:2.8:4.0	1:3.3:6.5			
	Proportion of total	~ 10	40	62.3	28	
D [a]	pyrolysis product (vol.-%)					not determined
	Proportion of total	–	–	–	54	85
E [b]	pyrolysis product (vol.-%)					

[a] Mixture of substances of higher molecular weight. [b] Low solubility in benzene.

information about the processes which bring about the increase in molecular size. The substances used in the investigation were an untreated reaction mixture from the pyrolysis of $Si(CH_3)_4$, the substances of group A obtained by column chromatography of the pyrolysis mixture, and the compounds $Si_4C_{10}H_{24}$ [Table 1, *(9)*], $Si_9C_{16}H_{36}$, and $((CH_3)_3Si)_2CH_2$ [Table 1, *(3)*].

The experiments showed that the untreated pyrolysis mixture changed appreciably even when heated to about 400 °C (increase in the average molecular weight, formation of benzene-insoluble components; group E), while only small quantities of gas are formed. When a sample of the pyrolysis mixture was heated at 430 to 490 °C for 46 hours, 72 % of the product was converted into benzene-insoluble residues, with formation of only very small quantities of methane and hydrogen. The separated group A exhibits similar behavior only at about 230 °C, though no benzene-insoluble material is formed [15].

On the other hand, $Si_4C_{10}H_{24}$, which has a tetrasilaadamantane skeleton *(9)*, was found to have an extremely high thermal stability, and showed practically no change when heated for 37 hours at 520 to 540 °C. No extensive decomposition occurred, even when the substance was heated at 550 to 560 °C (70 hours). Marked decomposition is observed only at 580 °C, and after 24 hours at this temperature a benzene-insoluble residue can be isolated (about 33 %). By far the greatest part of the benzene-soluble fraction consists of unchanged $Si_7C_{10}H_{24}$.

The crystalline compound $Si_7C_{16}H_{36}$, the structure of which has not yet been fully elucidated, resembles $Si_4C_{10}H_{24}$ in its thermal stability. It shows practically no change after 54 hours at temperatures up to 490 °C, and forms an insoluble residue (42 % of the original substance) only when heated at 560 °C (55 hours); the benzene-soluble fraction still contains the unchanged compound. The decomposition temperature of $[(CH_3)_3Si]_2CH_2$ is about 500 °C, *i.e.* somewhat lower than that of the more symmetrical, crystalline compounds $Si_4C_{10}H_{24}$ and $Si_7C_{16}H_{36}$.

These investigations [15] show that the observed molecular-weight changes in the pyrolysis mixtures are due to changes in carbosilanes of a few structural types.

3. Synthesis of Chlorinated Carbosilanes by Pyrolysis

Many carbosilanes of various molecular weights are obtainable by the pyrolysis of tetramethylsilane. Most of these compounds are unreactive, since they contain no functional groups. However, compounds with the same basic skeleton, but with reactive groups attached to the Si atoms, are required in many investigations. Compounds of this nature can be obtained by the pyrolysis of the three methylchlorosilanes [16]. The thermal decomposition of the methylchlorosilanes is reasonably fast at about 700 °C. The pyrolysis products are obtained in useful amounts by the principle used in the pyrolysis of tetramethylsilane. Of the products formed on pyrolysis of $(CH_3)_3SiCl$, some 60 vol-% consist of fractions that boil at temperatures between 163 and 200 °C at normal pressure, while 40 vol-% are oily and solid fractions that dissolve in non-polar solvents. About 85 % of the pyrolysis products of CH_3SiCl are colorless liquids, while 15 % are oils or solids that are fusible and colored. All the compounds that were formed on pyrolysis of the three methylchlorosilanes and that have boiling points below 250 °C have been detected by gas chromatography, and their relative proportions have been determined [17, 18].

The carbosilanes obtained from the methylchlorosilanes are listed in Table 3. All the possible chlorinated and methylated compounds having the basic structure $Si-CH_2-Si$ have been isolated from the pyrolysis products of $(CH_3)_3SiCl$. The distribution of the 1,3-disilapropanes *(17)* to *(26)* in the pyrolysis products of the three methylchlorosilanes are compared in Table 3. The 1,3-disilapropanes accounted for 32 % of the total pyrolysis product from $(CH_3)_3SiCl$, 43 % of that from $(CH_3)_2SiCl_2$, and 60 % of that from CH_3SiCl_3.

4. Reduction of the Chlorinated Carbosilanes

In order to investigate the high molecular weight products from the pyrolysis of the methylchlorosilanes, it was necessary to separate the various compounds from the mixture. However, even for substances containing three Si atoms per molecule, the distillative separation of Si-chlorinated carbosilanes is difficult, owing to the high boiling points of the compounds. The chromatographic methods are also unsuitable for the same reason. Attempts were therefore made to replace the chlorine by hydrogen in Si-chlorinated carbosilanes by treatment with $LiAlH_4$. The corresponding compounds with SiH groups boil at lower temperatures, and can be separated by distillation and gas chromatography. The hydrogenation takes place with no change in the Si–C–Si skeleton, as was shown by the investigation of Si-chlorinated 1,3-disilapropanes having known structure, and of 1,1,3,3,5,5-hexachloro-1,3,5-trisilacyclohexane, *(30)*, which crystallizes well [19].

The fractions of the pyrolysis products containing the compounds *(27)* to *(40)* were hydrogenated. Comparison of the proportions of the various compounds in the hydrogenated pyrolysis mixtures shows that the tendency toward the formation of six-membered rings with alternating Si and C atoms increases with the number of $SiCH_3$ groups in the starting compound.

In the high molecular weight compounds formed on pyrolysis of the methylchlorosilanes, the SiCl groups can again be converted into SiH groups without modification of the skeleton,

[16] *G. Fritz, D. Habel, D. Kummer*, and *G. Teichmann*, Z. anorg. allg. Chem. *302*, 60 (1959).

[17] *G. Fritz* and *D. Ksinsik*, Z. anorg. allg. Chem. *304*, 241 (1960).

[18] *G. Fritz* and *D. Ksinsik*, Z. anorg. allg. Chem. *322*, 46 (1963).

[19] *G. Fritz, H. J. Buhl*, and *D. Kummer*, Z. anorg. allg. Chem. *327*, 165 (1964).

Table 3. Carbosilanes from the pyrolysis of CH_3SiCl_3, $(CH_3)_2SiCl_2$, and $(CH_3)_3SiCl$. The compounds containing SiCl groups and the SiH compounds obtained from them by hydrogenation with $LiAlH_4$ are listed together.

	SiCl-containing compound in pyrolysis mixture	Hydrogenated compound	B.p. (°C/mm) of the SiH-comp.	Parts by volume in the pyrolysis mixture from CH_3SiCl_3	$(CH_3)_2SiCl_2$	$(CH_3)_3SiCl$
				with respect to $(Cl_3Si)_2CH_2 = 100$		
(17)	$Cl_3Si-CH_2-SiCl_3$	$H_3Si-CH_2-SiH_3$	17/757	100	100	100
(18)	$(CH_3)_2SiCl-CH_2-SiCl_3$	$(CH_3)_2SiH-CH_2-SiH_3$	70.5—71/768	2.5	—	0.8
(19)	$(CH_3)_2ClSi-CH_2-SiCl_3$	$(CH_3)_2HSi-CH_2-SiH_3$ (2:3)				
(20)	$(CH_3)Cl_2Si-CH_2-SiCl_2(CH_3)$	$(CH_3)H_2Si-CH_2-SiH_2(CH_3)$ (2:3)	71/768	6.8	33	44.7
(21)	$(CH_3)_3Si-CH_2-SiCl_3$	$(CH_3)_3Si-CH_2-SiH_3$	91—92/768	0.5	23.7	141
(22)	$(CH_3)_2ClSi-CH_2-SiCl_2(CH_3)$	$(CH_3)_2HSi-CH_2-SiH_2(CH_3)$	88.5/768	—	10.7	71.4
(23)	$(CH_3)_2ClSi-CH_2-SiCl(CH_3)_2$	$(CH_3)_2HSi-CH_2-SiH(CH_3)_2$	107/768	—	—	41.9
(24)	$(CH_3)_2ClSi-CH_2-SiCl(CH_3)_2$	$(CH_3)_2HSi-CH_2-SiH(CH_3)_2$ (1:3)				
(25)	$(CH_3)_3Si-CH_2-SiCl_2(CH_3)$	$(CH_3)_3Si-CH_2-SiH_2(CH_3)$ (1:3)	103/768	—	0.66	13.9
(26)	$(CH_3)_3Si-CH_2-SiCl(CH_3)_2$	$(CH_3)_3Si-CH_2-SiH(CH_3)_2$	120/768	—	—	13.6
				with respect to $(SiH_2-CH_2)_3 = 100$		
(27)	$Cl_3Si-CH_2-SiCl_2-CH_2-SiCl_3$	$H_3Si-CH_2-SiH_2-CH_2-SiH_3$	100/760	109	28	14
(28)	$Cl_3Si-CH_2-SiCl_2-CH_2-SiCl_2(CH_3)$	$H_3Si-CH_2-SiH_2-CH_2-SiH_2(CH_3)$	123/758	45	—	69
(29)	$Cl_3Si-CH_2-SiCl_2-CH_2-SiCl(CH_3)_2$ [a]	$H_3Si-CH_2-SiH_2-CH_2-SiH(CH_3)_2$ [a]	133/762	—	—	155
		$(CH_3)_3Si-CH_2-Si(CH_3)_3$	135/768	—	—	64
(30)	1,1,3,3,5,5-Hexachloro-1,3,5-trisilacyclohexane	1,3,5-Trisilacyclohexane	142/760	100	100	100
(31)	$Cl_3Si-CH_2-SiCl_2-Si(CH_3)_3$ [a]	$H_3Si-CH_2-SiH_2-CH_2-Si(CH_3)_3$ [a]	154/756	—	—	69
(32)	1,1,3,3,5-Pentachloro-5-methyl-1,3,5-trisilacyclohexane	1-Methyl-1,3,5-trisilacyclohexane	159/766	25	50	960
(33)	1,1,3,5-Tetrachloro-3,5-dimethyl-1,3,5-trisilacyclohexane	1,3-Dimethyl-1,3,5-trisilacyclohexane	166/764	—	—	1690
(34)	1,3,5-Trichloro-1,3,5-trimethyl-1,3,5-trisilacyclohexane	1,3,5-Trimethyl-1,3,5-trisilacyclohexane	180/764	—	—	1000
(35)	1,1,3-Trichloro-3,5,5-trimethyl-1,3,5-trisilacyclohexane	1,1,3-Trimethyl-1,3,5-trisilacyclohexane				
(36)	1,3-Dichloro-1,3,5,5-tetramethyl-1,3,5-trisilacyclohexane	1,1,3,5-Tetramethyl-1,3,5-trisilacyclohexane	190/764	—	—	168
(37)	1-Chloro-1,3,3,5,5-pentamethyl-1,3,5-trisilacyclohexane	1,1,3,3,5-Pentamethyl-1,3,5-trisilacyclohexane	201/767	—	—	65 *(29)+(19)*
(38)	1,1,3,3-Tetrachloro-1,3-disilaindan	1,3-Disilaindan	204/746	4	9	65 *(29)+(19)*
(39)	1,3,3-Trichloro-1-methyl-1,3-disilaindan	1-Methyl-1,3-disilaindan	210/767	—	—	59
(40)	1,3-Dichloro-1,3-dimethyl-1,3-disilaindan	1,3-Dimethyl-1,3-disilaindan	not determined	—	—	14
(41)	2,2,4,4,6,6,8,8-Octachloro-2,4,6,8-tetrasilabicyclo[3.3.0]oct-1(5)-ene [20a]	Methylation product 2,2,4,4,6,6,8,8-Octamethyl-2,4,6,8-tetrasilabicyclo[3.3.0]oct-1(5)-ene [20] [m.p. = 142]				
(42)	1,3,5,7-Tetrachloro-1,3,5,7-tetrasiladamantane [21] [c]	1,3,5,7-Tetrahydro-1,3,5,7-tetrasiladamantane				
(43)	$Si_7C_{12}H_{28}Cl_6$ [27]					
(44)	$Si_8C_8H_{16}Cl_{16}$ [27] [b]					

[a] The distribution of the CH_3 groups on the Si atoms of the molecule has not yet been established unambiguously.

[b] *(44)* consists of four condensed six-membered rings with alternating Si and C atoms. The Si valences that are not involved in the skeleton are occupied by Cl, and the carbon valences by H atoms. *(43)* has a similar structure.

[c] This compound has been obtained by the reaction of $SiCl_4$ and $(CH_3)_3SiCl$ in the presence of $AlCl_3$ at high pressures. — *A. Lee Smith* and *H. A. Clark*, J. Amer. chem. Soc. *83*, 3345 (1961).

so that these compounds containing SiH groups, which are less sensitive to hydrolysis, can also be separated. The mixture is again resolved into three groups of substances by chromatography on Al_2O_3 columns. Group C can be further resolved by elution with benzene-methanol mixtures having increasing methanol contents. The fractions obtained by chromatographic separation (molecular weights between 400 and 800) all contain compounds having relatively small differences in their molecular weights (*e.g.* 544 to 571; 817 to 834)[21].

5. Conclusions Concerning the Formation of Pyrolysis Products

The formation of compounds in the gaseous phase at about 700 °C is assumed to be a free-radical process[2,3,10]. The initial step of the decomposition is thought to be reaction (1). This is followed by reaction (2).

$$Si(CH_3)_4 \rightarrow (CH_3)_3\dot{S}i + \dot{C}H_3 \quad (1)$$

$$(CH_3)_3Si-CH_3 + \dot{C}H_3 \rightarrow (CH_3)_3Si-\dot{C}H_2 + CH_4 \quad (2)$$

These processes yield the free radicals required for the formation of the Si–C–Si skeleton. The parent compound is probably formed in accordance with (3).

$$(CH_3)_3Si-\dot{C}H_2 + \dot{S}i(CH_3)_3 \rightarrow (CH_3)_3Si-CH_2-Si(CH_3)_3 \quad (3)$$

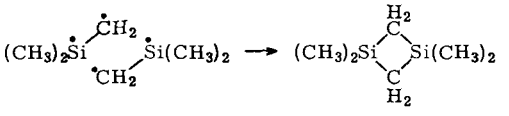
[20] *G. Fritz*, *E. Krahe*, and *H. G. v. Schnering*, unpublished.

[20a] *G. Fritz* and *R. Haase*, unpublished.

[21] *G. Fritz* and *W. König*, unpublished.

This does not explain the preferential formation of cyclic carbosilanes. The isolation of 1,3-disilacyclobutane from the pyrolysis products [11] seems particularly significant; this product could be formed by reactions (4) and (5).

$$(CH_3)_3Si-\dot{C}H_2 \rightarrow (CH_3)_2\dot{S}i-\dot{C}H_2 + \dot{C}H_3 \qquad (4)$$



(5)

The formation of the six-membered ring can also be explained as proceeding *via* the radical $(CH_3)_2\dot{S}i-\dot{C}H_2$.

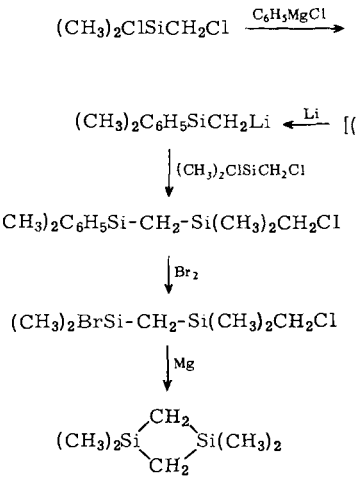
The Si-chlorinated carbosilanes could be formed in a similar manner from the three methylchlorosilanes in the gaseous phase [2,3]. As in the pyrolysis of $Si(CH_3)_4$, the SiC and CH bonds may be expected to be cleaved. However, the products isolated show that the SiCl bond must also be broken, since the pyrolysis products of $(CH_3)_3SiCl$ and $(CH_3)_2SiCl_2$ include compounds in which the Si atom carries more Cl atoms than in the starting material. Moreover, the 1,3-disilapropanes formed in the greatest quantities are those whose formation involves large transpositions, *e.g.* $Cl_3Si-CH_2-SiCl_3$ and $(CH_3)_3Si-CH_2-SiCl_3$ from $(CH_3)_3SiCl$ or $(CH_3)_2SiCl_2$. Further assumptions are necessary in order to explain the formation of these compounds. If it is assumed that SiCl bonds are broken, the formation of the compounds could be explained by the recombination of suitable radicals; however, this assumption is open to certain objections.

It should be stressed that we have never found pyrolysis products containing Si–Si bonds, which could possibly have arisen by the recombination of radicals such as $(CH_3)_3Si\bullet$ (see eq. (1)). Since the bond energy of the Si–C bond (76 kcal) is higher than that of the Si–Si bond (53 kcal), the arrangement Si–C–Si is energetically favored in relation to Si–Si–C. This is confirmed by a series of catalytic and even thermal rearrangements [22].

6. Synthesis of Carbosilanes Containing Functional Groups

The stepwise organometallic synthesis of carbosilanes with functional groups on the Si atom [2,3,23] is made difficult by the fact that functional groups on Si readily undergo undesirable side reactions with organolithium or organomagnesium compounds.

The obvious remedy was to carry out the synthesis of the organometallic compounds, and as far as possible their further reaction, with derivatives having protective groups on the Si atom. These groups must prevent undesirable condensations, and it must be possible to remove them at a later stage to give an Si atom carrying a functional group. A suitable group for this purpose is the $Si-C_6H_5$ group, which can be split by reaction with halogens or hydrogen halides, depending on the other substituents on the Si atom [24]. This principle was used for the preparation of a number of carbosilanes containing functional groups [25], *e.g.*:



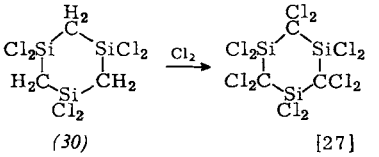
The four-membered ring has now also been synthesized from $(CH_3)_2ClSiCH_2Cl$ and Mg [25a].

The chemical properties of the carbosilanes are determined largely by the groups attached to the Si atoms and to the skeletal C atoms. The compounds in which the Si atoms are fully methylated are (generally) inert. Reactions are observed only under extreme conditions or where strained ring systems are involved. Thus 1,1,3,3-tetramethyl-1,3-disilacyclobutane undergoes ring cleavage with HBr. The corresponding six-membered ring compound does not exhibit this reaction.

Photochlorination leads to chlorination of the CH groups of the carbosilane skeleton, the reaction proceeding as far as steric factors allow [26,27] (cf. eqs. (6)–(8)). Intermediates can be isolated in only a very few cases [28], one such substance being $Cl_3Si-CHCl-SiCl_3$ [27a].

$$Cl_3Si-CH_2-SiCl_3 \xrightarrow{Cl_2} Cl_3Si-CCl_2-SiCl_3 \qquad (6)$$
(17)

$$(Cl_3Si-CH_2)_2SiCl_2 \xrightarrow{Cl_2} (Cl_3Si-CCl_2)_2SiCl_2 \qquad (7)$$
(27)



(8)

(30) [27]

[22] *K. Shiina* and *M. Kumada*, J. org. Chemistry *23*, 139 (1958).

[23] *G. Fritz* and *H. Burdt*, Z. anorg. allg. Chem. *314*, 35 (1962).

[24] *G. Fritz* and *D. Kummer*, Z. anorg. allg. Chem. *308*, 105 (1961); *310*, 327 (1961).

[25] *G. Fritz* and *W. Kemmerling*, Z. anorg. allg. Chem. *322*, 34 (1963); *G. Fritz*, *W. Kemmerling*, *G. Sonntag*, *H. J. Becker*, *E. A. V. Ebsworth*, and *J. Grobe*, Z. anorg. allg. Chem. *321*, 10 (1963).

[25a] *W. A. Kriner*, J. org. Chemistry *29*, 1601 (1964); *R. Müller*, *R. Kähne*, and *H. Beyer*, Chem. Ber. *95*, 3030 (1962); *H. Gilman*, personal communication.

[26] *R. Müller* and *G. Seitz*, Chem. Ber. *91*, 22 (1958).

[27] *G. Fritz*, *D. Habel*, and *G. Teichmann*, Z. anorg. allg. Chem. *303*, 85 (1960).

[27a] *G. Fritz* and *R. Riekens*, unpublished.

[28] *G. Fritz et al.*, unpublished.

These *C*-chlorinated carbosilanes are particularly interesting in their reaction with organometallic compounds. While methylation of *C*-chlorinated methylchlorosilanes with CH_3MgCl or CH_3Li leads mainly to the Si-methyl compound, *e.g.* the reaction of $(CH_3)_2ClSi-CHCl_2$ with CH_3MgCl yields $(CH_3)_3Si-CHCl_2$, a similar reaction is hardly ever observed with chlorosilanes in which the skeletal C atom is chlorinated. After the methylation of $(Cl_3Si)_2CCl_2$ with CH_3MgCl or CH_3Li, not even small quantities of the Si-methylated compound $[(CH_3)_3Si]_2CCl_2$ can be isolated. Reaction under a wide range of conditions leads instead to $[(CH_3)_3Si]_2CH_2$, $[(CH_3)_3Si]_2CHCH_3$, $[(CH_3)_3Si]_2C=CH_2$, and $[(CH_3)_3Si]_2C(CH_3)_2$, as well as other compounds that have not yet been fully characterized [29]. Although these transformations cannot be satisfactorily interpreted at present they have opened up new avenues in carbosilane chemistry.

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[29] *G. Fritz* and *J. Grobe*, Z. anorg. allg. Chem. *309*, 77 (1961).

Siloxane Compounds of the Transition Metals

BY F. SCHINDLER AND H. SCHMIDBAUR [*]

Heterosiloxanes of transition metals contain the characteristic grouping Si–O–X; in the compounds known so far, X may be Au, Zn, Cd, Hg, Ti, Zr, Hf, V, Nb, Ta, Cr, U, Re, Fe, Co, Ni, or Pt. Most of these compounds are obtained from silanols, metal silanolates, acyloxysilanes, disiloxanes, or alkoxysilanes, i.e. from compounds that already contain an Si–O bond. The transition metal may be introduced e.g. as a halide, as an organometallic compound, as an alkoxy compound, or as an oxide. Heterosiloxanes are also formed on reaction of many silicon compounds that do not contain oxygen with transition metal compounds containing oxygen. Some of these compounds, e.g. some titanosiloxanes, are very stable, whereas others decompose explosively. Oligomeric and polymeric heterosiloxanes exist in addition to the monomeric compounds.

The heterosiloxane grouping Si–O–X (X = hetero atom) is one of the most important structural units of inanimate nature. The various metal silicates are built up from such units, and profit from their high chemical and thermal stability. Numerous attempts have been made to prepare organometallic polymers from metal-substituted silicones, in order to make use of the advantageous properties of the heterosiloxane group. Heterosiloxanes of elements of the main groups were discussed in an earlier article [1]. The present article deals with the corresponding compounds of the transition elements, which were almost unknown until a few years ago. Efforts to synthesize new inorganic polymers [2, 3] have also led to fundamental investigations in this field.

[*] Dr. F. Schindler and Prof. Dr. H. Schmidbaur
Institut für Anorganische Chemie der Universität
Röntgenring 11
87 Würzburg (Germany)

[1] *H. Schmidbaur*, Angew.Chem.*77*, 206 (1965); Angew. Chem. internat. Edit. *4*, 201 (1965).

[2] *F. G. A. Stone* and *W. A. G. Graham*: Inorganic Polymers. Academic Press, New York 1962.

[3] *M. F. Lappert* and *G. J. Leigh*: Development in Inorganic Polymer Chemistry. Elsevier, Amsterdam 1962.

I. Siloxanes of Copper, Silver, and Gold

Preliminary experiments with copper and silver were not very promising. Thus the reaction of disodium diphenylsilanediolate with copper(II) chloride gives an intermediate product presumed to have the composition $[Si(C_6H_5)_2-O]_x[-Cu-O]_y$, but this immediately decomposes into copper(II) oxide and octaphenylcyclotetrasiloxane [4].

Attempts to prepare siloxanes of silver by reaction of silver perchlorate or nitrate with sodium trimethylsilanolate in many different solvents did not yield a definite silver trimethylsilanolate, but only silver oxide and hexamethyldisiloxane [5].

$$2\,AgClO_4 + 2\,NaOSi(CH_3)_3 \rightarrow 2\,NaClO_4 + Ag_2O + [(CH_3)_3Si]_2O$$

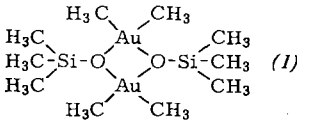
It is not certain whether $AgOSi(CH_3)_3$ occurs as an unstable intermediate in this reaction.

[4] *E. D. Hornbaker* and *F. Conrad*, J. org. Chemistry *24*, 1858 (1959).

[5] *H. Schmidbaur* and *M. Bergfeld*, unpublished; *M. Bergfeld*, Dissertation, Universität Würzburg 1967.

Attempts to prepare an aurosiloxane, on the other hand, were successful [6]. The reaction of dimethylgold bromide with sodium trimethylsilanolate in diethyl ether gives pentamethyl-aurosiloxane *(1)* in good yield.

$$2\ (CH_3)_2AuBr + 2\ NaOSi(CH_3)_3 \rightarrow 2\ NaBr +$$

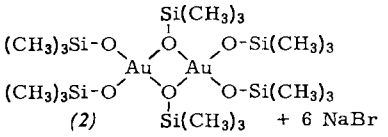


(1)

The colorless compound *(1)* (m.p. 37–39 °C, sublimation at 40 °C/0.001 mm Hg) is one of the few organogold compounds that evaporate without decomposition. It decomposes at 135 °C with deposition of a gold mirror, and molecular-weight determinations in benzene show it to be a dimer with a gold-oxygen four-membered ring system. Compound *(1)* was characterized by its IR and NMR spectra, some details of which are given in Table 1 [6]. The compound is diamagnetic, and the arrangement of the four ligands of the gold atoms is therefore assumed to be planar.

Anhydrous $AuBr_3$ reacts with sodium trimethylsilanolate to form the much less stable tris(trimethylsiloxy)gold *(2)*. This product forms yellow crystals, which decompose even at room temperature into

$$Au_2Br_6 + 6\ NaOSi(CH_3)_3 \rightarrow$$



(2)

$$+ 6\ NaBr$$

lower gold oxides, oxygen, and hexamethyldisiloxane [6]. IR and NMR data indicate a constitution having bridge-type and terminal siloxy groups.

Compound *(2)* is converted by an excess of $NaOSi(CH_3)_3$ into the complex sodium tetrakis(trimethylsiloxy)aurate(III), which can be isolated as the colorless salt, and which is insoluble in nonpolar organic solvents [6].

$$\{Au[OSi(CH_3)_3]_3\}_2 + 2\ NaOSi(CH_3)_3 \rightarrow 2\ Na\{Au[OSi(CH_3)_3]_4\} \quad (3)$$

Heterosiloxanes of monovalent gold, like those of monovalent silver, are unknown.

II. Siloxanes of Zinc, Cadmium, and Mercury

Siloxy compounds of elements of the Group II triad have not been extensively studied so far. Two articles deal with the incorporation of Zn, Cd, and Hg into polyorganometallosiloxanes [4,7], and two others describe low molecular weight mercurosiloxanes [8,9].

Recent investigations by the present authors [5,10,11] have shown that dimethylzinc and dimethylcadmium (but not dimethylmercury) react with trimethylsilanol at room temperature, with evolution of methane and formation of compounds containing Zn–O–Si and Cd–O–Si structural units:

$$4(CH_3)_2Zn + 4HOSi(CH_3)_3 \rightarrow 4CH_4 + [CH_3ZnOSi(CH_3)_3]_4 \quad (4)$$

$$4(CH_3)_2Cd + 4HOSi(CH_3)_3 \rightarrow 4CH_4 + [CH_3CdOSi(CH_3)_3]_4 \quad (5)$$

Molecular-weight determinations show that the resulting heterosiloxanes of zinc and cadmium are tetrameric. The proposed cubane structure of the com-

Table 1. Physical constants and IR and NMR data of heterosiloxanes of the Group I and II triads.

Compound	M.p. (°C)	B.p. (°C/mm)	NMR (Hz) [b]		IR (cm^{-1})				Ref.
			δCH_3M	δCH_3Si	νSiO	νSiC	νMC	νMO	
(1) $[(CH_3)_2AuOSi(CH_3)_3]_2$	37–39	40/0.001 [a]	−57.5	− 8.5	910,882	681	578	478	[6]
(2) $\{Au[(CH_3)_3SiO]_3\}_2$	−30 decomp.	—	—	−12.8 [e] −20.2 [f]	895,875	682	—	502	[6]
(3) $Na\{Au[OSi(CH_3)_3]_4\}$	−20 decomp.	—	—	—	—	—	—	—	[6]
(4) $[CH_3ZnOSi(CH_3)_3]_4$	150 decomp.	125/1 [a]	+35.0	−9.5	862	676	541	437	[10]
(5) $[CH_3CdOSi(CH_3)_3]_4$	145 decomp.	135/1 [a]	+18.2 [c]	−8.0	869	680	442	409	[10]
(6) $\{Zn[OSi(CH_3)_3]_2\}_n$	200 decomp.	—	—	—	875	681	—	455	[5]
(7) $\{Cd[OSi(CH_3)_3]_2\}_n$	180 decomp.	—	—	—	910,890	677	—	428	[5]
(8) $\{Hg[OSi(CH_3)_3]_2\}_n$	0 decomp.	—	—	− 5.8	900	685	—	497	[5]
(9) $C_6H_5HgOSi(C_6H_5)_3$	140–141	—	—	—	—	—	—	—	[9]
(10) $CH_3HgOSi(CH_3)_3$	52	50/1 [a]	−45.0 [d]	− 2.0	903	673	552	480	[11]

[a] Sublimation. [b] NMR data in CCl_4 against tetramethylsilane as an internal standard; Varian A 60, 60 MHz. [c] $J(^1H-C-^{111}Cd) = \pm 80.5$ Hz; $J(^1H-C-^{113}Cd) = \pm 84.0$ Hz. [d] $J(^1H-C-^{199}Hg) = \pm 196.5$ Hz. [e] Bridge trimethylsiloxy groups. [f] Terminal trimethylsiloxy groups.

[6] *H. Schmidbaur* and *M. Bergfeld*, Inorg. Chem. *5*, 2069 (1966).

[7] *K. A. Andrianov, G. L. Slininskii, A. A. Zhdanov, E. A. Kashutina*, and *V. Yu. Levin*, Vysokomolekul. Soedineniya *8*, 898 (1966); Chem. Abstr. *65*, 5546 (1966).

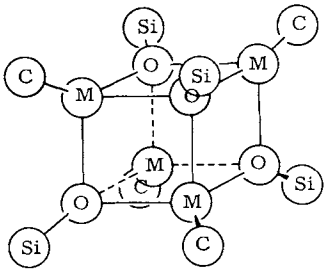
[8] *W. S. Tatlock* and *E. G. Rochow*, J. org. Chemistry *17*, 1555 (1952).

[9] *A. K. Ghosh, C. E. Hansing, A. J. Stutz*, and *A. G. MacDiarmid*, J. chem. Soc. (London) *1962*, 403.

[10] *F. Schindler, H. Schmidbaur*, and *U. Krüger*, Angew. Chem. *77*, 865 (1965); Angew. Chem. internat. Edit. *4*, 876 (1965).

[11] *H. Schmidbaur* and *F. Schindler*, Angew. Chem. *77*, 865 (1965); Angew. Chem. internat. Edit. *4*, 876 (1965).

pounds is confirmed by spectroscopic investigations and by (an almost completed) X-ray analysis. The corners of the distorted cube are occupied alternately by zinc or cadmium and oxygen atoms.

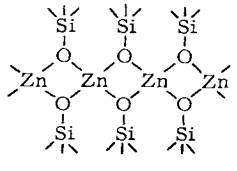


(4), M = Zn
(5), M = Cd

A similar structure has been suggested [12] and confirmed by X-ray analysis [13] for the recently prepared methylzinc methoxide ($CH_3Zn-OCH_3$). According to the crystallographic data, *(4)* forms monoclinic crystals of the space group P 2/n ($Z = 4$, $a = 17.625$ Å; $b = 19.839$ Å; $c = 9.85$ Å; $\beta = 97.49°$). The zinc-oxygen distances correspond to those in methylzinc methoxide (2.09 Å), while the silicon-oxygen distances are somewhat increased as a result of the coordination of the oxygen with three zinc atoms.

(4) and *(5)* are colorless crystalline substances; owing to the small size of their molecules they are readily soluble in organic solvents, and sublime under vacuum without decomposition. NMR and IR data and the physical constants of the compounds are listed in Table 1. Both compounds react with water to form methane, metal hydroxide, and trimethylsilanol.

Bis(trimethylsiloxy)zinc *(6)* and -cadmium *(7)* are formed in high yields as colorless, evidently polymeric compounds [5] by the metathetic reaction of $ZnCl_2$ and $CdBr_2$ with alkali metal trimethylsilanolates in diethyl ether. They are sparingly soluble in organic solvents, and do not sublime without decomposition. This behavior (which corresponds to that of zinc and cadmium alkoxides [12, 14]) and the spectroscopic data are compatible with a chain structure *(6)* or with a layer structure similar to that of lithium methoxide [14a].



(6)

The zinc atoms in both forms would have the coordination number 4. Attempts to sublime bis(trimethylsiloxy)zinc led to a surprising result. Above 110 °C, a colorless sublimate was formed that was positively identified as the tetramer *(4)*. The heating had evidently led to transmethylation, in which a methyl group was transferred from a silicon to a zinc atom [5]. The dimethylpolysiloxane required to balance the equation could also be detected in the reaction products.

$$\underset{(6)}{\{Zn[OSi(CH_3)_3]_2\}_n} \rightarrow \frac{n}{4}\ \underset{(4)}{[CH_3ZnOSi(CH_3)_3]_4} + [(CH_3)_2SiO]_n$$

This is one of the very few reactions in which organosilicon residues act as alkylating agents for other metals [15, 16]. The cadmium compound *(7)* does not exhibit this reaction under comparable conditions.

The first of the two articles that have so far dealt with the preparation of mercurosiloxanes [8] describes the reaction of $HgCl_2$ with sodium trimethylsilanolate in dioxane, which leads to the formation of impure, unstable bis(trimethylsiloxy)mercury *(8)*.

$$HgCl_2 + 2\ NaOSi(CH_3)_3 \rightarrow \underset{(8)}{Hg[OSi(CH_3)_3]_2} + 2\ NaCl$$

The compound has so far been characterized by IR spectroscopy only.

The other article [9], which was published soon afterwards, describes the preparation of tetraphenylmercurosiloxane *(9)* *via* the intermediate bis(triphenylsiloxy)mercury.

$$2(C_6H_5)_3SiONa + HgCl_2 \rightarrow [(C_6H_5)_3SiO]_2Hg + 2\ NaCl$$

$$x[(C_6H_5)_3SiO]_2Hg \rightarrow (x\text{-}1)\ \underset{(9)}{(C_6H_5)_3SiOHgC_6H_5} + (C_6H_5)_3SiO-[(C_6H_5)_2SiO]_x-HgC_6H_5$$

The same authors also synthesized *(9)* from phenylmercury chloride, potassium, and triphenylsilanol in diethyl ether.

$$(C_6H_5)_3SiOH + K + C_6H_5HgCl - 1/2\ H_2 \rightarrow \underset{(9)}{(C_6H_5)_3SiOHgC_6H_5} + KCl$$

Compound *(9)* forms colorless crystals having m.p. 140–141 °C. It reacts with HCl in diethyl ether to form C_6H_5HgCl and $(C_6H_5)_3SiOH$. When *(9)* is heated to 145 °C under nitrogen, diphenylmercury and a phenylpolysiloxane that contains mercury, $(C_6H_5)_3SiO[(C_6H_5)_2SiO]_x \cdot HgC_6H_5$, are formed.

The simplest mercurosiloxane $CH_3Hg-O-Si(CH_3)_3$ *(10)*, which cannot be prepared from dimethylmercury and trimethylsilanol, has become readily obtainable by the reaction of methylmercury halides with alkali metal trimethylsilanolates [11].

$$CH_3HgCl + NaOSi(CH_3)_3 \rightarrow NaCl + \underset{(10)}{CH_3Hg-O-Si(CH_3)_3}$$

Compound *(10)* is formed in excellent yields as a colorless sublimable compound, which is readily soluble in organic solvents, and which is even more sensitive to moisture than *(4)* and *(5)*. The results of molecular-weight determinations on solutions of *(10)* in benzene indicate a concentration-dependent equilibrium between monomer and oligomer. The measured molecular weight approaches the value for the monomer only at high dilution. On the other hand, X-ray analysis [17] shows that the compound is entirely tetrameric

[12] *G. E. Coates* and *D. Ridley*, J. chem. Soc. (London) *1965*, 1870.

[13] *H. M. M. Shearer* and *C. B. Spencer*, Chem. Commun. *1966*, 194.

[14] *W. L. German* and *T. W. Brandon*, J. chem. Soc. (London) *1942*, 526.

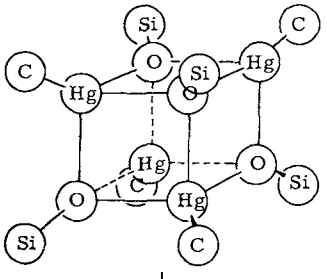
[14a] *P. J. Wheatley*, J. chem. Soc. (London) *1960*, 4270.

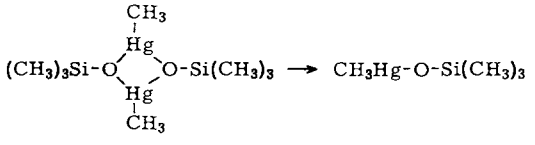
[15] *H. Schmidbaur* and *W. Findeiss*, Chem. Ber. *99*, 2187 (1966).

[16] *C. Dathe* and *R. Müller*, Chem. Ber. *98*, 235 (1965).

[17] *E. Hellner* and *G. Dittmar*, Lecture at the 7th Internat. IUC Congress (Internat. Union of Crystallography), Moscow 1966.

in the solid state. The distorted cubane structure of these molecules, in which the monomeric units are still clearly recognizable, is not retained in solution, in contrast to the behavior of the corresponding zinc and cadmium compounds. The tetramer undergoes degradation by the solvent into dimer and monomer. This clearly shows that mercury is a much weaker acceptor than zinc or cadmium.





The unit cell of the tetragonal crystals of *(10)* (space group P 4_2/nmc) has the following dimensions: a = 13.18 Å; c = 9.85 Å; d_{exp} = 2.2; d_{calc} = 2.37; Z = 8. The physical constants of the compound and its IR and NMR data are listed in Table 1.

According to recent investigations [5], the bis(trimethylsiloxy)mercury *(8)* obtained by the *Tatlock* and *Rochow* method [8], like the zinc and cadmium derivatives, is polymeric and has no definite melting point or decomposition point. However, attempted sublimation again resulted in intramolecular alkylation, which above 90 °C led to volatile tetramethylmercurosiloxane *(10)*.

$$\underset{(8)}{\{[(CH_3)_3SiO]_2Hg\}_n} \rightarrow n\ \underset{(10)}{CH_3HgOSi(CH_3)_3} + [(CH_3)_2SiO]_n$$

The methylmercury grouping in the sublimate could be detected by IR and NMR spectroscopy. A substance identical with that obtained from methylmercury chloride and sodium trimethylsilanolate was isolated.

No investigations on siloxy derivatives of monovalent mercury have so far been reported.

III. Siloxanes of Scandium, Yttrium, and Lanthanum

No heterosiloxanes of the elements of Group IIIb or of the lanthanide and actinide series are known as yet. The only exception is uranium, siloxy compounds of which were prepared and studied by *D. C. Bradley et al.* [18, 19]. This work will be discussed in Section VI.

[18] *D. C. Bradley, R. N. Kapoor,* and *B. C. Smith,* J. inorg. nuclear Chem. *24,* 863 (1962).

[19] *D. C. Bradley, R. N. Kapoor,* and *B. C. Smith,* J. chem. Soc. (London) *1963,* 204.

IV. Siloxanes of Titanium, Zirconium, and Hafnium

The titanosiloxanes are the most extensively studied group of heterosiloxanes of transition elements. Polymeric titanosiloxanes with a wide range of organic substituents both on the silicon and on the titanium have been prepared and studied by *K. A. Andrianov et al.*, as well as by other research groups. The incorporation of titanium into the inorganic skeleton of silicones can have a very favorable effect on the thermal stability of the compounds [20–23]. The stability of such compounds toward hydrolysis is fairly satisfactory, and is much better *e.g.* than that of the corresponding aluminosiloxanes [23–25].

A large number of polymeric and telomeric titanosiloxanes with alkyl and aryl substituents on the Si and Ti atoms [20–56]

[20] *A. I. Petrashko* and *K. A. Andrianov,* Vysokomolekul. Soedineniya *6,* 1405 (1964); Chem. Abstr. *61,* 16181 (1964).

[21] *K. A. Andrianov* and *A. A. Zhdanov,* Plastičeskie Massy *1962,* 24; Chem. Abstr. *57,* 15337 (1962).

[22] *J. B. Rust* and *H. H. Takimoto,* US.-Pat. 3013992 (1961); Chem. Abstr. *57,* 1091 (1962).

[23] *K. A. Andrianov,* Plastičeskie Massy *1960,* 23; Chem. Abstr. *55,* 12910 (1961).

[24] *A. A. Zhdanov* and *K. A. Andrianov,* Meždunarod. Simpozium po Makromol. Chim., Doklady, Moscow *1960,* Sect. 3, 440; Chem. Abstr. *55,* 10948 (1961).

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[27] *K. A. Andrianov, N. V. Varlamova, M. F. Borisov, A. G. Kolchina,* and *G. V. Grebenshchikova,* Plastičeskie Massy *1966,* 33; Chem. Abstr. *64,* 17727 (1966).

[28] *K. A. Andrianov, N. A. Kurasheva,* and *V. A. Avilov,* Izvest. Akad. Nauk SSSR, Ser. chim. *1965,* 1616; Chem. Abstr. *64,* 3586 (1966).

[29] *K. A. Andrianov* and *I. K. Kuznetsova,* Izvest. Akad. Nauk SSSR, Ser. chim. *1965,* 945; Chem. Abstr. *64,* 3588 (1966).

[30] *T. P. Avilova, V. T. Bykov, V. P. Marinin,* and *N. P. Shapkin,* Vysokomolekul. Soedineniya *7,* 2168 (1965); Chem. Abstr. *64,* 11328 (1966).

[31] *K. A. Andrianov, G. E. Golubkov, V. I. Elinek, N. A. Kurasheva, I. F. Manucharova, L. F. Litvinova,* and *B. K. Artemev,* Vysokomolekul. Soedineniya *7,* 680, 688 (1965); Chem. Abstr. *63,* 3057 (1965).

[32] *K. A. Andrianov, N. A. Kurasheva, I. F. Manucharova,* and *E. M. Berliner,* Izvest. Akad. Nauk SSSR, Neorgan. Materialy *1,* 294 (1965); Chem. Abstr. *63,* 5766 (1965).

[33] *Z. N. Nudel'man, K. A. Andrianov,* and *G. B. Kudryavitskaya,* Vysokomolekul. Soedineniya *4,* 440 (1962); Chem. Abstr. *62,* 6567 (1965).

[34] *A. N. Rodionov, E. Z. Asnovich, D. N. Shigorin,* and *K. A. Andrianov,* Vysokomolekul. Soedineniya, Geterotsepnye Vysokomolekul. Soedineniya *1964,* 81; Chem. Abstr. *61,* 4504 (1964).

[35] *K. A. Andrianov, M. A. Sipyagina,* and *T. I. Fridshtein,* Izvest. Akad. Nauk SSSR, Ser. chim. *1963,* 1672; Chem. Abstr. *59,* 15300 (1963).

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[37] *K. A. Andrianov,* USSR.-Pat. 148236 (1961); Chem. Abstr. *58,* 4659 (1963).

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[39] *K. A. Andrianov* and *M. A. Sipyagina,* Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1962,* 1392; Chem. Abstr. *58,* 2466 (1963).

[40] *D. C. Bradley* and *C. Prevedorou-Demas,* Canad. J. Chem. *41,* 629 (1963).

and with chelated Ti atoms[57–76] have been prepared and studied. However, a description of all the titanosiloxanes would be beyond the scope of the present article, and the reader is referred to monographs on the subject[2,3,77–85].

Low molecular weight titanosiloxanes can be prepared by the following methods:

a) By silylation of titanium alkoxides with acyloxysilanes[84,86–88]:

$$(RO)_4Ti + 4R'_3SiOCOR'' \rightarrow Ti(OSiR'_3)_4 + 4R''COOR$$

b) By silylation of titanium alkoxides with silanols[84,86,89–92]:

$$(RO)_4Ti + 4R'_3SiOH \rightarrow Ti(OSiR'_3)_4 + 4\ ROH$$

c) By heterolysis of siloxanes with titanium tetrahalides[84,93,94]:

$$TiX_4 + R_3SiOSiR_3 \rightarrow R_3SiOTiX_3 + R_3SiX$$

d) By silylation of titanium tetrahalides with silanols in the presence of tertiary amines[84]:

$$TiX_4 + 4R_3SiOH + 4R_3N \rightarrow Ti(OSiR_3)_4 + 4\ R_3HN^{\oplus}X^{\ominus}$$

[41] *J. B. Rust, C. L. Segal,* and *H. H. Takimoto*, US Dept. Commerce, Office Techn. Serv., PB Rep. 171522 (1959); Chem. Abstr. *58*, 14113 (91963).

[42] *K. A. Andrianov* and *I. F. Manucharova*, Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1962*, 420; Chem. Abstr. *57*, 11364 (1962).

[43] *H. J. Cohen* and *J. M. Hoyt*, US.-Pat. 3046267 (1962); Chem. Abstr. *57*, 13997 (1962).

[44] *K. A. Andrianov* and *N. A. Kurasheva*, Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1962*, 1011; Chem. Abstr. *57*, 12525 (1962).

[45] *K. A. Andrianov, Sh. V. Pichkhadze, V. V. Komarova,* and *Ts. N. Vardosanidze*, Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1962*, 833; Chem. Abstr. *57*, 15139 (1962).

[46] *K. A. Andrianov, Sh. V. Pichkhadze,* and *V. V. Komarova*, Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1962*, 724; Chem. Abstr. *57*, 16647 (1962).

[47] *J. B. Rust* and *H. H. Takimoto*, US.-Pat. 3013993 (1959); Chem. Abstr. *56*, 13098 (1962).

[48] *K. A. Andrianov*, Doklady Akad. Nauk SSSR *140*, 1310 (1961); Chem. Abstr. *56*, 8737 (1962).

[49] *K. A. Andrianov* and *Sh. V. Pichkhadze*, Vysokomolekul. Soedineniya *3*, 577 (1961); Chem. Abstr. *56*, 1585 (1962).

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[51] *K. A. Andrianov, N. P. Goshnikova,* and *E. Z. Asnovich*, Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1960*, 857; Chem. Abstr. *54*, 22008 (1960).

[52] *K. A. Andrianov* and *A. I. Petrashko*, Doklady Akad. Nauk SSSR *131*, 561 (1960); Chem. Abstr. *54*, 16375 (1960).

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[54] *A. I. Petrashko, K. A. Andrianov,* and *E. Z. Asnovich*, USSR.-Pat. 125681 (1960); Chem. Abstr. *54*, 15316 (1960).

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[61] *K. A. Andrianov* and *I. A. Lavygin*, Vysokomolekul. Soedineniya *7*, 1000 (1965); Chem. Abstr. *63*, 10122 (1965).

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[66] *B. P. Block* and *E. G. Meloni*, Inorg. Chem. *4*, 111 (1965).

[67] *K. A. Andrianov* and *I. A. Lavygin*, Izvest. Akad. Nauk SSSR Ser. chim. *1963*, 1857; Chem. Abstr. *60*, 2887 (1964).

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[92] *K. A. Andrianov* and *V. V. Astakhin*, Doklady Akad. Nauk SSSR *127*, 1014 (1959); Chem. Abstr. *54*, 266 (1960).

[93] *K. A. Andrianov* and *N. A. Kurasheva*, USSR.-Pat. 128020 (1960); Chem. Abstr. *55*, 1445 (1961).

[94] *K. A. Andrianov* and *N. A. Kurasheva*, Doklady Akad. Nauk SSSR *131*, 825 (1960); Chem. Abstr. *54*, 15054 (1960).

e) By degradation of dialkyl metatitanates with alkoxysilanes [84,95]:

$$(RO)_2Ti{=}O + (R'O)_4Si \rightarrow (R'O)(RO)_2TiOSi(OR')_3$$

f) By metathetic reaction of alkali metal [84,96,97] or heavy metal silanolates [84,98] with titanium halides:

$$TiX_4 + 4\ R_3SiOM^I \rightarrow Ti(OSiR_3)_4 + 4\ M^IX$$

The titanosiloxanes obtained in this way are listed in Table 2, together with their principal physical constants. The simple titanosiloxanes are colorless, distillable liquids or low-melting crystalline solids, most of which are readily soluble in organic solvents. The compounds are all monomeric, and with only a few exceptions, the titanium atom has the coordination number 4. A coordination number of 5 can be reached only in the presence of polydentate ligands such as $N(CH_2{-}CH_2OH)_3$ [89].

Table 2. Heterosiloxanes of titanium.

	Compound [a]	M.p. (°C)	B.p. (°C/mm)	Ref.
(11)	$Ti(OSiMe_3)_4$	—	110/10	[84,88]
(12)	$Ti(OSiEt_3)_4$	96	176—178/2.5	[84,91]
(13)	$Ti(OSiPh_3)_4$	501—505	370/1	[78,84,91,97,101]
(14)	$Ti(OSiEt_2Me)_4$	—	196/6	[84,91]
(15)	$Ti(OSiEtMe_2)_4$	—	140—142/5	[91]
(16)	$Ti(OSiPr_2Me)_4$	—	186/3	[84]
(17)	$Ti(OSiBu_2Me)_4$	99—101	195/3.5	[91]
(18)	$Ti(OSiPhMe_2)_4$		274—275/7	[84]
(19)	$Ti(OSiPh_2Me)_4$	—	370—374/6	[84,100]
(20)	$Ti(OSiPhEt_2)_4$	—	300—305/5	[91]
(21)	$TiCl(OSiMe_3)_3$	—	103—105/10	[84]
(22)	$TiCl_2(OSiMe_3)_2$	—	67/3	[84,94,102]
(23)	$TiCl_2(OSiMe_2Et)_2$	—	114—118/9	[102]
(24)	$TiCl_2(OSiMeEt_2)_2$	—	127—135/2	[102]
(25)	$TiCl_3(OSiMe_3)$	—	67/3	[84,94,102]
(26)	$TiCl_3(OSiMe_2Et)$	—	94—98/17	[102]
(27)	$TiCl_3(OSiMeEt_2)$	—	122—126/9	[102]
(28)	$TiBr_3(OSiMe_3)$	32—34	102—104/10	[102]
(29)	$TiClCp_2(OSiMe_3)$	137.7	—	[99]
(30)	$TiClCp_2(OSiPh_3)$	210—212	—	[96]
(31)	$TiCp(OSiMe_3)_3$	—	138—139/4	[99]
(32)	$TiCp_2(OSiPh_3)_2$	208—210	—	[96]
(33)	$Ti(OiPr)(OSiMe_3)_3$	—	91—93/8	[88]
(34)	$Ti(OiPr)_2(OSiMe_3)_2$	—	120/14	[84,88]
(35)	$Ti(OPr)_2(OSiEt_3)_2$	—	144—146/1.5	[92]
(36)	$Ti(OiPr)_3(OSiMe_3)$	—	114/13	[84]
(37)	$Ti(OBu)(OSiMe_3)_3$	—	76—77/2	[84]
(38)	$Ti(OBu)(OSiEt_3)_3$	—	182/4	[92]
(39)	$Ti(OBu)_2(OSiEt_3)_2$	—	186—188/6	[33,90]
(40)	$Ti(OBu)_3(OSiMe_3)$	—	176—177/8	[100]
(41)	$Ti(OPr)_3OSi(OPr)_3$	—	125—126/1	[84]
(42)	$Ti(OiBu)_3OSi(OiBu)_3$	—	75—78/10^{-5}	[84]
(43)	$Ti(OSiEt_3)(OC_2H_4)_3N$	166—168	—	[89]
(44)	$Ti(OSiPh_3)(OC_2H_4)_3N$	270—271	—	[89]
(45)	$Ti(OSiPh_2Me)(OC_2H_4)_3N$	172—174	—	[89]

[a] Abbreviations: Me = CH_3, Et = C_2H_5, Ph = C_6H_5, Pr = n-C_3H_7, Bu = n-C_4H_9, Cp = cyclopentadienyl, iPr = i-C_3H_7 iBu = i-C_4H_9.

According to investigations by *Andrianov* and *Zhdanov* [103], the Ti—O—Si linkage has a high resistance to hydrolysis. In compounds of the type $[(C_2H_5)_3SiO]_{3\text{ or }4}\ M^{III\text{ or }IV}$ (M = Ti, Al, Sn), the stability of the MOSi linkage to hydrolysis decreases in the order Ti > Al > Sn (ratio 2220:27.2:1). However, the stability of compounds of this type, as expected, also depends strongly on the nature of the organic substituent on the silicon. Bulky groups considerably increase the stability of a compound to hydrolysis.

Bradley et al. [86,104], in their work on titanosiloxanes, also studied analogous compounds of zirconium. Compounds containing Zr—O—Si linkages were prepared by two methods, which had also been successfully used for the preparation of titanosiloxanes. Zirconium tetraalkoxides react with trialkylsilanols in boiling benzene to form tetrakis(trialkylsiloxy)zirconium.

$$(RO)_4Zr + 4\ R'_3SiOH \rightarrow (R'_3SiO)_4Zr + 4\ ROH$$

If the alcohol is removed continuously by azeotropic distillation with benzene, the yields are greater than 70 %. Compounds of the same type can also be obtained from zirconium alkoxides and trialkylsilyl acetates. The yields in this case are higher than 50 %.

$$(RO)_4Zr + 4R'_3SiOCOCH_3 \rightarrow (R'_3SiO)_4Zr + 4CH_3COOR$$

Zirconosiloxanes can also be obtained readily and in high yields by elimination of alkali metal halide. Tetrakis(triphenylsiloxy)zirconium *(48)* has been prepared by this method [97].

$$ZrCl_4 + 4(C_6H_5)_3SiONa \rightarrow [(C_6H_5)_3SiO]_4Zr + 4NaCl \qquad (48)$$

The zirconosiloxanes are colorless, distillable substances and, like the titanosiloxanes, they are only slightly hydrolysed. Controlled partial hydrolysis in dioxane leads to polymeric organosiloxyzirconium oxides of varying composition [105], whereas total hydrolysis yields silanols and zirconium hydroxide. The zirconosiloxanes known so far, unlike the titanosiloxanes, are characterized by a tendency to associate that is strongly dependent on the bulk of the ligands R attached to the silicon. Molecular-weight determinations showed various degrees of oligomerization [86], the perethylated compound *(47)* being monomeric while the permethylated compound *(46)* is dimeric. This dimer is assumed to have a bridged structure in which the zirconium atom has a coordination number of 5.

[95] *A. N. Nesmeyanov, O. V. Nogina, A. M. Berlin,* and *Yu. P. Kudryavtsev,* Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1960,* 1206; Chem. Abstr. *55,* 352 (1961).

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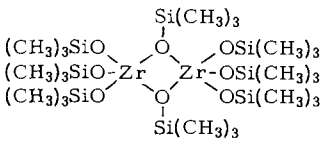
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(46)

However, the NMR spectrum of solutions of this substance in CCl_4 shows only one proton signal at room temperature, indicating a rapid transposition of the ligands on the zirconium atoms or else a very mobile oligomerization equilibrium (cf. *e.g.* [106]).

The reaction of diphenyldichlorosilane with propyl orthozirconates leads to polymers of the type $[(Si(C_6H_5)_2-O)_m-Zr(OC_3H_7)_2-O]_n$ [107].

Table 3. Heterosiloxanes of zirconium, hafnium, vanadium, niobium, and tantalum.

	Compound [a]	M.p. (°C)	B.p. (°C/mm)	Ref.
(46)	$[Zr(OSiMe_3)_4]_2$	*152*	*135/0.1*	*[86]*
(47)	$Zr(OSiEt_3)_4$	—	147/0.1	[86]
(48)	$Zr(OSiPh_3)_4$	410	$360/10^{-4}$ [b]	[97]
(49)	$Zr(OSiMe_2Et)_4$	105	105/0.1	[86]
(50)	$Zr(OSiMeEt_2)_4$	30	120/0.1	[86]
(51)	$Zr(OSiMe_2Pr)_4$	60	103/0.05	[86]
(52)	$Zr(OSiMe_2iPr)_4$	—	110/0.1	[86]
(53)	$Hf(OSiEtMe_2)_4$	—	—	[104]
(54)	$Hf(OSiPh_3)_4$	383	$360/10^{-4}$ [b]	[97]
(55)	$VO(OSiMe_3)_3$	−18	100/10	[113,117]
(56)	$VO(OSiEt_3)_3$	—	198–201/13	[111,117]
(57)	$VO(OSiPh_3)_3$	228	—	[114,115,117]
(58)	$VO(OSiMe_2Et)_3$	—	124–126/7	[117]
(59)	$VO(OSiMeEt_2)_3$	—	169–170/5	[117]
(60)	$VO(OSiPhEt_2)_3$	—	263–268/1.5	[117]
(61)	$VOCl(OSiMe_3)_2$	—	53/1	[118]
(62)	$VOCl_2(OSiMe_3)$	−39	35–36/1	[118]
(63)	$VS(OSiPh_3)_3$	200–202	—	[114]
(64)	$V(OSiPh_3)_4$	264–268	—	[114–116]
(65)	$V(OiPr)(OSiMe_3)_2$	—	63–67/1.5	[115]
(66)	$V(OiPr)_2(OSiMe_3)$	—	73–74/2.5	[115]
(67)	$Nb(OSiMe_3)_5$	—	120/0.1	[86]
(68)	$Nb(OSiMe_2Et)_5$	—	$140/10^{-4}$	[86]
(69)	$Ta(OSiMe_3)_5$	80	*84/0.05*	*[86]*
(70)	$Ta(OSiEt_3)_5$	210	210/0.1	[86]
(71)	$Ta(OSiMeEt_2)_5$	180	170/0.1	[86]
(72)	$Ta(OSiMe_2Et)_5$	135	135/0.1	[86]

[a] For abbreviations see Table 2; [b] Sublimation.

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Two groups of workers have so far reported on heterosiloxanes of hafnium. *Bradley et al.* [104] give the IR spectrum of $Hf[OSi(C_2H_5)(CH_3)_2]_4$ *(53)*, but do not describe either the preparation or the properties of this compound; *Gutmann et al.* [97] obtained tetrakis(triphenylsiloxy)hafnium *(54)* by reaction of sodium triphenylsilanolate with hafnium tetrachloride in boiling xylene.

$$4(C_6H_5)_3SiONa + HfCl_4 \rightarrow Hf[OSi(C_6H_5)_3]_4 + 4NaCl \qquad (54)$$

Tetrakis(triphenylsiloxy)hafnium forms white crystals having m.p. 383 °C, which can be recrystallized from benzene or toluene. The compound decomposes on melting, with deposition of carbon. There is no evidence that the siloxanes of hafnium tend to associate. The physical constants of some heterosiloxanes of zirconium and hafnium are listed in Table 3.

V. Siloxanes of Vanadium, Niobium, and Tantalum

Heterosiloxanes of pentavalent vanadium of the type $(R_3SiO)_3VO$, which may also be regarded as triorganosilyl vanadates, can be synthesized by eight different routes and isolated in the pure state. *M. G. Voronkov et al.* [91,108,109] used the reaction of triorganosilanols with vanadium pentoxide, which gives the desired products in yields of 50–80 % when the water is continuously removed from the equilibrium mixture.

$$6\ R_3SiOH + V_2O_5 \rightarrow 2\ (R_3SiO)_3VO + 3\ H_2O$$

The same silyl vanadates are also formed by the reaction of triorganosilanols with alkyl orthovanadates (yield approximately 90 %).

$$3\ R_3SiOH + R'_3VO_4 \rightarrow (R_3SiO)_3VO + 3\ R'OH$$

$VOCl_3$ may also be used as the vanadium component instead of V_2O_5 or R_3VO_4. The replacement of halogen by the triorganosiloxy residues of alkali metal silanolates leads almost quantitatively to the desired compounds.

$$VOCl_3 + 3\ R_3SiONa \rightarrow (R_3SiO)_3VO + 3\ NaCl$$

Even silanols react with $VOCl_3$ in the presence of hydrogen halide acceptors such as pyridine (yield 60–80 %).

$$VOCl_3 + 3\ R_3SiOH + 3\ C_5H_5N \rightarrow 3\ C_5H_5N^{\oplus}HCl^{\ominus} + (R_3SiO)_3VO$$

Schmidt and *Schmidbaur* independently obtained the compounds at the same time and by other routes [110].

Silver orthovanadate undergoes a heterogeneous but practically complete reaction with trimethylchlorosilane in benzene or methylene chloride:

$$Ag_3VO_4 + 3\ (CH_3)_3SiCl \xrightarrow{12\,^{\circ}C} [(CH_3)_3SiO]_3VO + 3\ AgCl \qquad (55)$$

Small quantities of silyl vanadate could also be obtained from V_2O_5 and hexamethyldisiloxane.

$$V_2O_5 + 3\ (CH_3)_3SiOSi(CH_3)_3 \rightleftarrows 2\ [(CH_3)_3SiO]_3VO \quad (55)$$

However, the yields in this reaction are unsatisfactory ($< 10\,\%$).

Other methods for the formation of V–O–Si linkages are the reaction of vanadium oxide chloride with lead silanolates [111] and the "alkoxy-acyloxy reaction" [112].

$$3\ Pb[OSi(C_2H_5)_3]_2 + 2\ VOCl_3 \rightarrow 2[(C_2H_5)_3SiO]_3VO + 3\ PbCl_2 \quad (56)$$

$$V(O\text{-}i\text{-}C_3H_7)_3 + (CH_3)_3SiOCOCH_3 \rightarrow (CH_3)_3SiOV(O\text{-}i\text{-}C_3H_7)_2 + CH_3COO\text{-}i\text{-}C_3H_7 \quad (66)$$

Thus nearly all the methods that have been used for the preparation of titanosiloxanes are also suitable for the preparation of heterosiloxanes of vanadium [113–116].

The physical constants of the compounds prepared by the above methods are listed in Table 3. The compounds with aliphatic substituents are colorless; they are very sensitive to moisture, and immediately become intensely red in presence of traces of water. The compounds are thermally relatively stable, and decompose only at high temperatures with elimination of hexaalkyldisiloxane and formation of polymeric trialkylsilyl metavanadates. The latter are brown compounds, are sparingly soluble in organic solvents, and

$$n(R_3SiO)_3VO \rightarrow n\ R_3SiOSiR_3 + (R_3SiOVO_2)_n$$

are hydrolysed only slowly [118]. Tris(trimethylsilyl)-vanadate *(55)* can be distilled without decomposition at 230 °C. The phenylated compounds are not only stable to heat, but also exhibit considerable stability to water and can therefore be purified in many cases by washing with water [114]. This stability is thought to be mainly due to steric effects.

Heterosiloxanes of tetravalent vanadium, such as *(64)*, are obtained by reaction of VCl_4 with alkali metal silanolates.

$$VCl_4 + 4\ (C_6H_5)_3SiONa \rightarrow 4\ NaCl + V[OSi(C_6H_5)_3]_4 \quad (64)$$

Tetrakis(triphenylsiloxy)vanadium *(64)* is the only member of this series that has been positively characterized. The compound is interesting because of the four oxygen atoms coordinated to the central vanadium atom, which is in the oxidation state +4 (cf. [119]). In the presence of atmospheric oxygen, *(64)* is slowly converted into tris(triphenylsilyl)orthovanadate *(57)* [114].

$$2V[OSi(C_6H_5)_3]_4 + 1/2\ O_2 \rightarrow 2[(C_6H_5)_3SiO]_3VO + [(C_6H_5)_3Si]_2O$$
(64) *(57)*

[119] *G. F. Kokoszka, H. C. Allen jr.*, and *G. Gordon*, Inorg. Chem. 5, 91 (1966).

Reaction with sulfur yields the corresponding thiovanadate *(63)* [114], which, like its oxygen analogues, is stable to cold water and is thermally very stable even above 200 °C.

$$2V[OSi(C_6H_5)_3]_4 + 1/8\ S_8 \rightarrow [(C_6H_5)_3SiO]_3VS \quad (63)$$
$$+ [(C_6H_5)_3SiO]_3VO + (C_6H_5)_3SiOSi(C_6H_5)_3 \quad (57)$$

Reactions of $VOCl_3$ with hexamethyldisiloxane led to the first trimethylsiloxy derivatives of monochloro- and dichlorovanadic acids [110, 118].

$$(CH_3)_3SiOSi(CH_3)_3 + VOCl_3 \rightarrow (CH_3)_3SiCl + (CH_3)_3SiOVOCl_2 \quad (62)$$

$$2(CH_3)_3SiOSi(CH_3)_3 + VOCl_3 \rightarrow 2(CH_3)_3SiCl + [(CH_3)_3SiO]_2VOCl \quad (61)$$

The cleavage of the siloxane takes place in stages, and if the trimethylchlorosilane is not removed from the equilibrium, the reaction stops at the dichlorovanadate stage *(62)*. If the equilibrium is displaced, the monochlorovanadate *(61)* is formed. The two silylchlorovanadates can also be obtained by the reaction of trimethylchlorosilane with trimethylsilyl orthovanadate or -chlorovanadate.

Finally, orthovanadate and dichlorovanadate coproportionate readily:

$$[(CH_3)_3SiO]_3VO + (CH_3)_3SiOVOCl_2 \rightarrow 2[(CH_3)_3SiO]_2VOCl \quad (61)$$

(61) and *(62)* are pale yellow and yellow liquids, respectively, which become brilliant red on contact with traces of moisture. They are hydrolysed in water, with formation of hydrogen chloride, trimethylsilanol, and vanadic acid. They can be distilled under vacuum without decomposition, but they decompose at high temperatures with elimination of trimethylchlorosilane.

Heterosiloxanes of vanadium have been suggested and patented for use as catalysts for the cracking of petroleum, as corrosion inhibitors, and as fuel and dye additives [40, 113, 116]. However, their effectiveness has not yet been confirmed.

Polymers containing the structural unit V–O–Si [120] are formed *e.g.* in the reaction of VCl_4 with diphenylsilanediol [115].

Whereas vanadium forms siloxanes of the types $(R_3SiO)_4V$ and $(R_3SiO)_3VO$, niobium and tantalum form only heterosiloxanes having the general formulae $(R_3SiO)_5Nb$ and $(R_3SiO)_5Ta$ [86, 104]. These compounds can be synthesized by the same methods as are used for Ti, Zr, and V compounds, *e.g.*:

$$(RO)_5Nb + 5R'_3SiOCOCH_3 \rightarrow (R'_3SiO)_5Nb + 5CH_3COOR$$
$$(RO)_5Ta + 5R'_3SiOH \rightarrow (R'_3SiO)_5Ta + 5ROH$$

The compounds of this class that are listed in Table 3 are colorless liquids or crystalline solids, which can be volatilized under vacuum without decomposition. They are all monomeric, and the metal atoms have a coordination number of 5. It is not known whether

the arrangement of the ligands is trigonal-bipyramidal or tetragonal-monopyramidal. No spectroscopic studies have so far been carried out. Heterosiloxanes of niobium and tantalum are all sensitive to hydrolysis and alcoholysis. Their properties are very similar to those of the corresponding alkoxides.

It was recently reported by *Bradley et al.*[121] that careful hydrolysis of pentakis(trimethylsiloxy)tantalum, unlike that of compounds of the type $El(OR)_5$ (where El = element of Group Va of the periodic system), but like that of $Ti[OSi(CH_3)_3]_4$ and of $Zr[OSi(CH_3)_3]_4$, yields soluble polymers of the type $\{TaO_x[OSi(CH_3)_3]_{(5-2x)}\}_n$. Other polymeric siloxanes of Nb and Ta are described in a report mentioned earlier[120].

VI. Siloxanes of Chromium, Molybdenum, Tungsten, and Uranium

In most of the heterosiloxanes of chromium that have been described so far, the element is present in the hexavalent state. Working with chromosiloxanes (silyl chromates) has proved to be extremely dangerous, and very often leads to serious explosions[122–124]. Consequently, these compounds must not be handled carelessly.

Bis(trimethylsilyl)chromate $[(CH_3)_3SiO]_2CrO_2$ *(73)* is a brilliant orange-red liquid, which can be prepared in good yields from anhydrous chromium trioxide and hexamethyldisiloxane.

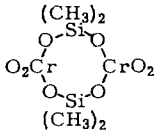
$$(CH_3)_3SiOSi(CH_3)_3 + CrO_3 \rightarrow [(CH_3)_3SiO]_2CrO_2 \qquad (73)$$

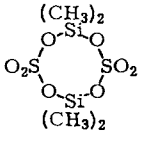
This heterolysis of the disiloxane bridge by chromium trioxide proceeds in a manner similar to the cleavage with sulfur trioxide or selenium trioxide[125–127]. Complete reaction of the chromium trioxide is observed in an excess of siloxane, even under mild conditions[124]. The product can be purified by careful vacuum distillation, but this can lead to explosion for no apparent reason. Even when no explosion occurred, the compound was found to decompose slowly with deposition of dark, lower chromium oxides. Bis(trimethylsilyl)chromate (b.p. 60 °C/0.2 mm Hg and $n_D^{20} = 1.4937$) is immediately hydrolysed by water to chromic acid and trimethylsilanol.

$$[(CH_3)_3SiO]_2CrO_2 + 2\,H_2O \rightarrow 2\,(CH_3)_3SiOH + H_2CrO_4$$

The quantitative determination of the chromic acid may be used for the analysis of the compound.

Experiments with dimethylpolysiloxane and octamethylcyclotetrasiloxane instead of hexamethyldisiloxane[118] have shown that CrO_3 can also be incorporated into these compounds to give products that are deep yellow silicone oils, in which some of the Si–O–Si groups have not been converted into Si–O–CrO_2–O–Si bridges. Before the reaction is complete, decomposition with deposition of lower chromium oxides again takes place. Owing to the danger of explosion, no attempt was made to separate by distillation the pure dimethylsilyl chromate, which, like the corresponding sulfate, should be dimeric with an eight-membered ring structure.





The product obtained is probably best described by the general formula:

$$[-O-Si(CH_3)_2]-[CrO_4-Si(CH_3)_2]_a-[O-Si(CH_3)_2-]_b \qquad (a, b = 1, 2, 3 \ldots)$$

F. C. Saunders[122] reported a violent explosion when a mixture of methylpolysiloxanes was heated with CrO_3.

Solutions of chromosiloxanes in an excess of hexamethyldisiloxane can be used as oxidizing agents for organic compounds[118]. CrO_3 is a milder oxidizing agent in this form than in *e.g.* glacial acetic acid. The fact that the oxidation can be carried out in homogeneous nonaqueous or aprotic solvents is often an advantage. The dangerous silyl chromates need not be isolated for this purpose, the substance in question simply being allowed to react with CrO_3 in hexamethyldisiloxane.

Compounds containing the Cr–O–Si grouping have also been obtained by other routes. Thus the reaction of chromyl chloride with sodium triphenylsilanolate yields bis(triphenylsilyl) chromate having m.p. 138 to 140 °C[115].

$$CrO_2Cl_2 + 2NaOSi(C_6H_5)_3 \rightarrow [(C_6H_5)_3SiO]_2CrO_2 + 2NaCl \qquad (74)$$

Siloxy compounds of tetravalent chromium can be prepared from Cr^{IV} alkoxides and silanols[128].

$$Cr(OC_4H_9)_4 + 4(C_2H_5)_3SiOH \rightarrow [(C_2H_5)_3SiO]_4Cr + 4C_4H_9OH \qquad (75)$$

The silyl chromates prepared are listed, together with their physical constants, in Table 4.

Silyl chromates of the type $R_3Si-O-CrO_2-O-SiR_3$ have been used as catalysts for the polymerization

[120] *M. M. Chamberlain*, US Dept. Commerce, Office Techn. Serv., AD 601415 (1964); Chem. Abstr. *62*, 1311 (1965).

[121] *D. C. Bradley* and *C. Prevedorou-Demas*, J. chem. Soc. (London) *A 1966*, 1139.

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[123] *E. W. Abel*, Z. Naturforsch. *15b*, 57 (1960).

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[127] *M. Schmidt*, *I. Ruidisch*, and *H. Schmidbaur*, Chem. Ber. *94*, 2451 (1961).

[128] *J. S. Basi* and *D. C. Bradley*, Proc. chem. Soc. (London) *1963*, 305.

Table 4. Heterosiloxanes of chromium, uranium, rhenium, iron, cobalt, and platinum.

	Compound [a]	M.p. (°C)	B.p. (°C/mm)	Ref.
(73)	$CrO_2(OSiMe_3)_2$	−20	60/0.2	[123, 124]
(74)	$CrO_2(OSiPh_3)_2$	138–140	–	[115]
(75)	$Cr(OSiEt_3)_4$	–	–	[128]
(76)	$UCl_2(OSiEt_2Me)_2$	–	260/0.01	[18]
(77)	$U(OSiMe_3)_5$	–	150/0.1 [b]	[18]
(78)	$U(OSiEt_3)_5$	–	180/0.1 [b]	[19]
(79)	$U(OSiMe_2Et)_5$	–	155/0.1 [b]	[19]
(80)	$U(OSiMeEt_2)_5$	–	160/0.1 [b]	[19]
(81)	$U(OSiMe_3)_6$	–	180/0.1 [b]	[19]
(82)	$U(OSiEt_3)_6$	–	195/0.05 [b]	[19]
(83)	$U(OSiMe_2Et)_6$	–	165/0.1 [b]	[19]
(84)	$U(OSiMeEt_2)_6$	–	175/0.1 [b]	[19]
(85)	$ReO_4(SiMe_3)$	79.5–80.5	70/1 [b]	[134]
(86)	$[Fe(OSiMe_3)_3]_2$	179–181	–	[135, 139]
(87)	$Li[Fe(OSiMe_3)_3]_4$	–	–	[135, 139]
(88)	$Na[Fe(OSiMe_3)_3]_4$	–	–	[135, 139]
(89)	$K[Fe(OSiMe_3)_3]_4$	–	–	[135, 139]
(90)	$Me_4Sb[Fe(OSiMe_3)_3]_4$	193	190/1 [b]	[135, 138]
(91)	$Co(OSiMe_3)_2$	–	160–180/1 [b]	[146]
(92)	$Me_3PtOSiMe_3$	98	–	[5]

[a] For abbreviations see Table 2; [b] Sublimation.

of olefins [129, 130]. (For polymeric chromosiloxanes see [120].)

Attempts to prepare halogenochromic acid derivatives of the silanols have been unsuccessful [118]. The reaction of the acid anhydrides sulfur trioxide and selenium trioxide with halogenosilanes [131, 132] could not be observed in the case of CrO_3 and trimethylchlorosilane.

$$SO_3 + (CH_3)_3SiCl \rightarrow (CH_3)_3SiO{-}SO_2{-}Cl$$

$$CrO_3 + (CH_3)_3SiCl \rightarrow (CH_3)_3SiO{-}CrO_2{-}Cl$$

Whereas no reaction could be detected below 50 °C, a redox reaction with evolution of chlorine took place above 50 °C.

Descriptions of the preparation of chromosiloxanes from siloxanes and CrO_2Cl_2 in the patent literature are particularly interesting in this connection [133]. Such a reaction would have to proceed *via* silyl chlorochromates. However, it would be necessary to establish that these reactions can be carried out in the desired manner.

Thus of the analogous series of compounds

$Cl_3TiOSi(CH_3)_3$ $Cl_2OVOSi(CH_3)_3$

$ClO_2CrOSi(CH_3)_3$ $O_3MnOSi(CH_3)_3$

only the first two can be prepared, whereas the last two (see below) autoxidize spontaneously.

Attempts to prepare heterosiloxanes of molybdenum and of tungsten by conventional methods were unsuccessful for a long time. Neither the reaction of siloxanes with molybdenum trioxide nor the reaction of alkylchlorosilanes with silver molybdate led to the desired compounds [118].

Molybdenum dioxide dichloride reacted with hexamethyldisiloxane, but isolation of the desired product was prevented by a subsequent redox reaction with separation of molybdenum blue. However, compounds containing the system Mo–O–Si are reported to be formed by the reaction of sodium triphenylsilanolate with the dimethylformamide complex of $MoO(OH)_2Cl_2$ [115] but the compounds formed have not yet been fully characterized.

Polyheterosiloxanes of tungsten have been prepared by *M. M. Chamberlain* [120]. However, no definite low molecular weight siloxy compounds of tungsten have been reported as yet.

Heterosiloxanes of the actinide element uranium have been studied by *D. C. Bradley et al.* [18, 19]. The compounds were prepared by methods that have already been mentioned several times:

$$U(OC_2H_5)_5 + 5R_3SiOH \rightarrow U(OSiR_3)_5 + 5C_2H_5OH$$

$$U(OC_2H_5)_6 + 6R_3SiOH \rightarrow U(OSiR_3)_6 + 6C_2H_5OH$$

$$UCl_4 + 2(C_2H_5)_2CH_3SiOLi \rightarrow Cl_2U[OSi(C_2H_5)_2CH_3]_2 + 2LiCl \quad (76)$$

The resulting compounds of pentavalent uranium are yellow-brown to yellow-green, whereas those of the hexavalent metal are orange-red to red sublimable solids; the only known derivative of tetravalent uranium is a green distillable solid. Molecular-weight determinations in boiling benzene showed that the permethylated silanolate of pentavalent uranium is associated; it is almost dimeric on average (n = 1.77). Pentakis(triethylsilyl)uranate(v), on the other hand, is strictly monomeric. A similar dependence of association on the substituent has already been mentioned in connection with the heterosiloxanes of zirconium. The silanolates of hexavalent uranium are all monomeric, irrespective of the nature of the organic substituent. This observation seems quite plausible in view of the steric conditions.

VII. Siloxanes of Manganese, Technetium, and Rhenium

No heterosiloxanes of manganese are known as yet. Several attempts have been made to prepare the fundamentally feasible compounds $R_3SiOMnO_3$ of heptavalent manganese from trimethylchlorosilane and silver permanganate and from hexamethyldisiloxane and dimanganese heptoxide [118]. However these reactions always resulted in reduction of the heptavalent manganese and deposition of manganese dioxide. As in the case of chromium(VI) compounds, explosions occur when these compounds are handled carelessly.

Reactions of this type were not carried out with technetium compounds. Owing to the much weaker oxidizing power of Tc^{VII} compared with that of manganese, however, it should be possible to prepare silyl pertechnates, and these should be reasonably stable.

[129] Union Carbide Corp., Belg. Pat. 637740 (1963); Chem. Abstr. *62*, 9255 (1965).

[130] Union Carbide Corp., Netherlands Pat. 298323 (1963); Chem. Abstr. *64*, 14308 (1966).

[131] *M. Schmidt* and *H. Schmidbaur*, Angew. Chem. *70*, 657 (1958).

[132] *M. Schmidt* and *H. Schmidbaur*, Chem. Ber. *95*, 47 (1962).

[133] *F. E. Granchelli* and *G. B. Walkers*, US.-Pat. 2863891 (1958); French Pat. 1179740 (1959).

The remarkably stable rhenium siloxane *(85)* was prepared in very good yields several years ago [134].

$$(CH_3)_3SiCl + AgReO_4 \xrightarrow{-AgCl} (CH_3)_3SiReO_4 \quad (85)$$

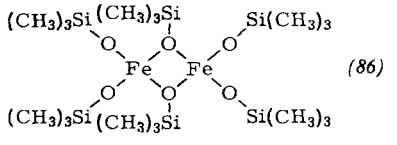
$$1/2\ [(CH_3)_3Si]_2O + 1/2\ Re_2O_7 \rightarrow$$

Trimethylsilyl perrhenate forms colorless crystals having m.p. 79.5–80.5 °C, which are very soluble in organic solvents. Hydrolysis leads to trimethylsilanol and to quantitative formation of perrhenic acid, which can be titrated alkalimetrically.

VIII. Siloxanes of Iron, Cobalt, Nickel, and Platinum

A number of low molecular weight heterosiloxanes of trivalent iron have become known in recent years [135–140]. Dimeric tris(trimethylsiloxy)iron *(86)* is formed in good yields [125,139] in accordance with the following equation:

$$2\ FeCl_3 + 6\ NaOSi(CH_3)_3 \longrightarrow 6\ NaCl +$$



(86)

The compound forms yellow-green, wax-like crystals having m.p. 179–181 °C, which are very readily soluble in aprotic organic solvents.

Like the corresponding aluminum and gallium derivatives [141,142], the compound has a structure with a four-membered iron-oxygen ring system. The 3-coordinate oxygen atoms in this dimer give the compound a distinctly unsaturated character, which becomes particularly noticeable on addition of alkali metal or pseudoalkali silanolates. The four-membered ring system is opened and each of the iron atoms acquires an additional silanolate ligand. In this way the metal retains a coordination number of four without the need for unstable bridge bonds.

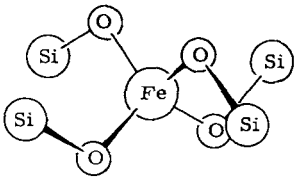
The alkali metal or pseudoalkali tetrakis(trimethylsiloxy)ferrates [135,137,139,140], *(87)–(90)*, are formed in accordance with the equation:

$$\underset{(86)}{\{Fe[OSi(CH_3)_3]_3\}_2} + 2\ MOSi(CH_3)_3 \rightarrow 2\ M\{Fe[OSi(CH_3)_3]_4\}$$

(87), M = Li *(89)*, M = K
(88), M = Na *(90)*, M = $(CH_3)_4Sb$

The ionic compounds *(87)–(89)* are pale yellow, and are very sparingly soluble in organic solvents. They do not melt or sublime below about 200 °C, at which temperature they decompose slowly with deposition of Fe_2O_3. The well-formed crystals of the ionic tetramethylstibonium tetrakis(trimethylsiloxy)ferrate *(90)* [137,140] are readily soluble in polar organic solvents, but only slightly soluble in nonpolar solvents. They melt at 193 °C and sublime at 190 ° C/1 mm Hg.

Crystallographic investigations on *(90)* [143] indicated an orthorhombic structure having the space group P_{mmn} with $a = 13.50_8$ Å; $b = 11.95_8$ Å; $c = 9.81$ Å; $U = 1584.9$ Å^3; $d_{exp.} = 1.25$; $d_{calc.} = 1.246$.



The compound *(90)* is therefore isostructural with the corresponding tetrakis(trimethylsiloxy)aluminates and gallates [143]. The four oxygen atoms are arranged tetrahedrally around the iron atom.

The recently prepared complex of this iron siloxane with trimethylamine oxide has a similar structure. This coordination compound is formed almost quantitatively in accordance with

$$(86) + 2\ (CH_3)_3NO \rightarrow [(CH_3)_3Si{-}O]_3Fe{-}O{-}N(CH_3)_3.$$

The pale yellow crystals, which are very sensitive to hydrolysis and to autoxidation, have m.p. 86–90 °C and can be distilled at 145–148 °C/1 mm Hg. The donor strength of trimethylamine oxide is evidently sufficiently great to displace the bridge siloxy oxygen atoms from the coordination with the iron atom and to open the four-membered ring [143a].

Only two articles have been published on polymeric siloxanes of iron [144,145]. *K. A. Andrianov et al.* [144] obtained polyheterosiloxanes containing Fe–O–Si structural units from anhydrous $FeCl_3$ and $C_6H_5Si(OH)_2ONa$ and by the action of aqueous NaOH and iron(III) ammonium sulfate on a polyphenylsiloxane prepared from $H_2O/C_4H_9OH/(C_6H_5)SiCl_3$. The preparation of polyferrosiloxanes by treatment of the monoalkali metal salt of an organosilandiol or -triol with FeX_3 is described in a patent [145]. The resulting compounds which contain the structural unit $-Fe(OSiR_3)-OSiR_2-OSiR_2-O-$ were not characterized further.

Little is known as yet about heterosiloxanes of cobalt and nickel. $CoCl_2$ and sodium trimethylsilanolate give the deep blue, wax-like crystalline bis(trimethylsiloxy)-

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[137] *H. Schmidbaur*, Angew. Chem. *75*, 137 (1963); Angew. Chem. internat. Edit. *2*, 94 (1963).
[138] *H. Schmidbaur*, Chem. Ber. *97*, 459 (1964).
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[142] *H. Schmidbaur*, Chem. Ber. *96*, 2692 (1963).
[143] *P. J. Wheatley*, J. chem. Soc. (London) *1963*, 3200.
[143a] *F. Schindler* and *H. Schmidbaur*, unpublished.
[144] *K. A. Andrianov*, *T. N. Ganina*, and *N. N. Sokolov*, Vysokomolekul. Soedineniya *4*, 678 (1962); Chem.Abstr.*58*, 9239 (1963).
[145] Distillers Co. Ltd., Brit. Pat. 978666 (1962); Chem. Abstr. *62*, 6650 (1965).

cobalt *(91)* [146], in accordance with the following equation:

$$CoCl_2 + 2\ NaOSi(CH_3)_3 \rightarrow Co[OSi(CH_3)_3]_2 + 2\ NaCl$$
(91)

Compound *(91)* sublimes at 160–180 °C/1 mm Hg, is paramagnetic, and is extremely sensitive to oxygen and moisture; its structure has not yet been elucidated.

In addition to this compound, a number of polymers having Co–O–Si and Ni–O–Si structural units have been described; these are reported to have extremely high thermal stabilities and to be slowly hydrolysed only in hot water. These polymers are obtained from dialkyldialkoxysilanes and cobalt or nickel acetate. The reaction of diorganosilanediolates with cobalt chloride leads to compounds of this type [147, 148].

An article by *Andrianov* and *Zhdanov* [149] is particularly interesting in this connection. According to these authors, compounds containing Co–O–Si and Ni–O–Si structural units could not be obtained by the reaction of $RSi(OH_2)ONa$ with $CoCl_2$ or $NiCl_2$ in butanol. The addition of $AlCl_3$ in the case of $CoCl_2$ yields a violet polymer, while with $NiCl_2$ a green polymer is obtained; however, in addition to the desired structural units, these compounds also contain Al–O–Si bonds. The thermochemical properties of polycobaltsiloxanes have recently been studied [7].

Heterosiloxanes of the light and heavy platinum metals have so far been almost completely ignored. The first success was reported only very recently in the case of the heterosiloxanes of platinum [5]. Trimethylplatinum chloride reacts with lithium tetramethylsilanolate in tetrahydrofuran with deposition of LiCl and formation of a hexamethylplatinosiloxane *(92)*, which can be isolated with some difficulty:

$$(CH_3)_3PtCl + LiOSi(CH_3)_3 \rightarrow (CH_3)_3Pt{-}O{-}Si(CH_3)_3 + LiCl$$
(92)

The compound *(92)*, which forms colorless crystals having m.p. 98 °C, does not sublime without decomposition but can be recrystallized from petroleum ether. Above 100 °C *(92)* decomposes with deposition of metallic platinum. The NMR spectrum ($\delta_{CH_3(Pt)} = -69$ Hz; $\delta_{CH_3(Si)} = -6.5$ Hz; J (^1H–C–^{195}Pt) = 78.5) confirms the proposed composition, as does the IR spectrum (νSiO = 904; νSiC = 671, 615; νPtC = 584, 558; νPtO = 440).

Compound *(93)* represents an important addition to the homologous series of the heterosiloxanes of the heavy metals: $Me_3PtOSiMe_3$; $Me_2AuOSiMe_3$; $MeHgOSiMe_3$; $TlOSiMe_3$; $Me_2TlOSiMe_3$; $Me_3PbOSiMe_3$; $Me_2BiOSiMe_3$ (Me = CH_3) [5].

Note: A monograph on "Organoelement Compounds of Silicon" by *S. N. Borisov, M. G. Voronkov,* and *E. Ya. Lukevits* has now been published (Izd. Khimiya, Leningrad 1966), in which the subject of the present article is dealt with at length.

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Translated by Express Translation Service, London

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[148] *C. Schneider* and *G. Berg*, Makromolekulare Chem. *54*, 171 (1962).

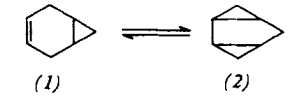
[149] *K. A. Andrianov* and *A. A. Zhdanov*, Izvest. Akad. Nauk SSSR, Otdel. chim. Nauk *1959*, 1590; Chem. Abstr. *54*, 8687 (1960); see also *D. C. Bradley* in [2].

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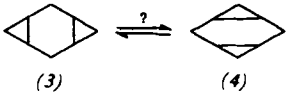
Valence Isomerizations of Hydrocarbons Containing Three-Membered Rings

By *E. Wiskott* and *P. v. R. Schleyer* [*]

Several examples of light induced valence isomerizations of the general type *(1)* → *(2)* have been reported recently [1a]. It is known that reverse reactions *(2)* → *(1)* can sometimes take place thermally [1b]. Thermal automerizations (degenerate isomerizations) [1c] of type *(3)* ⇌ *(4)* are of particular



(1) *(2)*



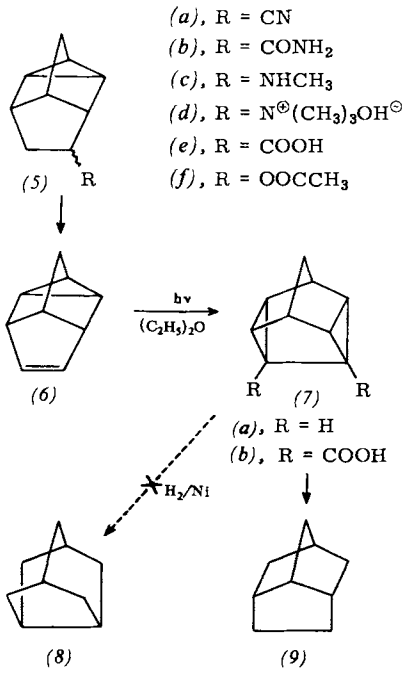
(3) *(4)*

interest, but transformations of this type are formally forbidden by the Woodward-Hoffmann rules [2], and attempts to detect such rearrangements have failed [3]. Only one exception is known to us, and this involves a compound activated by carboxyl substituents [4]. Stimulated by recent literature reports [5, 6] we herewith present our own observations on molecules representative of these two classes.

Tetracyclo[4.3.0.$0^{2,4}$.$0^{3,7}$]non-8-ene *(6)* [6–8], the starting material for our investigations, was prepared by two different methods from the readily available nitrile *(5a)* [9]. The first route involved the following steps: Partial hydrolysis of *(5a)* to the amide *(5b)*; Hofmann rearrangement of the latter in methanol to a methyl urethane followed by $LiAlH_4$ reduction to methylamine *(5c)*; and quaternization of *(5c)* to *(5d)*. Hofmann elimination of *(5d)* gave the desired olefin in 22 % overall yield, calculated from *(5a)*. The second route (based on the method of *LeGoff* and *Slee* [8]) was somewhat simpler: Hydrolysis of the nitrile *(5a)* gave an acid *(5e)* which could be converted to the acetate *(5f)* by the action of lead tetraacetate. Pyrolysis of *(5f)* at 500 °C gave *(6)* in 70 % yield. The overall yield of *(6)* calculated from *(5a)* was 32 %.

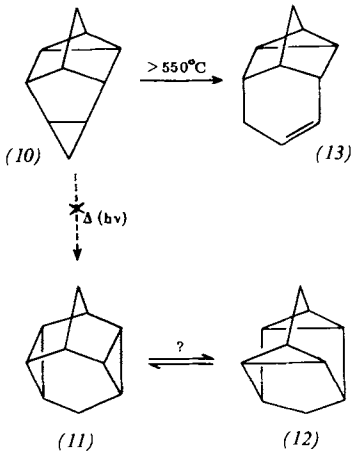
When *(6)*, a compound of type *(1)*, was irradiated in ether (450 W Hanovia lamp, no filter), pentacyclo[4.3.0.-$0^{2,4}$.$0^{3,8}$.$0^{5,7}$]nonane *(7a)*, m.p. 85–87 °C, was produced. A yield of 30 % was realized using gas chromatographic isolation.

Very recently, failure of a similar attempt to convert *(6)* into *(7a)* has been reported [6]. This failure was due, evidently, to the use of acetone as the solvent, *i.e.* the experiment was



conducted under conditions which favor dimerization rather than isomerization. A description of a different preparation of *(7a)*, by bisdecarboxylation of *(7b)*, has just appeared[5]. The physical and spectroscopic properties of *(7a)* produced by the two routes are in agreement.

We had hoped to be able to prepare noradamantane *(8)* by hydrogenation of *(7a)*. However, with Raney-nickel catalyst under high pressure conditions, brendane *(9)*[10] was the main product and only a trace, at most, of noradamantane *(8)* was formed[11]. Both cyclopropane rings were reduced from the same side of the molecule, a reduction course also observed with triasterane *(14)*[12].



Cyclopropanation[13] of *(6)* gave pentacyclo[4.4.0.0^{2,4}.0^{3,7}.0^{8,10}]decane *(10)*, b.p. 170–172 °C, in 65 % yield. NMR in CCl_4 at 60 MHz: τ = 7.94 (2H); 8.61 (2H); 8.76 (1H); 8.80–9.05 (5H); 9.45–10.20 (2H). The mass spectrum of *(10)* gave a parent peak at *m/e* = 132, a base peak at *m/e* = 118, and additional prominent peaks at *m/e* = 39, 54, 78, 91, 104, and 116.

All our attempts to isomerize *(10)*, a compound of type *(3)*, to "tetradehydroadamantane" *(11)* failed. Thermally *(10)* was stable below 550 °C. Above that temperature only rearrangement to an olefin, probably *(13)*, occurred. After irradiation of *(10)* for 200 hours under the conditions used for *(6)*, only starting material was recovered. We are now attempting to isomerize derivatives of *(10)*, activated by suitable substituents.

In view of the failure of *(10)* to isomerize to *(11)*, and of *(14)* and *(15)* to interconvert[3], the ready transformation of *(11)* into *(12)* also seems unlikely. As mentioned, all of these valence isomerizations are of the type *(3)* $\rightleftharpoons$ *(4)* which the Woodward-Hoffmann rules[2] indicate to be forbidden processes.

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[*] Dr. E. Wiskott and Prof. P. v. R. Schleyer
Department of Chemistry
Princeton University
Princeton, New Jersey 08540 (U.S.A.)

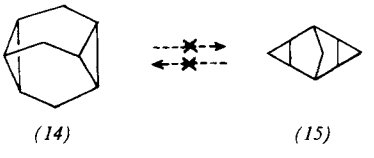
[1a] *H. Prinzbach, W. Eberbach*, and *G. v. Veh*, Angew. Chem. *77*, 454 (1965); Angew. Chem. internat. Edit. *4*, 436 (1965); *P. K. Freeman, D. G. Kuper*, and *V. N. M. Rao*, Tetrahedron Letters *1965*, 3301; *H. Prinzbach, W. Eberbach, M. Klaus, G. v. Veh*, and *U. Scheidegger*, *ibid. 1966*, 1681; *R. Askani*, Chem. Ber. *98*, 3618 (1965); *C. F. Huebner, E. Donoghue, L. Dorfman, E. Wenkert, W. E. Streth*, and *S. W. Donely*, Chem. Comm. *1966*, 419.

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[2] *R. Hoffmann*, personal communication.

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Synthesis of Oligonucleotides by Use of Phosphoric Triesters [1]

By *F. Eckstein* and *I. Rizk* [*]

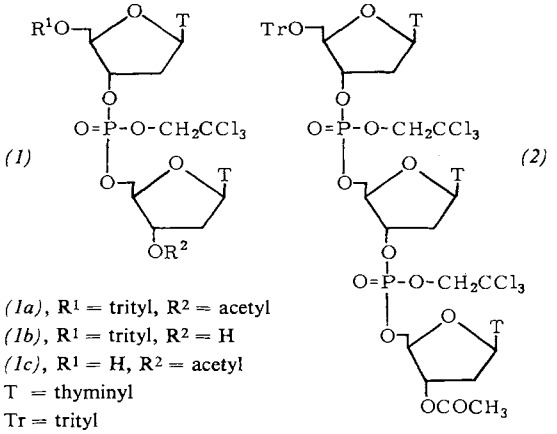
In the synthesis of higher oligonucleotides by-products arise that can be traced to activation of the internucleotide bond by the condensing agent[2]. Esterification of the free OH groups on the phosphate bridges should repress these side reactions and, further, make it possible to separate the products on silica gel.

We therefore activated the pyridinium salt of 2,2,2-trichloroethyl 5′-trityl-3′-thymidylic acid ($NH_4^{\oplus}$ salt: m.p. 226 °C)[3,4] (0.5 mmole) with 2,4,6-triisopropylbenzenesulfonyl chloride (1 mmole) in pyridine (3 ml) (12 h at room temperature)

and then condensed the product with 3′-*O*-acetylthymidine (0.5 mmole) (further 12 h at room temperature)[5]. We were then able to isolate the triester *(1a)*[4] in 55% yield by preparative thin-layer chromatography of the reaction mixture (Merck-Kieselgel PF 254, chloroform/methanol = 93:7 v/v).

Reduction of *(1a)* with Zn dust in 80% acetic acid (20 min at room temperature) and subsequent removal of the trityl and acetyl groups gave TpT[6] (90% yield).

Hydrolysis of *(1a)* with concentrated ammonia (2 h) gave tritylthymidine, thymidine, and *(1b)* in the relative yields 25:20:55, together with phosphoric acid diesters. Acid hydrolysis (80% acetic acid, 100 °C, 10 min) afforded exclusively *(1c)*.



(1) *(2)*

(1a), R^1 = trityl, R^2 = acetyl
(1b), R^1 = trityl, R^2 = H
(1c), R^1 = H, R^2 = acetyl
T = thyminyl
Tr = trityl

Replacing the acetylthymidine in the condensation by *(1c)* yields 55% of the oligonucleotide ester *(2)*[4] (amorphous, m.p. 143 °C). Fission of the trichloroethyl group by reduction with Zn dust and 80% acetic acid and removal of the trityl and acetyl groups gives TpTpT[6] (85% yield).

RF values on Merck DC-prepared silica gel plates F_{254}, chloroform/methanol = 93:7 v/v

5′-Tritylthymidine	0.63	*(1a)*	0.86
3′-Acetylthymidine	0.52	*(1b)*	0.38
(2)	0.57	*(1c)*	0.42

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[*] Dr. F. Eckstein and Dipl.-Chem. I. Rizk
Max-Planck-Institut für experimentelle Medizin,
Abteilung Chemie
Hermann-Rein-Str. 3
34 Göttingen (Germany)

[1] Part XI of Syntheses of Oligo- and Poly-nucleotides. – Part X: *F. Cramer, W. Frölke*, and *H. Matzura*, Angew. Chem. 79, 580 (1967); Angew. Chem. internat. Edit. 6, 562 (1967).

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[5] Cf. *R. L. Letsinger* and *V. Mahadevan*, J. Amer. chem. Soc. 88, 5319 (1966).

[6] Degradation by snake venom phosphodiesterase gave the required ratio thymidine:thymidine-5′-phosphoric acid.

Synthesis of Metal-Boron Coordination Compounds by Oxidative Addition

By *G. Schmid, W. Petz, W. Arloth*, and *H. Nöth*[*]

Complex metal hydrides or metal alkyls are formed by oxidative addition of H_2, HX, or RX, respectively, (X = halogen) to d^8- and d^{10}-metal compounds in low oxidation states[1,2].

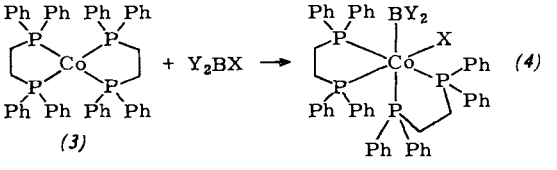
For instance, (i) the planar complex $[(C_6H_5)_3P]_2Ir(CO)Cl$ is converted by HCl into the octahedral iridium(III) complex $[(C_6H_5)_3P]_2IrH(CO)Cl_2$[1], and (ii) reaction of RX with the tetrakis(triphenylphosphine)platinum(0)[3] results in loss of 2 mol. equiv. of $(C_6H_5)_3P$ to give halogenoalkylbis(triphenylphosphine)platinum(II)[4].

We have found that the method of oxidative addition is eminently suited for the synthesis of covalent metal-boron compounds. Titanocene *(1)*[5] reacts with boron halides Y_2BX in ether at room temperature; the deep green of the solution of *(1)* changing to the purple color of the compound *(2)*.

$$[(\pi\text{-}C_6H_5)_2Ti]_2 + 2\ Y_2BX \longrightarrow 2\ (\pi\text{-}C_5H_5)_2Ti\begin{matrix}X\\BY_2\end{matrix}$$

(1) *(2)*

Bis(tetraphenyldiphosphinoethane)cobalt(0) behaves similarly; for example, in benzene it is oxidized by diphenylboron chloride to *cis*-diphenylborochlorobis(tetraphenyldiphosphinoethane)cobalt(II) *(4a)*. The boron halides BCl_3, BBr_3, and BI_3 may be used in place of diphenylboron chloride.



(3) *(4)*

Tetrakis(triphenylphosphine)platinum(0) *(5)* in boiling cyclohexane[7] reacts with diphenylboron chloride to yield triphenylphosphine and crystalline diphenylborochlorobis(triphenylphosphine)platinum(II) *(6a)*.

$$[(C_6H_5)_3P]_4Pt + Y_2BX$$

(5)

$$\longrightarrow 2\ (C_6H_5)_3P + [(C_6H_5)_3P]_2Pt\begin{matrix}X\\BY_2\end{matrix}$$

(6)

Sufficient Lewis-acidity on the part of the boron halide is of decisive importance for the success of the above synthesis. The weakly acidic compounds $(C_4H_9)_2BCl$, $[(CH_3)_2N]_2BCl$, $B[N(CH_3)_2]_3$, and $(C_6H_5)_2B{-}N(C_2H_5)$ do not react.

Surprisingly, bis(tetraphenyldiphosphinoethane)platinum(0)[8] reacts with diphenylboron chloride or bromide in boiling cyclohexane according to:

$$(TPE)_2Pt + 2(C_6H_5)_2BX \rightarrow (TPE)Pt{\cdot}2(C_6H_5)_2BX + TPE.$$

(7a), X = Cl
(7b), X = Br

The structures of the pale yellow products *(7a)*, m.p. 214 °C, and *(7b)*, m.p. 210 °C (decomp.), are not yet known. Reaction with pyridine results in loss of one mol. equiv. of $(C_6H_5)_2BX$ and formation of *cis*-diphenylborotetraphenyldiphosphinoethaneplatinum(II) halides. Therefore, we classify *(7a)* and *(7b)* as diphenylboron halide adducts of the compound *(8)*.

$$[(H_5C_6)_2P{-}CH_2{-}CH_2{-}P(C_6H_5)_2]PtX[B(C_6H_5)_2]$$

(8)

Evidence for the structure of the newly prepared compounds is provided by their chemical behavior and by elemental analysis, molecular-weight determinations, magnetic measurements, and spectrochemical data.

	X	Y	M.p. (°C)	Color	Yield (%)
(2a)	Cl	C_6H_5	300 (decomp.)	black-violet	80
(2b)	Br	Br	300 (decomp.)	black-violet	75
(2c)	Cl	Cl	300 (decomp.)	black-violet	80
(4a)	Cl	C_6H_5	115 [a]	red-brown	92
(4b)	Br	Br	120	red-brown	95
(4c)	Cl	Cl	115 (decomp.)	red-brown	97
(6a)	Cl	C_6H_5	244 (decomp.)	beige	87
(6b)	Br	C_6H_5	198–200	pale yellow	88
(6c)	Br	Br	306	white	85
(8a)	Cl	–	208 (decomp.)	white	65
(8b)	Br	–	150	white	70

[a] Magnetic moment: 4.8 BM.

Since tetrakis(triphenylphosphine)platinum(0) reacts with Si_2Cl_6 to give the compound $[(C_6H_5)P]_2Pt(SiCl_3)_2$, m.p. 180 °C (decomp.), and also reacts with metal-halide complexes of the type L_nMX_m (L = phosphine, X = halogen) to give $[(C_6H_5)_3P]Pt(X)-MX_{m-1}L_n$ [9], it may be predicted that not only boron halides, but also other non-metal halides, as well as metal halide complexes, may react with the systems that we have investigated and thus provide a simple route to numerous new metal-element compounds.

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[*] Dr. G. Schmid, Dipl.-Chem. W. Petz, W. Arloth, and Prof. Dr. H. Nöth
Institut für Anorganische Chemie der Universität
Gutenbergstr. 18
355 Marburg (Germany)

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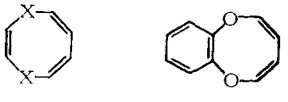
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1,6-Benzodioxocin: Synthesis and Properties

By *W. Schroth* and *B. Werner* [*]

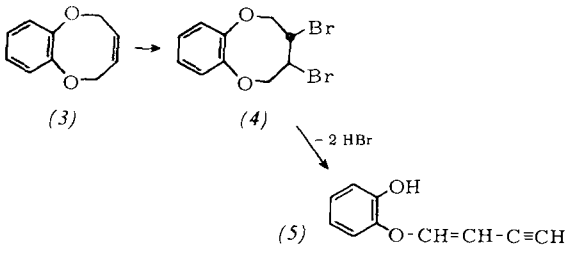
Heterocyclic compounds of the type *(1)*, X = O, N–R, S (1,4-diheterocins) may be formally regarded as 10 π-electron systems. We have prepared and investigated a member of this series [1], namely, 1,6-benzodioxocin *(2)*.



(1) *(2)*

The substance used as starting material was 2,5-dihydro-1,6-benzodioxocin *(3)* [2], which was formed (along with 2-vinyl-2,3-dihydro-1,4-benzodioxin and 2,3:10,11-dibenzo-1,4,9,12-tetraoxacyclohexadeca-all-*cis*-2,6,10,14-tetraene) on reaction of pyrocatechol with *cis*-1,4-dichloro-2-butene.

Double dehydrobromination of *(4)* [2,3], the *trans* dibromo-adduct obtained from *(3)*, with potassium t-butoxide does not yield *(2)*, but gives 1-(*o*-hydroxyphenoxy)but-1-en-2-yne *(5)* (b.p. 124 °C/10 mm). The elimination involves 3-bromo-2,5-dihydro-1,6-benzodioxocin (m.p. 30 °C) as an intermediate, which is formed by reaction of *(4)* with 1,5-diazobicyclo[4.3.0]non-5-ene [4].



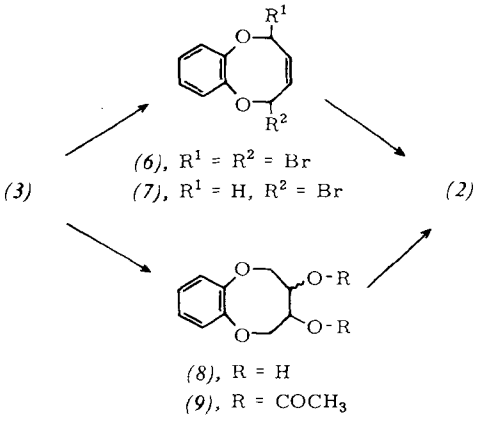
(3) *(4)* *(5)*

Compound *(2)* may be prepared by the following methods:

a) By bromination of *(3)* with two mol. equiv. of *N*-bromosuccinimide to form *(6)*, which is not isolated but is reduced with zinc dust in dimethylformamide. Yield approximately 10 % (with respect to *(3)*).

b) By monobromination of *(3)* with *N*-bromosuccinimide to form 2-bromo-2,5-dihydro-1,6-benzodioxocin *(7)*, which subsequently is treated with triethylamine.

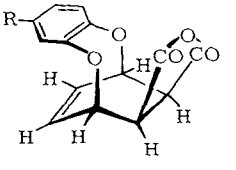
c) By oxidation of *(3)* to *cis*- and *trans*-3,4-dihydroxy-2,3,4,5-tetrahydro-1,6-benzodioxocin *(8)* [1] (*cis* compound: m.p. 112 °C; *trans* compound: m.p. 111 °C), acetylation to the diacetoxy derivatives *(9)* (*cis* compound: m.p. 62 °C; *trans* compound: m.p. 88 °C), and pyrolysis (450 °C). Yield up to 3 % (with respect to *(3)*).



(8), R = H
(9), R = $COCH_3$

Compound *(2)* is a colorless oil (b.p. 109 °C/13 mm) which crystallizes on cooling (m.p. 5 °C). The ^1H–NMR signals [5] of the heterocyclic ring protons in *(2)* lie in the "olefinic range" (τ = 3.05 and 4.65, both signals being split into double doublets with J = 5 and 2 Hz, respectively); the resonance of the benzene-ring protons lies at τ = 2.40. The fact that the UV absorption of *(2)* (λ_{max} = 277, 272 nm; log ε_{max} = 3.47, 3.49 in cyclohexane) is at shorter wavelengths than that of *(3)* (λ_{max} = 282, 275; log ε_{max} = 3.30, 3.33 in cyclohexane) indicates reduced coplanarity, *i.e.* hindered conjugation of the hetero ring with the benzene ring, in compound *(2)*. Thus, in spite of satisfying the $4n+2$ rule (n = 2), π-electron delocalization in the heterocyclic ring of *(2)* takes place to a limited extent only, if at all [6].

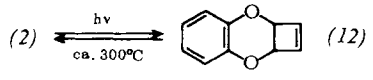
At 190 °C (bath temperature), *(2)* reacts with maleic anhydride to give the Diels-Alder adduct *(10)*, m.p. 220 °C; ^1H–NMR: τ = 3.20 (aromatic-ring protons), 3.82 (olefinic protons), 4.86 (CH-O), and 6.07 (CH-CO-O), relative areas = 2:1:1:1. Proof of structure is provided by hydrolysis (HBr/acetic acid) to phthalic acid. The formulated *exo* configuration of *(10)* is in agreement with the fact that no bromo-



(10), R = H
(11), R = Br

lactonic acid is formed on treatment with hypobromous acid; instead, bromination of the benzene ring occurs. Dehydration under vacuum at 150 °C yields *(11)*, m.p. 263; ^{1}H–NMR τ = 3.10, 3.19 (aromatic-ring protons), 3.56 (olefinic protons), 4.83 (CH–O), and 5.72 (CH–CO–O), relative areas = 3:2:2:2.

On being irradiated with UV light (50 h, 20 °C) compound *(2)* undergoes disrotatory valence isomerization to 3,4-benzo-2,5-dioxabicyclo[4.2.0]octa-3,7-diene *(12)*, m.p. 63 °C; ^{1}H–NMR: τ = 3.21 (aromatic-ring protons), 3.80 (olefinic protons), 4.81 (CH–O), relative areas = 2:1:1. Thermally



induced isomerization of *(12)* back to *(2)* requires temperatures of about 300 °C. At these temperatures decomposition starts to take place and small amounts of *(12)* are cleaved to 1,4-benzodioxin[7] and acetylene.

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[*] Doz. Dr. W. Schroth and Dipl.-Chem. B. Werner
Institut für Organische Chemie der Universität
Weinbergweg
X 402 Halle (Germany)

[1] Cf. *W. Schroth, K. Kränke*, and *J. Reinhardt*, Angew. Chem. *75*, 303 (1963); Z. Chem. *3*, 119 (1963).

[2] Cf. *W. Schroth, J. Reinhardt, K. Kränke*, and *B. Strecken-bach*, Z. Chem. *3*, 228 (1963).

[3] The *trans* position of the bromine atoms provides proof for the formation of *threo*-2,3-dibromobutane-1,4-diol (m.p. 87 °C) on ozonolysis of the benzene ring and mild acid hydrolysis.

[4] *H. Oediger, H. J. Kabbe, Fr. Möller*, and *K. Eiter*, Chem. Ber. *99*, 2012 (1966); we thank Dr. *Eiter* for a sample of authentic material.

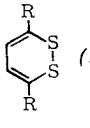
[5] We thank Dr. *G. Engelhardt*, Berlin-Adlershof, and Dr. *A. Zschunke*, Leipzig, for recording the NMR spectrum and for discussions.

[6] Quantum-theoretical calculations: *A. T. Balaban* and *Z. Simon*, Rev. roum. Chim (Bucharest) *10*, 1059 (1965), especially page 1071.

1,2-Dithiins, a New Type of Heterocycle [1]

By *W. Schroth, F. Billig*, and *G. Reinhold*[*]

The, as yet, unknown 1,2-dithiins *(1)* have a disulfide structure in cyclic conjugation and thus formally represent an 8-π electron system. To account for the great lability of the recently synthesized[2] parent compound *(1a)* (a red oil that is easily polymerized and splits off sulfur with the formation of thiophene) it was necessary to investigate the 3,6-disubstituted derivatives.

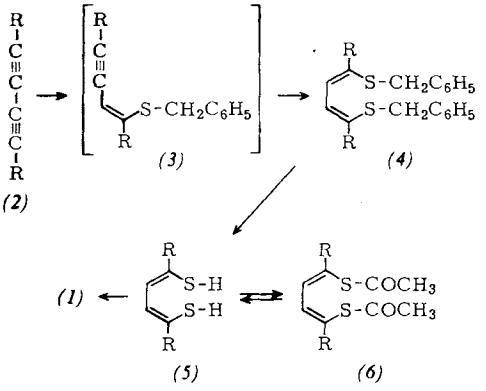


(1)

	R	M.p. (°C) [B.p. (°C/mm)]	λ_{max} [a] (nm)	log ε
(1a)	H	[45/4]	451	2.88
(1b)	C_6H_5	143	468	3.12
(1c)	*p*-CH_3–C_6H_4	162	470	3.46
(1d)	*p*-CH_3O–C_6H_4	179	467	4.43
(1e)	2-Thienyl	123	481	3.76

[a] In the visible spectral region; in cyclohexane.

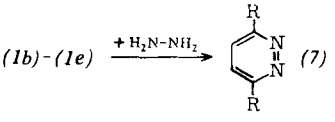
The synthesis of such derivatives was accomplished by nucleophilic addition of phenylmethane thiol to butadiynes *(2)* to give *cis,cis*-1,4-bis(benzylthio)butadienes *(4)*. Reductive debenzylation of *(4)* with sodium in liquid ammonia (–70 °C) gives the *cis,cis*-1,4-dimercaptobutadienes *(5)*, which on oxidation (with air) in alkaline solution give the desired products. In a few cases (R = *p*-CH_3–C_6H_4, *p*-CH_3O–C_6H_4, CH_3) the mono-addition products *(3)* were obtained.



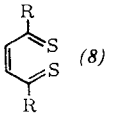
	R	*(3)* M.p. (°C)	*(4)* M.p. (°C)	*(5)* M.p. (°C) [B.p. (°C/mm)]	*(6)* M.p. (°C)
(a)	H	–	129	[38/0.3]	148
(b)	C_6H_5	–	118	99	159
(c)	*p*-CH_3–C_6H_4	91	136	138	193
(d)	*p*-CH_3O–C_6H_4	73	157	148	167
(e)	2-Thienyl	–	116	–	156
(f)	CH_3	55	98	–	–

The relatively unstable dithiols *(5)* are stored as the diacetyl compounds *(6)* from which they can be regenerated by the action of dilute alkalis.

The 3,6-disubstituted 1,2-dithiins *(1b)–(1e)* are obtained as deep red crystals. They may be reduced with sodium tetrahydridoborate or with sodium in liquid ammonia to give the dithiols *(5)*. They readily split off sulfur (especially rapidly on heating or on UV irradiation) to form the 2,5-disubstituted thiophenes. This reaction predominates in all attempts to prepare Diels-Alder adducts of the compounds *(1b)–(1e)* with maleic anhydride or tetracyanoethylene. Oxidation of *(1b)* with hydrogen peroxide in glacial acetic acid leads to the 1,4-diphenylbutadiene-1,4-disulfonic acid (m.p. 108 °C; IR: strong absorption at 1170–1200 and 3400–3450 cm^{-1}). When the compounds *(1b)–(1e)* react with hydrazine in pyridine, or in dimethylformamide, H_2S is evolved and 3,6-disubstituted pyridazines *(7)* are formed.



Compounds of type *(1)* (R = acetylene/olefin side chains) have recently been detected in plants, presumably as precursors of natural thiophene derivatives[3]. The spontaneous elimination of sulfur and their light absorption in the visible region suggested the formulation of the valence isomer *(8)*[3a,4].



We consider that the following facts bear out the cyclic disulfide structure *(1)*: (i) If the compound *(1a)* had the structure *(8)*, then an NMR signal of the thioaldehyde hydrogen atoms would lie at very low field strengths[5] – this was not the case (the chemical shifts are τ = 3.87 and 4.03;

1,4-dithiin: $\tau = 4.05$); (ii) If the compounds *(1b)–(1e)* were to have the structure *(8)*, they would be aromatic thioketones, which absorb at considerably greater wavelengths (at 600 nm)[6].

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[*] Doz. Dr. W. Schroth
Institut für Organische Chemie der Universität
Weinbergweg
X 402 Halle (Germany)
Dipl.-Chem. F. Billig and Dipl.-Chem. G. Reinhold
Institut für Organische Chemie der Universität
Liebigstr. 18
X 701 Leipzig (Germany)

[1] Part 12 of Organosulfur Compounds. – Part 11: *W. Schroth, B. Streckenbach,* and *B. Werner,* Z. Chem. *7*, 152 (1967).

[2] *W. Schroth, H. Langguth,* and *F. Billig,* Z. Chem. *5*, 353 (1965).

[3] [a] *F. Bohlmann* and *K.-M. Kleine,* Chem. Ber. *98*, 3081 (1965); *F. Bohlmann,* Fortschr. chem. Forsch. *6*, 89 (1966).

[b] *J.T. Mortensen, J. Sörensen,* and *N. A. Sörensen,* Acta chem. scand. *18*, 2392 (1964).

[4] Quantum-mechanical calculations show a negative bond order (–0.03 to –0.04) between the S atoms of the compounds *(1)* which corresponds to a weakening of the S–S bond. We thank Dr. *J. Fabian,* Dresden, for calculations and discussions.

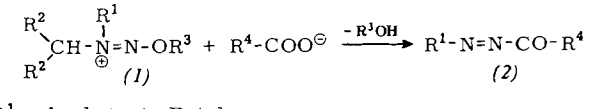
[5] In the range $\tau = 0$ to 1; cf. *S. McKenzie* and *D. H. Reid,* Chem. Commun. *1966*, 401.

[6] Cf. *R. Mayer, J. Morgenstern,* and *J. Fabian,* Angew. Chem. *76*, 157 (1964); Angew. Chem. internat. Edit. *3*, 277 (1964).

The Synthesis of Carbonylazo Compounds by the Reaction of Alkoxydiazenium Salts with Carboxylates [1]

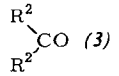
By *Th. Eicher, S. Hünig,* and *H. Hansen*[*]

Alkoxydiazenium salts are easily accessible by the alkylation of nitrosamines with trialkyloxonium salts, or $AgClO_4$/alkyl halide[2]. The reaction of carboxylates with alkoxydiazenium cations *(1)*, in which R^1 is an aromatic or tertiary aliphatic residue[3], generally leads to the formation of carbonylazo compounds *(2)* in high yield. Equivalent amounts of the carbonyl compound *(3)* are also formed[4].



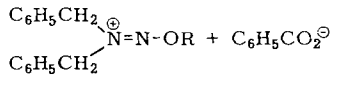
(1) *(2)*

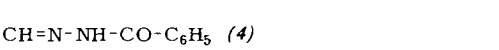
R^1 = Aryl, tert.-Butyl
R^2 = H, CH_3, C_6H_5
R^3 = CH_3, C_2H_5
R^4 = Aryl, Alkyl



(3)

The carbonylazo compounds are not obtained from cations *(1)* when R^1 is a substituent with an α-hydrogen atom, *e.g.* CH_3, $CH_2C_6H_5$; in this case the isomers of the acylhydrazones *(4)* are formed by proton migration[5].





(4)

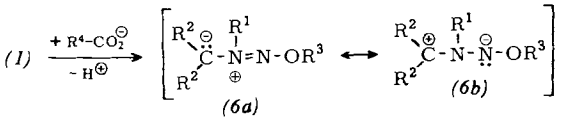
The carbonylazo compounds *(2)* are isolated as red substances after the usual techniques of product recovery by chromatography or crystallization. When difficulties are encountered in purification of the crude compounds *(2)* they are reduced with sodium dithionite to the stable hydrazides *(5)* which are easier to obtain pure.

R^1–NH–NH–CO–R^4

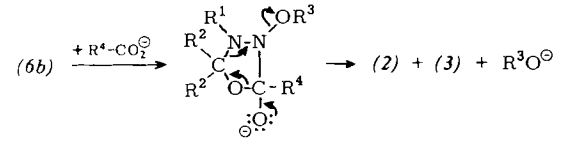
R^1	R^4	*(2)* Yield (%)	*(2)* M.p. (°C)	*(5)* Yield (%)	*(5)* M.p. (°C)
C_6H_5	C_6H_5			93	163–165 [a]
p-CH_3O–C_6H_4	C_6H_5	90	68–69	84	138–139 [b]
p-Cl–C_6H_4	C_6H_5	98	73–74	96	156–157
p-CH_3O–C_6H_4	p-O_2N–C_6H_4	84	148–150		
p-CH_3O–C_6H_4	CH_3			50	133–134 [c]
$(CH_3)_3C$	C_6H_5			75	94–96

[a] *E. Fischer,* Liebigs Ann. Chem. *190*, 126 (1878).
[b] *S. Goldschmidt* and *J. Bader,* Liebigs Ann. Chem. *473*, 125 (1929).
[c] *J. Altschul,* Ber. dtsch. chem. Ges. *25*, 1842 (1892).

Although the investigations of the mechanism of the reaction have not yet been completed, the following scheme is a plausible representation of the formation of compounds *(2)* and *(3)* from *(1)*:



(6a) *(6b)*



(7)

Deprotonation of *(1)* leads to the dipolar entity *(6)*, which, in the ground state, might have the structure *(6b)* on account of the differences between the electronegativities of the participating centers. The carboxylate anion is alkylated by *(6)* and undergoes simultaneous N–C ring closure to form the intermediate *(7)* which yields *(2)* and *(3)* *via* a seven-center cyclic fragmentation.

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[*] Dr. Th. Eicher, Prof. Dr. S. Hünig,
and Dipl.-Chem. H. Hansen
Institut für Organische Chemie der Universität
Röntgenring 11
87 Würzburg (Germany)

[1] Part 1 of Reactions of Alkoxydiazenium Salts.

[2] *S. Hünig, L. Geldern,* and *E. Lücke,* Angew. Chem. *75*, 476 (1963); Angew. Chem. internat. Edit. *2*, 327 (1963); Revue de Chimie (Roumaine) *7*, 935 (1962).

[3] The sodium salts are made to react in acetonitrile or water/methylene chloride (1:1 v/v). Reaction time: 2–3 h, temperature: 0 °C, molar ratio *(1)*: carboxylate = 1:1–1:10.

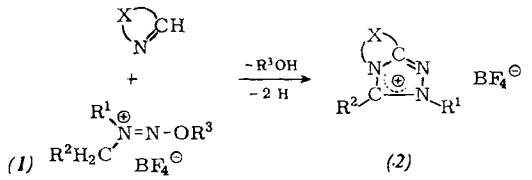
[4] See *E. Fahr* and *H. Lindt,* Angew. Chem. *78*, 376 (1966); Angew. Chem. internat. Edit. *5*, 372 (1966).

[5] Unpublished work; co-author *L. Geldern,* 1962.

Synthesis of *s*-Triazolium Cations by Reaction of Alkoxydiazenium Salts with Nitrogen Heterocycles [1]

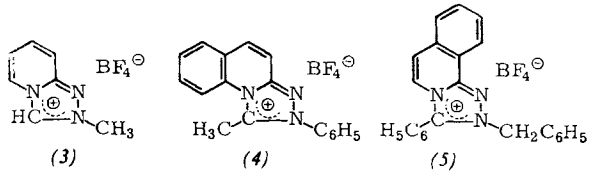
By *Th. Eicher, S. Hünig,* and *P. Nikolaus*[*]

Alkoxydiazenium cations[2] of the type *(1)*, in an organic or an aqueous medium, add smoothly to nitrogen heterocycles such as pyridine, quinoline, isoquinoline, phenanthridine, or benzthiazole to form heterocyclo[2,1-*c*]-*s*-triazolium salts *(2)*. The reaction proceeds *via* formal loss of alcohol and two hydrogen atoms.

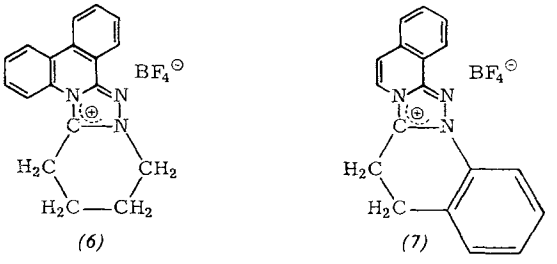


(1) R^2H_2C $BF_4^\ominus$ (2)

R^1 = Aryl, Alkyl
R^2 = Aryl, Alkyl
R^3 = CH_3, C_2H_5



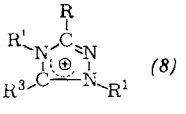
(3) (4) (5)



(6) (7)

	M.p. (°C)	Yield (%)
(3)	157–158	67
(4)	275–277	30
(5)	241–242	76
(6)	289–291	32
(7)	319–320	46

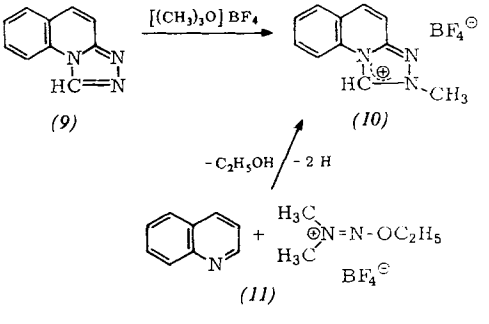
The compound *(1)* also adds on Schiff bases resulting in formation of the non-anellated *s*-triazolium cations *e.g. (8)* [*(8)*, R = R^1 = R′ = R^3 = C_6H_5: m.p. *ca.* 340 °C (decomp.), yield 58%].



(8)

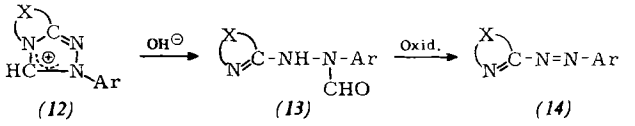
The assignment of the structure *(2)* is based on the NMR spectra, the assumption being made that an alkyl- or aryl-migration is improbable. The following chemical findings provide additional evidence:

a) The alkylation of 5,6-benzpyrido[2,1-*c*]-*s*-triazole *(9)* with trimethyloxonium tetrafluoroborate forms the same triazolium cation *(10)* as is formed in the reaction of 2-ethoxy-1,1-dimethyldiazenium tetrafluoroborate *(11)* with quinoline.



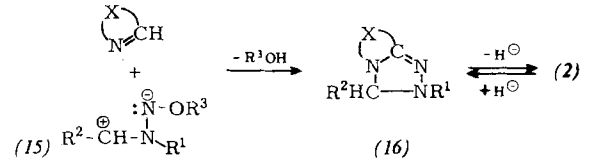
(9) *(10)* *(11)*

b) Alkaline fission of triazolium cations of the type *(12)* and subsequent oxidation leads, *via* the formylhydrazine *(13)*, to the 2-arylazoheterocycle *(14)* [3], thus confirming the presence of the heterocycle-*N*–*N*-aryl grouping in the cation *(12)*. The reaction sequence, heterocycle + *(1)* → *(12)* → *(14)* is simultaneously a new route for the direct introduction of azoaryl residues into heterocycles.



(12) *(13)* *(14)*

The formation of *(2)* probably proceeds also *via* the dipole *(15)* [4].



(15) *(16)*

The expected adduct *(16)* is not obtained as it is immediately dehydrogenated to *(2)* by *(1)*. This step can be proved in a separate experiment, since *(16)* can be prepared by the action $NaBH_4$ on *(2)* [3].

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[*] Dr. Th. Eicher, Prof. Dr. S. Hünig,
and Dipl.-Chem. P. Nikolaus
Institut für Organische Chemie der Universität
Röntgenring 11
87 Würzburg (Germany)

[1] Part 2 of Reactions of Alkoxydiazenium Salts. – Part 1: [4].

[2] *S. Hünig, L. Geldern,* and *E. Lücke,* Angew. Chem. *75,* 476 (1963); Angew. Chem. internat. Edit. *2,* 327 (1963).

[3] *P. Nikolaus,* Planned Dissertation.

[4] *Th. Eicher, S. Hünig,* and *H. Hansen,* Angew. Chem. *79,* 681 (1967); Angew. Chem. internat. Edit. *6,* 699 (1967).

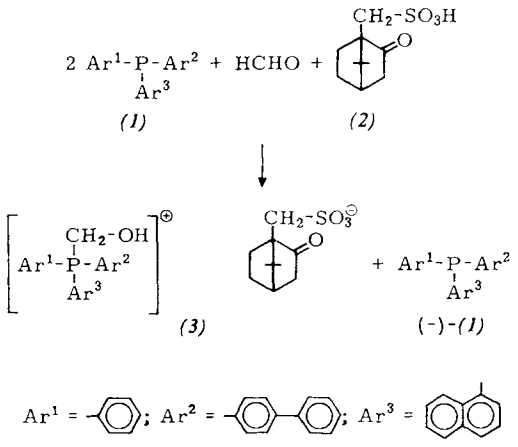
Resolution of Chiralic Triarylphosphines [1]

By *G. Wittig, H. J. Cristau,* and *H. Braun* [*]

Unsymmetrical tetraaryl phosphonium salts have been prepared several times [2], yet hitherto these compounds could not be resolved into enantiomers. We have now succeeded in separating a triarylphosphine into its optical antipodes. In order to accomplish this we made use of the fact that phosphines in the presence of acid and paraformaldehyde react to give α-hydroxymethylphosphonium salts [3]. The "method of half quantities" [4] proved especially well suited in our work for the resolution of these optical isomers. This procedure may be illustrated by the case of the resolution of *p*-biphenylyl-α-naphthylphenylphosphine *(1)* [5] (racemate m.p. 192–193 °C).

11 mmole of paraformaldehyde was suspended in a benzene solution of 20 mmole of the phosphine *(1)*, and a solution of 10 mmole of (+)-camphor-10-sulfonic acid *(2)* added. The mixture was stirred for 1h and then allowed to stand overnight, during which time the salt *(3)* crystallized out (yield 92%). The supernatant liquor was decanted off, the solvent was removed under vacuum, and the residue was chromatographed on Al_2O_3 (Brockmann) (eluent benzene).

The phosphine (–)-*(1)* (8.6 mmoles or 86%; m.p. 194 to 195 °C; $[\alpha]_{578}^{24} = -5.2°$; c = 3.38 in methylene chloride) was thus obtained. The camphor sulfonate *(3)* remaining behind after decantation (9.2 mmole; m.p. 111–112 °C) exhibited, after a triple recrystallization, a rotation value of $[\alpha]_{578}^{25.4} = +19.0°$ (*c* = 3.86 in methylene chloride). Cleavage of *(3)* to the phosphine (+)-*(1)* was accomplished with triethylamine in benzene (yield 93%; m.p. 195–196 °C; $[\alpha]_{578}^{25.4} = +8.7°$; *c* = 3.11 in methylene chloride) [6].



If a molecular ratio of 1:1:1 of the components was used, the separation of the diastereoisomers was unsuccessful. It was impossible to apply the above technique to aliphatic or aliphatic-aromatic phosphines, possibly because of the greater basicity of these compounds.

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[*] Prof. Dr. G. Wittig, H. J. Cristau, and cand. chem. H. Braun
Organisch-Chemisches Institut der Universität
Tiergartenstr.
69 Heidelberg (Germany)

[1] Cf. *L. Horner, F. Schedlbauer*, and *P. Beck*, Tetrahedron Letters *1964*, 1421.

[2] *G. Wittig* and *H. Matzura*, Angew. Chem. *76*, 187 (1964); Angew. Chem. internat. Edit. *3*, 231 (1964); *H. Matzura*, Dissertation, Universität Heidelberg 1964.

[3] *J. de Girard*, C. R. hebd. Séances Acad. Sci. *94*, 215 (1882).

[4] *W. J. Pope* and *C. S. Gibson*, J. chem. Soc. (London) *101*, 939 (1912).

[5] *G. Wittig* and *H. Matzura*, unpublished.

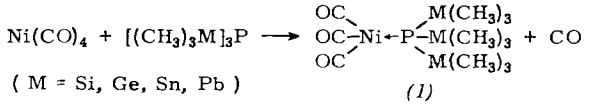
[6] There are indications that the phosphines are not 100% optically pure.

Tricarbonyl(organometalophosphine)nickel(0)

By *H. Schumann* and *O. Stelzer* [*]

The stability of organometalophosphines of type $(R_3M)_nPR_{3-n}$ (M = Si, Ge, Sn, or Pb) is ascribed to participation of the "free" electron pair on the phosphorus in the covalent M–P bond [1]. All previous attempts to prepare organometalophosphines with tetra- or quinque-valent phosphorus have been unsuccessful. Fission of the metal-phosphorus bond occurs on utilization of the "free" electron pair, for instance, by quaternization of the phosphorus or by oxidation.

By treatment of tetracarbonylnickel with tris(trimethylsilyl)-, tris(trimethylgermanyl)-, tris(trimethylstannyl)-, or tris(trimethylplumbyl)-phosphine in tetrahydrofuran at room temperature, it has now been possible to synthesize carbonylnickel(0) complexes *(1)* which represent the first stable organometal-substituted phosphines with tetravalent phosphorus.



The compounds, which are formed in quantitative yield as colorless crystals after four hours' stirring under a nitrogen atmosphere, can be isolated in high purity on distilling off the solvent. In contrast to the starting phosphines they are astonishingly stable to air; but they decompose, in some cases at very low temperatures, with separation of metal.

(1), M	Decomp. temp. (°C)	$J[^1HCM^{31}P]$ (Hz)	ν CO (cm^{-1})	ν PM_3 (cm^{-1})	ν NiP (cm^{-1})
Si	30	5.2	2074 1995	363	478
Ge	100	4.65	2070 1996	362	454
Sn	90	3.35	2057 1968	345	448
Pb	85	2.9	2049 1960	321	446

The considerable increase in the coupling constants $J[^1HCM^{31}P]$ of the complexes in comparison with those of the free organometalophosphines (Si, 4.62 Hz; Ge, 4.00 Hz; Sn, 1.95 Hz; Pb, 0 Hz) confirms the increase in s-character of the P–M bonds on going from the p^3 hybridized phosphorus atom of the free phosphines to the sp^3 hybridized phosphorus in the complexes. The IR spectrum shows the two CO stretching vibrations required by the C_{3v} symmetry [2]; these bands being shifted, as expected, to longer wavelengths with increase in the size of the phosphine ligands. In addition to the internal vibrations of the trimethylmetal groups there are two bands between 4000 and 280 cm^{-1} which we ascribe to $\nu_{as}PM_3$ (E) and νPNi (A_1) of the atomic grouping M_3PNi (C_{3v}). The small long-wave shift of $\nu_{as}PM_3$, compared with the tris(organometalo)phosphines, shows that the M–P bond is only slightly weakened by complex formation. The stability of the new compounds towards oxygen confirms the hypothesis that on oxidation of organometalophosphines the oxygen attacks the "free" electron pair of the phosphorus [3]. In the complexes *(1)*, this electron pair is no longer open to electrophilic attack, owing to coordination to the nickel.

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[*] Priv.-Doz. Dr. H. Schumann and cand. chem. O. Stelzer
Institut für Anorganische Chemie der Universität
Röntgenring 11
87 Würzburg (Germany)

[1] *H. Schumann*, Habilitations Thesis, Universität Würzburg, 1967.

[2] *W. F. Edgell* and *M. P. Dunkle*, Inorg. Chem. *4*, 1629 (1965).

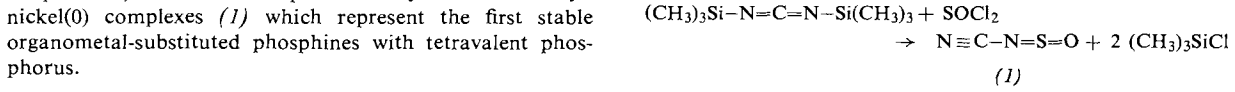
[3] *H. Schumann, P. Jutzi, A. Roth, P. Schwabe*, and *E. Schauer*, J. organometal. Chem., in press.

Thionylcyanamide

By *O. J. Scherer* and *R. Schmitt* [*]

Silicon-nitrogen compounds are extremely useful for the preparation of new types of thionyl imide [1] and fluorosulfur imide derivatives [2].

On treatment of bis(trimethylsilyl)carbodiimide with thionyl chloride at −70 °C (molar ratio 1:1, no solvent) and removal of the chlorotrimethylsilane in a water-pump vacuum, one obtains as residue a liquid that decomposes explosively with

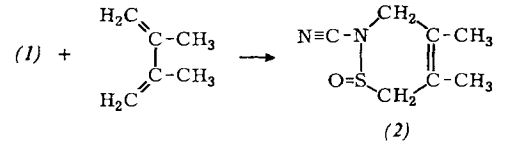


the greatest ease (storage in a refrigerator or distillation under reduced pressure leads to explosions). However, if the reaction mixture is worked up in an oil-pump vacuum, thionylcyanamide *(1)* is obtained as a yellow liquid (b.p. 23–24 °C/4 mm, m.p. −37 °C) in 60 % yield.

The product *(1)* is moderately soluble in CCl_4, readily so in $CHCl_3$, CH_2Cl_2, ether, or benzene, but insoluble in petroleum ether. Traces of water or alcohol lead to explosive decomposition. Although compound *(1)* can be kept for several days in the refrigerator (closed vessels) without decomposi-

tion, polymerization with simultaneous loss of sulfur dioxide occurs within a few hours under the influence of daylight at room temperature; the same occurs when the substance is warmed to 90–100 °C. IR spectrum: ν(CN)2190, ν_{as} (NSO) 1260, ν_s (NSO) 1170, δ(NSO) 620 cm^{-1}.

Compound *(1)* reacts exothermally with an ethereal solution of 2,3-dimethylbutadiene to give the cyclic product *(2)*.



(2)

The thiazine derivative *(2)* forms colorless crystals (m.p. 97–98 °C, yield 90 %).

Treating *(1)* with bis(trimethylsilyl)methylamine in ether at −70 °C gives bis(trimethylsilyl)carbodiimide (yield *ca.* 80 %), as well as *N*-methylthionylimide (which forms polymers).

(1) + $[(CH_3)_3Si]_2NCH_3$

→ $(CH_3)_3Si{-}N{=}C{=}N{-}Si(CH_3)_3 + CH_3NSO$

Thionylcyanamide (Caution during the preparation – explosive decomposition possible – use a protective shield!):

7.15 g (61 mmoles) of thionyl chloride is added dropwise to 11.2 g (60 mmoles) of bis(trimethylsilyl)carbodiimide[3] at −70 °C, with stirring, over a period of 5–10 min. The reaction mixture is then allowed to warm to 0 °C within about 45 min. The chlorotrimethylsilane is at once distilled off under oil-pump vacuum and the residue is fractionally distilled. Yield 3.2 g (60 %); b.p. 23–24 °C/4 mm; m.p. −37 °. A brown polymeric solid remains as distillation residue. If bis(trimethylsilyl)carbodiimide is added dropwise to a large excess of thionyl chloride, again only thionylcyanamide is formed.

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[*] Priv.-Doz. Dr. O. J. Scherer and cand. chem. R. Schmitt
Institut für Anorganische Chemie der Universität
Röntgenring 11
87 Würzburg (Germany)

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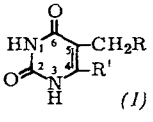
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C-C Condensations with the Uracilylmethyl Cation [1]

By *R. Brossmer* [*]

5-Arylmethyl derivatives of uracil can be simply prepared: *In statu nascendi*, the cation that is readily formed from 5-(hydroxymethyl)uracil[2] by catalytic amounts of acid reacts smoothly (forming a C–C bond) with phenols and naphthols and their derivatives and with compounds that can be substituted electrophilically. 5-Benzyl- and 5-(naphthylmethyl)-uracils *(1)* result. The condensation is not hindered by fairly large substituents R′, *e.g.* phenyl, on C–4 of uracil. Analogous reactions occur with free nucleosides or those protected in the sugar portion.



(1)

R	R′	Yield (%)[3]	M.p. (°C)
4-Hydroxyphenyl	H	95	330
3-Chloro-4-hydroxyphenyl	H	88	295–296
3-Chloro-6-hydroxyphenyl	H	90	340 (decomp.)
2-Hydroxy-3,5-dimethylphenyl	H	86	300–303
2-Hydroxy-5-formylphenyl	H	75	295–297
4-Hydroxyphenyl	CH_3	95	310
4-Hydroxyphenyl	C_6H_5	78	150 (decomp.)
4-Hydroxynaphthyl	H	91	298

These products have hitherto been accessible, if at all, only by total synthesis involving several steps[4].

5-(4-Hydroxybenzyl)uracil: 5-Hydroxymethyluracil (1 g) and then concentrated hydrochloric acid or trifluoroacetic acid (0.3 ml) are added to molten phenol (15 g). The mixture is stirred for 0.5 to 1 h at 80 to 100 °C. Dissolution occurs after a few minutes, then a thick precipitate separates. After the mixture has been cooled, precipitation is completed by addition of ether. Yield 1.45 g (95 %); recrystallized from 70 % ethanol or water, the product has m.p. 330 °C.

5-(4-Hydroxybenzyl)-3-(2,3,5-tri-O-benzoyl-β-D-ribofuranosyl)uracil: 5-(Hydroxymethyl)-3-(2,3,5-tri-*O*-benzoyl-β-D-ribofuranosyl)uracil (0.5 g) and concentrated hydrochloric or trifluoroacetic acid (0.2ml) are added to molten phenol (20 g). The mixture is kept for 1 h at 80 to 100 °C, then treated with water (1 liter) and decanted; the precipitate is dissolved in a little methanol and the solution is allowed to flow into water (*ca.* 800 ml). Yield, 0.40 g (71 %). Recrystallized from methanol, the product has m.p. 155 °C (decomp.).

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[*] Priv.-Doz. Dr. R. Brossmer
Max-Planck-Institut für Medizinische Forschung
Institut für Chemie
Jahnstr. 29
69 Heidelberg (Germany)

[1] Pyrimidines, Part V. – Part IV: *R. Brossmer* and *D. Ziegler*, Angew. Chem. *79*, 322 (1967); Angew. Chem. internat. Edit. *6*, 369 (1967).

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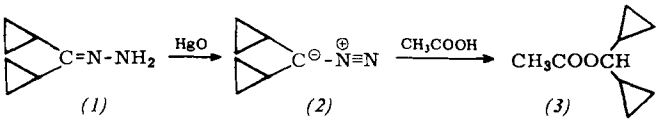
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Dicyclopropyldiazomethane

By *H. M. Ensslin* and *M. Hanack* [*]

There have been two recent reports[1,2] on the preparation of cyclopropyldiazomethane. Dicyclopropyldiazomethane can also be obtained; its preparation is indeed simpler than that of cyclopropyldiazomethane. A solution of freshly distilled dicyclopropyl ketone hydrazone *(1)* (24 g; readily accessible[3] from dicyclopropyl ketone and 80 % hydrazine hydrate in presence of barium oxide) in anhydrous ether is cooled to 0 °C and added rapidly, with stirring at 0 °C, to a suspension of yellow mercuric oxide (56.2 g, 1.33 equivalents) in ether (20 ml) containing 3 M ethanolic sodium hydroxide (10 drops). The solution becomes deep red instantaneously; after 5 min it is filtered and dried over KOH at −40 °C. The IR spectrum of the etheral solution shows a weak band at



(1) *(2)* *(3)*

2260 cm^{-1}, which is characteristic of a diazo group[1,4]. The cyclopropane rings are indicated by a band at 3090 cm^{-1}. If the ether is pumped off at −20 °C, the product *(2)* remains as a brick-red oily liquid with an odor of decay. The IR spectrum of *(2)* in $CDCl_3$ at −20 °C shows an intense diazo band at 2225 cm^{-1}. Compound *(2)* begins to decompose even while the spectrum is being measured; at −15 °C decomposition sets in with violent evolution of nitrogen. However, it can be kept for several days in ether at −50 °C.

The ethereal solution of *(2)* was added dropwise to a solution of acetic acid in ether at −20 °C. The course of the reaction could be followed by the evolution of nitrogen; it yielded dicyclopropylmethyl acetate *(3)*, whose IR spectrum and retention time in the gas chromatograph agreed with those of an authentic specimen[5].

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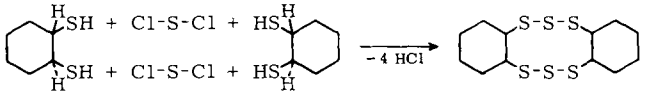
[*] Dr. H. M. Ensslin and Priv.-Doz. Dr. M. Hanack
Chemisches Institut der Universität
Wilhelmstr. 31
74 Tübingen (Germany)

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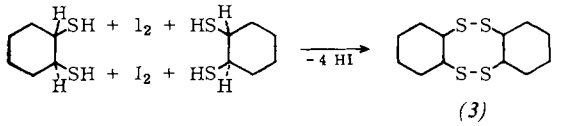
New Sulfur-containing Cyclic Compounds

By *F. Fehér* and *B. Degen*[*]

trans-1,2-Cyclohexanedithiol *(1)*[1] reacts with dichloromonosulfane or iodine with ring formation, if the dilution method is used.



(1) *(2)*

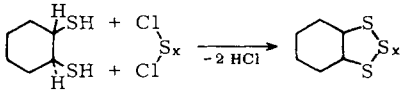


(3)

	M.p. (°C)	Yield (%)	λ_{max} (mμ) in cyclohexane	log ε
(2)	216–218	5.9	274	3.36
(3)	191.5–192	52	242	2.95

It yields perhydrodibenzo-1,2,3,6,7,8-hexathiecin *(2)* and perhydrodibenzo-1,2,5,6-tetrathiocin *(3)*, respectively, which are stable, colorless substances that can be recrystallized from chlorobenzene. They can also be obtained by reaction of bis(2-chlorocyclohexyl)-trisulfane or -disulfane with sodium trisulfide or disulfide, respectively[2], but then only in poor yield.

Reaction of the dithiol *(1)* with chlorosulfanes S_xCl_2 ($x \geq 2$)[3] in very dilute solution gives bicyclic sulfur compounds *(4)*.



(4)

	(4), M.p. (°C)	*(4)*, Yield (%)	*(4)*, λ_{max}(mμ) in cyclohexane	log ε
$x = 2$	88.5–89	74	232; 277	3.65; 3.24
$x = 3$	66.5–67	75	231; 278	3.92; 3.48
$x = 4$	81–82	9	232; 279	3.70; 3.26
$x = 5$	128–129	7.5	288	3.75

In the mass spectra, fragments appear at mass numbers that correspond to compounds *(2)*, *(3)*, and *(4)*; in addition, key fragments are found that are formed by successive loss of one sulfur atom at a time. From compounds *(4)* with $x = 3$, 4, or 5, a metastable fragment with mass number 131 is found. In the 400 to 500 cm^{-1} region of the IR spectrum the bands due to S–S stretching vibrations are well developed. The ^1H–NMR spectra of *(4)* are appreciably more complicated than that of cyclohexane.

1-Substituted 1,2-cyclohexanedithiols do not give cyclic compounds on reaction with S_xCl_2; nor does *o*-benzenedithiol.

Preparation of (4):

0.2 mole of 1,2-cyclohexanedithiol and 0.2 mole of S_xCl_2 are dissolved separately, each in 100 ml of an anhydrous ether/carbon disulfide mixture (3:1). The solutions are added simultaneously from two dropping funnels, during a period of 12 h at room temperature and with stirring, to 3.5 liters of anhydrous ether. Finally, the HCl is removed in a stream of nitrogen, insoluble polymeric products are filtered off, and the solution is concentrated to 100 ml. The stable crystals that separate are recrystallized from ether. — Compounds *(2)* and *(3)* are obtained similarly.

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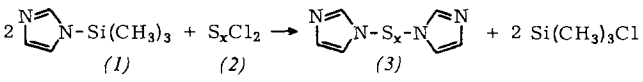
[*] Prof. Dr. F. Fehér and Dipl.-Chem. B. Degen
Institut für Anorganische Chemie der Universität
Zülpicher Str. 47
5 Köln (Germany)

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Preparation of Diimidazolylsulfanes and Di(aziridinyl)sulfanes

By *F. Fehér* and *B. Degen*[*]

Silylation of imidazole by hexamethyldisilazane affords *N*-(trimethylsilyl)imidazole *(1)*[1]. The silylated heterocycle *(1)* is suitable for reaction with chlorosulfanes *(2)*[2], since the chlorotrimethylsilane formed thereby is readily removed from the reaction mixture; furthermore, no side reactions occur. The diimidazol-1-ylsulfanes *(3)* are precipitated in analytically pure form.

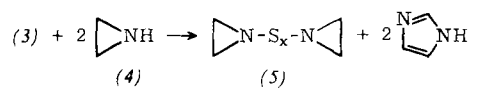


(1) *(2)* *(3)*

$x =$	1	2	3	4	5
(3), m.p. (°C)	111	91–92	88	75	73–74 (decomp.)
(3), yield (%)	92	90	82	77	70

If stoichiometric amounts of compounds *(1)* and *(2)* in anhydrous benzene are used under a nitrogen atmosphere with exclusion of moisture, higher chlorosulfanes ($x \geq 3$) being dissolved in a little anhydrous carbon disulfide, then the sulfanes separate at once in pure crystalline form.

The silyl derivative of ethyleneimine *(4)* is obtained pure only with difficulty. So it is interesting that use of the products *(3)* make it possible to transfer the sulfur chain to *(4)*.



(4) *(5)*

$x =$	1	2	3	4	5
(5), n_D^{20}	1.4892	1.5794	1.6550	1.7170	1.7720
(5), λmax (mμ) in cyclohexane	212; 275	258	225; 290	230; 298	232; 305
(5), log ε	3.41; 2.51	3.41	3.88; 3.41	4.00; 3.51	4,79 3.78

The ring bonds in compound *(5)* can conjugate with the sulfur chain, as is shown by the bathochromic shift of the absorption maxima of *(5)* in comparison with those of dipiperidinosulfanes[3]. Attempts to distil compound *(5)* often led to violent explosions.

Di(aziridin-1-yl)sulfanes (5):

Diimidazol-1-ylsulfane *(3)* (0.02 mole) was suspended in anhydrous n-pentane (50 ml) and treated with *(4)* (0.04 mole) at 5 to 10 °C. After storage at −20 °C for 5 h the crystalline imidazole was filtered off and the solvent was removed from the filtrate by distillation in a vacuum. The pure compound *(5)* remained as residue.

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[*] Prof. Dr. F. Fehér and Dipl.-Chem. B. Degen
Institut für Anorganische Chemie der Universität
Zülpicher Str. 47
5 Köln (Germany)

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Rearrangement of Electronegatively Substituted Guanidines to Semicarbazones

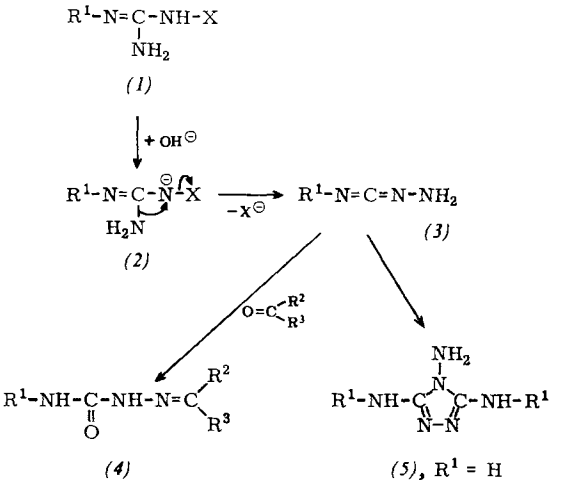
By *A. Heesing* and *H. Schulze* [*] [1]

Hydroxylamine-*O*-sulfonic acids and *N*-chloroamines react with ketones in alkaline solution, yielding oxaziridines[2]. On the other hand, diaziridones are formed from *N*-chloroureas in strongly basic media[3].

Nevertheless, we have found that with the guanidine derivatives *(1a)*–*(1d)* the guanidine system rearranges to the semicarbazone system *(4)*. Hydroxyguanidine-*O*-sulfonic acids *(1a)* and *(1b)* and the *N*-chloroguanidines *(1c)* and *(1d)* react with aldehydes and ketones in aqueous alkaline solution, forming the semicarbazones *(4)*.

Semicarbazone formation occurs only if the carbonyl compound and the base are both present. With sodium hydroxide alone, the guanidine derivative does not give a semicarbazide, so that the latter does not come into question as an intermediate. Instead, decomposition of *(1a)* by alkali gives a high yield of guanazine (3,4,5-triamino-1,2,4-triazole) *(5)* [4].

The reaction mechanism is thus as follows: An anion *(2)* is first formed, which, however, is not stabilized by migration of a hydrocarbon group (as in the Hoffmann degradation of *N*-chloroamides or in the rearrangement of *N*-chloroamidines[5]) but rather an amino group migrates with simultaneous elimination of a sulfate or chloride ion. The intermediate product, an aminocarbodiimide *(3)*, dimerizes in absence of a reaction partner to give guanazine *(5)*, but in presence of carbonyl compounds it is trapped, the semicarbazone *(4)* being formed.



(1) *(2)* *(3)* *(4)* *(5)*, R^1 = H

	R^1	X	R^2	R^3	*(4)*, Yield (%)
(1a) [6]	H	O–SO_3H	C_6H_5	H	74
(1a)	H	O–SO_3H	$-(CH_2)_5-$		61
(1a)	H	O–SO_3H	C_6H_5	CH_3	68
(1b) [6]	C_4H_9	O–SO_3H	C_6H_5	H	62
(1c) [7]	$H_5C_6-CH_2$	Cl	CH_3	CH_3	15
(1d) [7]	n-C_4H_9	Cl	C_6H_5	H	43

Benzylidenesemicarbazone:

1.0 ml (10 mmoles) of benzaldehyde and 15 ml of 2 N NaOH are added to a solution of 1.55 g of hydroxyguanidine-*O*-sulfonic acid *(1a)* in 15 ml of water. The mixture is shaken vigorously and, after about 10 minutes, the semicarbazone crystallizes in almost pure form. – When working with *N*-chloroguanidines *(1c)* and *(1d)* it is advisable to add a little methanol to aid dissolution.

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[*] Doz. Dr. A. Heesing and Dipl.-Chem. H. Schulze
Organisch-Chemisches Institut der Universität
Hindenburgplatz 55
44 Münster (Germany)

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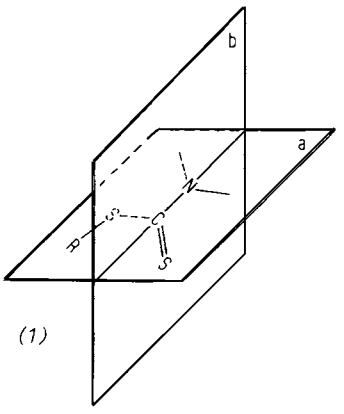
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Quadrant Rule for the n → π* Cotton Effect of Dithiourethanes from Optically Active Amines

By *H. Ripperger* [*]

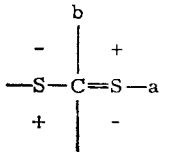
Relations between spatial structure and optical activity of chiral amine derivatives are still largely unknown. The dithiourethane chromophore is coplanar because of mesomerism[2–4]. Dipole moments indicate that we are concerned chiefly with the conformation *(1)* [5]. The geometry of the chromophore and of the n- and π*-orbitals[2] lead one to



(1)

expect that the contributions of individual atoms to the n → π* Cotton effect at about 340 nm will change sign on the planes a and b. It is possible also that importance attaches to the nodal surfaces of the n-orbital on the side of the chromophore remote from the nitrogen, but this can be neglected when the group R is symmetrical.

According to the experimental results, the signs are as given in *(2)*[**]. The same signs have been found for lactones[6].



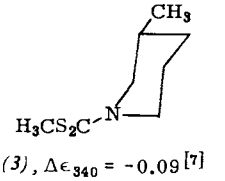
(2)

The inequality of the formal double and single C–S bonds has been neglected in the present discussion of the quadrant rule for dithiourethanes, as it was for lactones; this simplification seems permissible since both C–S bonds have partial double bond character, although to unequal extents. With this assumption, it becomes immaterial which of the two conformations that differ by rotation of 180° around the N–CS_2 bond is considered.

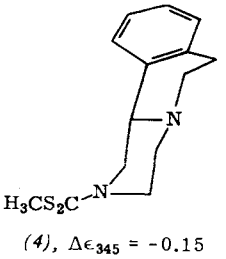
The Cotton effects for compounds *(3)* to *(6)* can be estimated by means of the quadrant rule displayed in *(2)*. This leads to a negative effect for *(3)* because of the methyl group, and for *(4)* because of the benzene ring in a negative quadrant, but to a positive effect for *(5)* and *(6)* because of the methyl group in the β-position and the 18-methyl and 12-methylene groups in a positive quadrant. Here it is to be noted that atoms in plane a or b make no contribution to the Cotton effect, that atoms in mirror-image positions relative to these planes cancel their effects, and that the effect of an atom decreases with increase in its distance from the chromophore.

The quadrant rule can also be applied to pyrrolidines and open-chain compounds. Dioxane was used as solvent in the measurements of the circular dichroism of each of the compounds except *(4)*; in the case of *(4)* methanol was used as solvent.

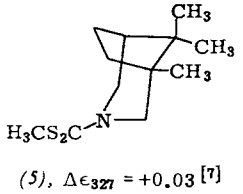
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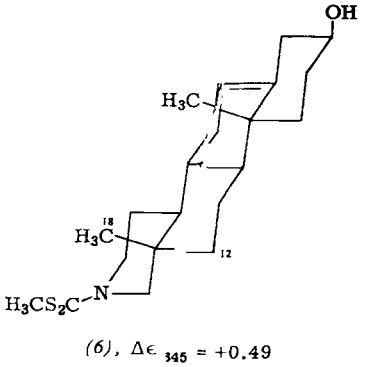
(3), $\Delta\epsilon_{340} = -0.09$[7]



(4), $\Delta\epsilon_{345} = -0.15$



(5), $\Delta\epsilon_{327} = +0.03$[7]



(6), $\Delta\epsilon_{345} = +0.49$

[*] Dr. H. Ripperger
Institut für Kulturpflanzenforschung der Deutschen Akademie der Wissenschaften zu Berlin
Kreis Aschersleben
X 4325 Gatersleben (Germany)

[**] Projection plane perpendicular to planes a and b; N atom behind the C atom.

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(Halogenocarbonyl)sulfur Pseudohalides

By *A. Haas* and *H. Reinke*[*]

We have been able to obtain the hitherto unknown (halogenocarbonyl)sulfur pseudohalides by treating (halogenocarbonyl)sulfur halides with silver pseudohalides. The synthesis of these compounds was of interest because they can be used for the preparation of further (halogenocarbonyl)sulfur compounds.

We first obtained (fluorocarbonyl)sulfur chloride *(2)*, in 70 % yield, by fluorinating the chlorine compound *(1)*[11] with antimony trifluoride in tetrahydrothiophene dioxide at 85 to 90 °C. The product was isolated by fractional distillation.

$$\underset{(1)}{Cl\text{–}CO\text{–}SCl} \xrightarrow{SbF_3} \underset{(2)}{F\text{–}CO\text{–}SCl}$$

Compounds *(1)* and *(2)* react with silver cyanate, in absence of a solvent, at 20 °C to give 60 % yields of the isocyanates *(3)*, X = Cl or F, which are then distilled off from the solids in a vacuum and are purified by fractional distillation. The isocyanates are hydrolysed completely in moist air to the *N,N'*-bis(halogenocarbonylthio)ureas *(4)*, X = Cl or F. Methanolysis of these ureas gives the methoxy derivative *(4)*, X = CH_3O, quantitatively.

X–CO–S–NCO *(3)* X–CO–S–NH–CO–NH–S–CO–X *(4)*

Compounds *(1)* and *(2)* react completely with silver isothiocyanate at room temperature. However, only (fluorocarbonyl)-sulfur thiocyanate *(5)* could be isolated – in 80 % yield by fractional condensation at −40 °C. It decomposes slowly at room temperature in accordance with:

$$\underset{(5)}{F\text{–}CO\text{–}S\text{–}SCN} \rightarrow COF_2 + COS + S + (SCN)_x$$

	^{19}F-NMR δ (ppm)[a]	B.p. (°C/mm)	M.p. (°C)	IR-absorption bands (cm^{-1}) [b]
F–CO–SCl	−33.24	46/740	−97	1857 (s) νC=O; 1055 (s) 751 (m) ; 570 (m) 1844 (s) νC=O; 1050 (s) νCF; 747 (m) νC–C + δC–F; 564 (m) νS–Cl
F–CO–NCS	−16.05 (−70 °C)	63.5	−73	1044 (s) 740 (m) 558 (m) 1966 (vs) ν_{as}NCS; 1848 (vs) νC=O; 1237 (s) ν_{s}NCS; 1028 (vs) νC–F; 762 (m) νC–S + δC–F 1018 (vs)
F–CO–S–SCN	−43.45	—	−27	2160 (m) ν_{as}SCN; 1820 (vs) νC=O; 1035 (vs) νC–F; 739 (s) νC–S + δC–F
F–CO–S–NCO	−23.46	74	−86	2245 (s) ν_{as}NCO; 1840 (s) νC=O; 1365 (w) ν_{s}NCO; 1080 (s) νC–F; 1820 (s) 1058 (s) 753 (m) νC–S + δC–F 740 (m)
$(F–CO–S–NH)_2CO$	—	—	125 (decomp.)	3250 (ms) νNH; 1805 (s) νC=O; 1505 (ms) δN–H; 1059 (s) νC–F; 1665 (s) 741 (m) νC–S + δC–F; 650 (vbr) γNH (not flat)
Cl–CO–S–NCO	—	110/748	—	2250 (s) νNCO; 1800 (vs) νCO; 830 (vs) νC–Cl
$(Cl–CO–S–NH)_2CO$	—	—	135 (decomp.)	3230 (s) νNH; 1780 (s) 1490 (s) δNH; 831 (s) νC–Cl; 655 (mbr) 1770 (s) νCO; γNH (not flat) 1665 (s)
$(CH_3O–CO–S–NH)_2CO$	—	—	194	3225 (s) νNH; 1730 (s) 1491 (s) δNH; 1450 (m) δCH_3O; 1647 (s) 1429 (ms) $\delta_{as}CH_3$ 1203 (s) 674 (m) γNH (not flat) 1191 (s) νC–O;

[a] Referred to CCl_3F as internal standard. [b] br = broad, m = medium, s = strong, vs = very strong, w = weak.

COS and $(SCN)_x$, together with small amounts of phosgene and S_2Cl_2 are found after reaction of *(1)* with AgSCN. We assume that both chlorine atoms in *(1)* react with AgSCN. Reaction of *(1)* with silver cyanide is explosive; Cl–CO–S–CN could not be isolated. Reaction of *(2)* with AgCN is also very violent but, when less than 5 g of *(2)* is used, $S(CN)_2$, COS, COF_2, and F–CO–NCS are obtained. We postulate the following reactions:

$$(2) + AgCN \longrightarrow F\text{-}CO\text{-}S\text{-}CN \xrightarrow{80\text{–}90\%} S(CN)_2 + COS + COF_2$$

$$F\text{-}CO\text{-}S\text{-}CN \xrightarrow{10\text{–}20\%} F\text{-}CO\text{-}NCS$$

The Table lists the physical properties of the new compounds. The vapor pressure of F–CO–SCl is reproduced by the following equation:

$$\log p = 7.316 - 1426/T$$

Thence b.p. 48.5 °C/760 mm can be calculated, in agreement with the experimental value. The heat of vaporization of this compound is calculated to be 6521 kcal $mole^{-1}$. The Trouton constant is 20.3 cal $degree^{-1}$ $mole^{-1}$.

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[*] Doz. Dr. A. Haas and Dipl.-Chem. H. Reinke
Anorganisch-Chemisches Institut der Universität
Hospitalstr. 8–9
34 Göttingen (Germany)

[1] French Pat. 1372911, California Research Corp.; Chem. Abstr. *62*, 1363 (1965); German Pat. 1224720, Farbenfabriken Bayer.

A Halogen-deficient Phase in the System Tellurium-Iodine

By *A. Rabenau, H. Rau,* and *P. Eckerlin*[*]

Dedicated to Professor F. Asinger on his 60th Birthday

The halides of sulfur, selenium, and tellurium constitute an interesting group of compounds because of their structural and bonding relations[1]. Their systematics are, however, not yet firmly founded. Only monohalides and compounds of high halogen content have been described.

During hydrothermal synthesis of tellurium crystals in concentrated hydriodic acid[2], we observed the occurrence of needle-shaped crystals with a metallic sheen. Their structure did not agree with that of any of the compounds described for the tellurium-iodine system[3]. Analysis showed a tellurium: iodine ratio greater than one.

Larger amounts of the crystals are formed regularly when tellurium-iodine mixtures containing less than 40 wt-% of iodine are heated with concentrated hydriodic acid in a temperature gradient. Reaction occurs in sealed quartz ampoules; the temperature must be below 210 °C. Crystals obtained under various conditions contain between 35 and 48% of iodine, which indicates a considerable phase width. The crystals are insoluble in non-oxidizing acids, in alkali hydroxide solutions, and in organic solvents, but dissolve in hot concentrated sulfuric or nitric acid.

Single-crystal studies show a monoclinic structure with a = 15.44 Å, b = 4.17 Å, and c = 12.05 Å, β = 128.1 °. D_{calc} = 5.55 g/cm^3; $D_{obs.}$ = 5.57 g/cm^3.

It has so far not been possible to obtain this phase by solid-state reactions of tellurium with iodine, which indicates strong kinetic hindrance. However, crystals of this phase have also been observed on forced sublimation with very pure argon as carrier gas[4].

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[*] Priv.-Doz. Dr. A. Rabenau, Dr. H. Rau, and
Dr. P. Eckerlin
Philips Zentrallaboratorium GmbH
Weisshausstr.
51 Aachen (Germany)

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Isomeric Chlorides and Fluorides of Sulfenic Acids

By *F. Seel, W. Gombler,* and *R. Budenz*[*]

We have proved that substitution of chlorine bonded to carbon in perchloromethane sulfenyl chloride, CCl_3SCl *(1)*, and in the chlorofluoromethane sulfenyl chlorides, $CFCl_2SCl$ *(2)*, and CF_2ClSCl *(3)* by fluorine proceeds *via* previously

unknown sulfenyl fluorides. The intermediate products are sufficiently stable to permit a study of their NMR and IR spectra at −50 °C (as liquids) and at room temperature (as gases at low pressure (≈10 mm)). The fluorination of *(1)*, *(2)*, and *(3)* has been effected in the gas phase at 150 °C with active potassium fluoride[1]. The ^{19}F–NMR spectra of the condensed products thus obtained exhibit the unusually high positive shifts characteristic of sulfenyl fluorides[2], as well as the multiplet structure expected for the CF–SF and F_2–SF groupings (Table 1). It is evident from the IR spectra that the carbon atoms of the C–SF, CF–SF, and CF_2–SF groupings are converted by chlorine into perhalomethyl groups. IR spectra of the sulfenyl fluorides show a band of type C in a constant position at 790 cm^{-1} which is assigned to S–F stretching.

At room temperature, rapid rearrangement of the liquid sulfenyl fluorides, $CF_nCl_{3-n}SF$ to the isomeric sulfenyl chlorides, $CF_{n+1}Cl_{2-n}SCl$ (n = 0,1,2) takes place.

Finally, our experiments demonstrate a decrease in the rate of substitution of chlorine by fluorine at the sulfur atom as the number of fluorine atoms on the carbon atom increases. We were also able to prepare the concluding member of the series, trifluoromethanesulfenyl fluoride.

Table 1. Chemical shifts (δ ppm.) and coupling constants (J Hz) for the ^{19}F–NMR spectra of perhalomethane sulfenyl halides (based on $CFCl_3$ as external reference).

	δ (F_C)	δ (F_S)	J (F_C–F_S)
Cl_3C–SF	–	249	–
FCl_2C–SCl	27.9	–	–
FCl_2C–SF	31 (doublet)	265 (doublet)	4.85
F_2ClC–SCl	37.5	–	–
F_2ClC–SF	45 (doublet)	297 (triplet)	6.85
F_3C–SCl	51	–	–
F_3C–SF	58 (doublet)	351 (quartet)	27
$(F_3C)_2CF$–SF [2]	73.9 158.9 (multiplets)	361 (multiplet)	22 10

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[*] Prof. F. Seel, W. Gombler, and R. Budenz
Insitut für Anorganische Chemie der Universität
66 Saarbrücken 15 (Germany)

[1] Obtained by the decomposition of potassium fluorosulfite. *F. Seel* and *D. Gölitz*, Z. anorg. allg. Chem. *327*, 28 (1964).

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Anomalous Course of the Neutralization of Periodic Acid by Sodium Hydroxide

By *K. F. Jahr* and *E. Gegner*[*]

Recently we showed[1] that the volume-contraction or -dilatation of a solution that occurs during a titration can be measured directly and used for indication of the end point. In neutralization of acids that proceeds normally one always observes a dilatation that has the same value for almost all strong acids. However, on neutralisation of free periodic acid H_5IO_6, we observed an anomalous course: a very strong dilatation up to the first equivalence point (consumption of 1 $OH^{\ominus}$) is followed by a strong contraction up to the second equivalence point (consumption of 2 $OH^{\ominus}$) (see Fig. 1).

We interpret the shape of this titration curve as due to the peculiarity of I(VII), which can adopt various coordination numbers towards oxygen, and we assume that the neutralization to the first equivalence point:

$$H_5IO_6 + OH^{\ominus} = H_4IO_6^{\ominus} + H_2O$$

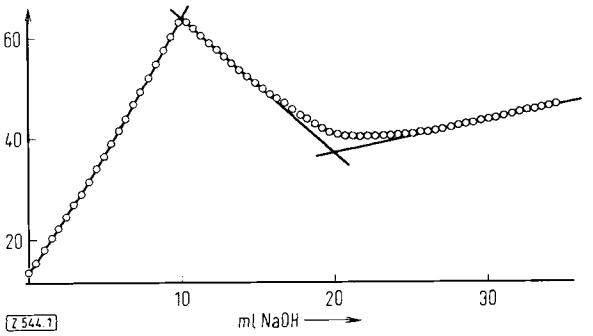


Fig. 1. Dilatometric titration of 100 ml of 0.1 M H_5IO_6 with 1 N NaOH.

Ordinate: Position of meniscus (cm).

is superposed by a change in coordination and thus by a dehydration that also occurs with dilatation:

$$H_4IO_6^{\ominus} = IO_4^{\ominus} + 2\,H_2O$$

The considerable volume contraction between the first and the second equivalence points can then be explained by resolvation, which occurs with a further change in coordination:

$$H_2O + IO_4^{\ominus} + OH^{\ominus} = H_3IO_6^{2\ominus}\ [**]$$

The slow further rise in the titration curve after the second equivalence point indicates further, incomplete neutralization of a weak acid. There are no other inflections.

That iodine can occur with various coordination numbers (4, 5, and 6) in periodates is proved by preparation of neutral anhydrous salts and by evaluation of their IR spectra[2]. Further, the central iodine atom does not retain its original coordination number during dissociation of periodic acid H_5IO_6 in aqueous solution; *Crouthamel et al.*[3], by pH measurements and spectrophotometric studies, and *Siebert*[4], by measurement of Raman spectra, have demonstrated the decomposition of $H_4IO_6^{\ominus}$ and the presence of the anion $IO_4^{\ominus}$; *Kustin* and *Lieberman*[5] have studied the kinetics of the decomposition $H_4IO_6^{\ominus} = IO_4^{\ominus} + 2\,H_2O$ in detail by the temperature-jump method and have found that on addition of alkali the anion $IO_4^{\ominus}$ is converted into the anion $H_3IO_6^{2\ominus}$ with addition of water. In agreement with these findings, crystalline salts are known that contain this anion, *e.g.* $Na_2H_3IO_6$, whereas salts of the type $M^IH_4IO_6$ have not hitherto been prepared.

In favorable circumstances the dilatometric indicator method thus makes it possible to observe addition or loss of water directly in aqueous solutions.

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[*] Prof. Dr. K. F. Jahr and Dr. E. Gegner
Institut für Anorganische Chemie der Freien Universität
Fabeckstr. 34/36
1 Berlin 33 (Germany)

[**] In a paper published while this communication was at the press, *H. Siebert* (Fortschr. chem. Forsch. *8*, 478 (1967)) formulates, instead of $H_3IO_6^{2\ominus}$, the binuclear ion $H_2I_2O_{10}^{4\ominus}$, whose formation from $IO_4^{\ominus}$, however, also involves addition of water.

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Dimethylfluorophosphine

By *F. Seel, K. Rudolph*, and *W. Gombler* [*]

Dimethylfluorophosphine, $(CH_3)_2PF$ *(1)*, could be obtained in the low pressure (<10 mm) reaction of gaseous dimethylchlorophosphine *(2)* [1] with active potassium fluoride [2] at 140 °C, thus closing the gap in the series PF_3, CH_3PF_2 [3], and $(CH_3)_3P$. Compound *(1)* melts at −109 °C, its boiling point is 26 °C/760 mm, and its vapor pressure is given by the equation $\log p$ (mm) = 7.46−1370/T (°K). The Trouton constant of *(1)* is 21.0 cal deg^{-1} mole^{-1}.

The most abundant fragments in the mass spectrum of *(1)* are CH_3PF^+ and $(CH_3)_2PF^+$. The IR spectrum of the vapor exhibits bands characteristic of a methyl compound which is closely related to the starting material (ν_{CH} = 2980, 2910 cm^{-1}; δ_{CH} = 1415, 1290 cm^{-1}; ρ_{CH} = 940, 875 cm^{-1}). The stretching frequencies of the C_2PF skeleton are found at 835, 760, and 690 cm^{-1}. In the ^{31}P–NMR spectrum the expected 1–1 doublet is observed, each component being split into a septet due to spin-spin coupling between ^{31}P and the protons of the two methyl groups. Likewise, the septets to be expected on account of F–P and F–H coupling are observed in the ^{19}F spectrum. The proton resonance in the methyl region consists of a doublet of doublets, due to H–F and H–P coupling. Chemical shifts and coupling constants are listed in Table 1.

Table 1. ^{31}P-, ^{19}F-, and H^1-NMR data for dimethylfluorophosphine

^{31}P (ext. H_3PO_4)			^{19}F (ext. $CFCl_3$)			^{1}H (ext. TMS)		
δ_P (ppm)	J_{P-F} (Hz)	J_{P-H} (Hz)	δ_F (ppm)	J_{F-P} (Hz)	J_{F-H} (Hz)	δ_H (ppm)	J_{H-P} (Hz)	J_{H-F} (Hz)
−187	820	6.0	+195.5	823	18.5	−1.45	5.9	18.5

Dimethylfluorophosphine is an extremely reactive compound which ignites spontaneously in air. It disproportionates cleanly at room temperature in accordance with the equation

$$3\,(CH_3)_2PF \rightarrow \underset{(3)}{(CH_3)_2PF_3} + \underset{(4)}{(CH_3)_2P{-}P(CH_3)_2}$$

to give dimethyltrifluorophosphorane *(3)* and tetramethylbiphosphine *(4)*. The identity of *(3)* was established from its ^{19}F–NMR spectrum [4], whereas *(4)* was identified by its ^{1}H- and ^{31}P–NMR spectra [5]. Hydrolysis of *(1)*, as well as of *(2)*, leads to formation of dimethylphosphine oxide, $(CH_3)_2P(O)H$.

In a manner analogous to methyldifluorophosphine [6], *(1)* combines with hydrogen fluoride in a 1:1 molar ratio to give a product containing a P–H bond, which is characterized by a proton NMR signal at −7.45 ppm. (J_{H-P} = 733 Hz), and by an IR band at 2435 cm^{-1}. *(1)* and *(2)* react with transition metals, even at low temperature, to form colored coordination compounds which are currently being investigated.

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[*] Prof. F. Seel, K. Rudolph, and W. Gombler
Institut für Anorganische Chemie der Universität
66 Saarbrücken 15 (Germany)

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p-Isothiocyanatobenzenesulfonyl Isocyanate: a Bifunctional Compound with Selective Reactivity

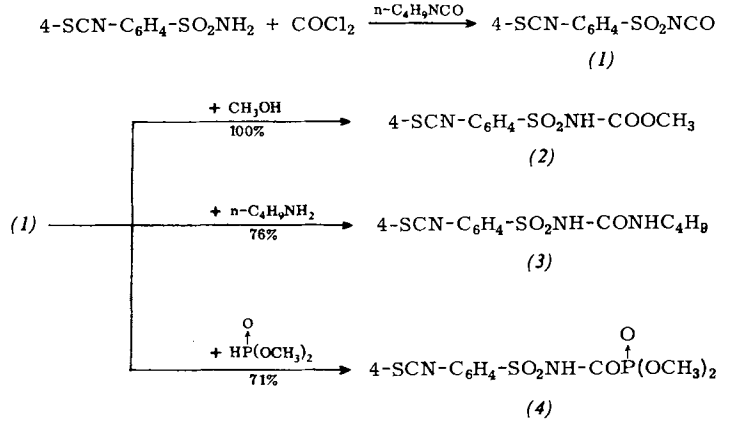
By *H. Ulrich, B. Tucker*, and *A. A. R. Sayigh* [*]

Few compounds are known containing two cumulene functions in which the reactivity of the two double-bond systems is so different that selective reaction can be achieved at only one of the two groups. We recently reported the synthesis of isocyanatobenzenesulfonyl isocyanates in which the reactivity of the sulfonyl isocyanate function was appreciably greater than that of the isocyanate group [1]. The difference between the two groups should be considerably larger in isothiocyanatobenzenesulfonyl isocyanates.

p-Isothiocyanatobenzenesulfonyl isocyanate *(1)* can be obtained by direct phosgenation of *p*-isothiocyanatobenzenesulfonamide in the presence of n-butyl isocyanate as catalyst. On treatment of *(1)* with alcohols, amines, or dialkyl phosphites at room temperature, reaction occurs at the sulfonyl isocyanate group with formation of the 1:1 adducts *(2)*, m.p. 150–153 °C, *(3)*, m.p. 152–156 °C, and *(4)*, m.p. 152 to 153 °C.

When the urethane *(2)* is heated with methanol in the presence of triethylenediamine (DABCO) as catalyst, the 1:2 adduct, m.p. 168–170 °C, is obtained in 47.5% yield. Under similar conditions, the urea *(3)* reacts with methanol with formation of the mixed 1:2 adduct, m.p. 75 °C (yield 92.5%); and the mixed 1:2 adduct, m.p. 140–142 °C (yield 56%), results from *(3)* and isopropylamine.

Reagents can be chosen that permit synthesis of a series of mixed 1:2 adducts, which are only very difficulty accessible by other routes.



p-Isothiocyanatobenzenesulfonyl isocyanate (1):

Phosgene is passed (1 g/min; 90 min) into a boiling solution of *p*-isothiocyanatobenzenesulfonamide[2] (21.4 g, 0.1 mole) and *n*-butyl isocyanate (8.56 g) in *o*-dichlorobenzene (500 ml). Nitrogen is passed through the mixture, and then the solvent and catalyst are removed in a vacuum. Vacuum-distillation of the residue gives 19 g (79 %) of *p*-isothiocyanatobenzenesulfonyl isocyanate, b.p. 140 °C/0.2 mm, m.p. 64–67 °C; IR, $\lambda_{max}^{CHCl_3}$ = 2232 cm^{-1} (NCO) and 2128–2041 cm^{-1} (NCS).

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[*] Dr. H. Ulrich, B. Tucker, and Dr. A. A. R. Sayigh
The Upjohn Company, Donald S. Gilmore Research Laboratories
North Haven, Connecticut, U.S.A.

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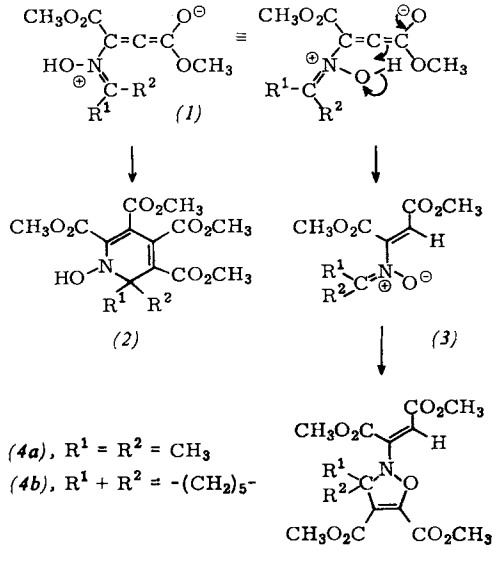
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Cycloaddition of Ketoximes

By *E. Winterfeldt* and *W. Krohn*[*]

We have treated the oximes of cyclohexanone and acetone with dimethyl acetylenedicarboxylate in dimethylformamide or dimethyl sulfoxide at room temperature for 15 h. Pouring the mixtures into water gives in each case a 75 % yield of a product that, on the basis of analysis and mass spectra, is to be regarded as a 2:1 adduct.

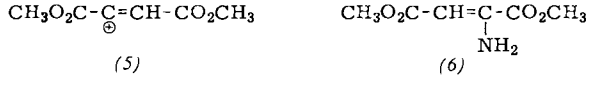
Basically, there are two ways for formation of such an adduct: (i) Formation of the 1:1 adduct *(1)* and subsequent cycloaddition to give *(2)*; and (ii) proton shift to give *(3)* with subsequent cycloaddition resulting in the formation of *(4)*.



(4a), $R^1 = R^2 = CH_3$
(4b), $R^1 + R^2 = -(CH_2)_5-$

Whilst the analytical data ($C_{15}H_{19}NO_9$ for the product from acetoxime)[1] are in agreement with either possible mechanism, the spectral data indicate structure *(4a)*.

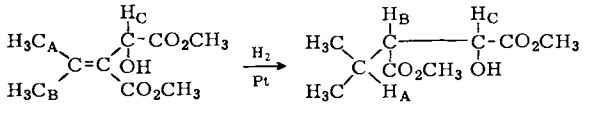
The intense peak (base peak) in the mass spectrum occurs at *m/e* = 143 and corresponds to fragment *(5)*; further important peaks lie at *m/e* = 342 (M − CH_3) and 298 (M − CO_2CH_3). The UV spectrum (in metnanol) with a maximum at 280 nm is not compatible with structure *(2)*.



(5) *(6)*

The IR spectrum shows bands at 1620, 1675, 1730, and 1750 cm^{-1} (no OH band) and thus accords well with structure *(4)*, as does also the NMR spectrum [τ = 8.44 (6), 6.37 (3), 6.28 (3), 6.18 (3), 6.15 (3), 4.51 and 3.89 (together 1)]. The NMR spectrum also indicates that *(4a)* is a mixture of *cis*- and *trans*-compounds in which the maleic ester configuration (the product of *cis*-addition) largely predominates (85 %). The failure of the protons with τ = 4.51 and 3.89 to undergo exchange with deuterated methanol excludes the presence of an OH group.

The following degradation reactions prove structure *(4a)*: Hydrogenation affords *(6)* (reductive N–O fission and allyl-hydrogenolysis), which proved to be identical with authentic material. Reduction with zinc in 10 % methanolic sulfuric acid at room temperature (30 min) yields *(7)* (reductive ring fission and Hofmann degradation), which gives *(8)* on hydrogenation.



(7) *(8)*

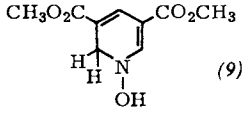
(7), IR: 3530, 1750, 1640 cm^{-1}.

NMR: H_3C_A τ = 8.03 (3); H_3C_B τ = 7.92 (3); CO_2CH_3 τ = 6.35 (3), 6.27 (3); H_C τ = 5.12 (1); OH τ = 7.0 (1).

(8), IR: 3550, 1750 cm^{-1}.

NMR: CH_3 τ = 9.0 (3), d*J* = 6.5, 9.06 (3), d*J* = 6.5; H_A τ = 7.78 (1); H_B τ = 7.52 (1), tr. *J* = 7; H_C τ = 5.71 (1), d*J* = 7; CO_2CH_3 τ = 6.25 (3), 6.38 (3); OH τ = 7.12 (1).

The structure *(4a)* is thus established for the adduct of acetoxime. Analogous spectral data for the adduct of cyclohexanone oxime permit it to be allotted structure *(4b)*. This



(9)

finding is remarkable because the investigations of *Ochiai et al.*[2] suggested that compound *(9)* of dihydropyridine type occurs as intermediate in the reaction of propiolic ester with formaldehyde oxime, and this product can be envisaged as formed by 1,4-addition.

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[*] Prof. Dr. E. Winterfeldt and W. Krohn
Organisch-Chemisches Institut der Technischen Universität
Strasse des 17. Juni 115
1 Berlin 12 (Germany)

[1] The elemental composition was derived from high resolution of the molecular ion peak in the mass spectrum. We thank Dr. *D. Schumann* for his willing help.

[2] *M. Ochiai*, *M. Obayashi*, and *K. Morita*, Tetrahedron *23*, 2641 (1967).

N-(Cyano)phenylphosphonimidic Difluoride and *N*-(Cyano)diphenylphosphinimidic Fluoride

By *O. Glemser*, *E. Niecke*, and *J. Stenzel*[*]

2,4-Difluoro-1,3,2,4-diazadiphosphetidines are formed on treatment of bis(trialkylsilyl)-nitrogen compounds with Lewis-acid phosphorus fluorides[1]. The stability of the four-membered ring apparently prevents formation of a compound with a phosphorus-nitrogen double bond, so that

hitherto only one representative of the phosphorus fluorides, namely *N*-methyldiphenylphosphinimidic fluoride, has been known [2]. By treatment of bis(trimethylsilyl)carbodiimide [3] with tetrafluoro(phenyl)phosphorane [4] and diphenylphosphinic trifluoride, we have now synthesized the two phosphorus fluoride imides *(1)* and *(2)*.

$$(CH_3)_3Si{-}NCN{-}Si(CH_3)_3 + H_5C_6{-}PF_4 \rightarrow 2\,(CH_3)_3SiF + H_5C_6{-}PF_2{=}NCN \quad (1)$$

$$(CH_3)_3Si{-}NCN{-}Si(CH_3)_3 + (C_6H_5)_2PF_3 \rightarrow 2\,(CH_3)_3SiF + (C_6H_5)_2PF{=}NCN \quad (2)$$

The compounds *(1)* and *(2)* are formed quantitatively when carbodiimide is added dropwise to the phosphorus fluoride (molar ratio 1:1 [5]) with stirring and warming [*(1)* at 30 °C, *(2)* at 70 °C]. A large part of the trimethylsilyl fluoride escapes from the mixture during the reaction, and the remainder is pumped off under vacuum (1 mm).

The composition of compounds *(1)* and *(2)* is proved by the results of elemental analyses and by determination of the molecular weight [mass spectroscopic: for *(1)*, *m/e* = 186; for *(2)*, *m/e* = 244] [6].

The phosphorus fluoride imides *(1)* and *(2)* are viscous, high-boiling liquids that fume in air and undergo considerable decomposition on distillation in a vacuum – their separation by distillation was therefore not attempted.

The IR spectra (capillary film) of *(1)* and *(2)* in the NaCl region showed the following bands, as well as those of the phenyl group:

$H_5C_6{-}PF_2NCN$: 2230 ν(NC≡N); 937, 908, 814 ν_{as},ν_{sym}(PF), ν(N–CN)

$(C_6H_5)_2{-}PFNCN$: 2210 ν(NC≡N); 885, 815 ν(N–CN), ν(PF)

The ^{31}P–NMR spectrum [6] of *(1)* contains a triplet, and that of *(2)* a doublet. As expected, the ^{19}F–NMR signal is a doublet for both compounds. Coupling of the *ortho*-protons on the phenyl group with the fluorine was not observed, nor was P–H coupling over two carbon atoms.

	$\delta^{31}P$(ppm)[a]	J_{PF}(Hz)	$\delta^{19}F$(ppm)[a]	J_{FP}(Hz)
$H_5C_6{-}PF_2NCN$	−15.3	1140	66.5	1132
$(C_6H_5)_2PFNCN$	−50.3	1074	82.1	1064

[a] 85 % H_3PO_4 and $CFCl_3$, respectively, were used as external standard.

The center of the signal for the *para*-proton on the phenyl ring of *(1)* is at −7.41 ppm, and of *(2)* is at −7.18 ppm, referred to $(CH_3)_4Si$ as external standard.

Comparison of the $\delta^{31}P$ values of difluorodiazadiphosphetidines (of the order of 45–70 ppm) with those of the phosphorus fluoride imides shows that the phosphorus nucleus is more strongly shielded in the cyclic compounds.

Thus the difference in the coordination number of the phosphorus in the difluorodiazadiphosphetidines (v) and in the phosphorus fluoride imides (iv) has its effect on the PF coupling constants. Whereas J_{PF} for the former is at 900 Hz, for the latter one obtains values some 200 Hz greater.

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[*] Prof. Dr. O. Glemser, Dipl.-Chem. E. Niecke, and Dipl.-Chem. J. Stenzel
Anorganisch-Chemisches Institut der Universität
Hospitalstr. 8/9
34 Göttingen (Germany)

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[2] *R. Schmutzler*, Chem. Commun. *1965*, 19.
[3] *J. Pump* and *U. Wannagat*, Angew. Chem. *74*, 117 (1962); Angew. Chem. internat. Edit. *1*, 112 (1962). – Preparation in molten salts: *J. Stenzel* and *W. Sundermeyer*, Chem. Ber., in the press.
[4] We thank Dr. *Schmutzler* for both the phosphorus fluorides.
[5] The molar ratio 1:1 must be adhered to as closely as possible, as separation of starting material from *(1)* is exceedingly difficult, and that from *(2)* was only partially achieved.
[6] We thank Dr. *Marsmann* for the ^{31}P–NMR spectra and *D. Böhler* for the mass-spectrometric investigations.

Synthesis of Sulfur Difluoride (Difluorophosphinyl)-imide and Sulfur Oxide Difluoride (Fluorosulfonyl)imide

By *O. Glemser*, *H. W. Roesky*, and *P. R. Heinze* [*]

Phosphorodifluoridamide *(1)*, prepared by ammonolysis of pyrophosphoryl tetrafluoride [1], reacts with sulfur tetrafluoride at 40 °C to give a 55 % yield of sulfur difluoride (difluorophosphinyl)imide *(2)*, which decomposes even at room temperature to phosphoryl fluoride and thiazyl fluoride.

$$\underset{(1)}{OPF_2NH_2} + SF_4 \rightarrow \underset{(2)}{OPF_2N{=}SF_2} + 2\,HF$$

$$(2) \rightarrow POF_3 + NSF$$

Fluorosulfonyl amide *(3)* reacts with sulfinyl tetrafluoride at 130 °C in presence of sodium fluoride as HF trap, to give a 30 % yield of sulfur oxide difluoride (fluorosulfonyl)imide *(4)* [2].

$$\underset{(3)}{FSO_2NH_2} + SOF_4 \rightarrow \underset{(4)}{FSO_2N{=}SOF_2} + 2\,HF$$

Compound *(2)* is a clear liquid with a pungent odor and has b.p. 45 °C/80 mm and m.p. −41 °C. Even in absence of moisture it decomposes within a few hours, becoming deep red. The vapor pressure accords with

$$\log p_{mm} = -(1904/T) + 7.887$$

with a heat of vaporization of 8.7 kcal mole^{-1} and a Trouton constant of 22.9 cal deg^{-1} mole^{-1}; b.p. (extrap.) = 108 °C. The composition of the compound is proved by the results of elemental analysis and by the mass spectrum. The ^{19}F–NMR spectrum of *(2)* shows four triplets of equal intensity.

Signal	Position (Hz)	Chem. shift [a]	Coupling constant
A	+3207	δ_{SF} = −57.1 ppm	$J_{P\text{-}F(S)}$ = 28 Hz
B	+3235		
C	−4457	δ_{PF} = +69.9 ppm	J_{PF} = 1026 Hz
D	−3431		J_{FF} = 4.5 Hz

[a] Referred to CCl_3F as external standard at 30 °C.

The IR spectrum (recorded in the gas phase) showed the following bands: 1392 vs ν(PO), 1352 vs ν(SN), 957 s ν_{as}(PF), 920 s ν_s(PF), 798 s ν_{as}(SF), 731 s ν_s(SF), 696 m ν(PN) cm^{-1} [3]; weak bands at 630, 566, 529, and 488 cm^{-1} are ascribed to deformation vibrations.

Because of the dependence of the strength of P–O and P–F bonds on the sum of the electronegativities of the halogens in phosphoryl halides, the IR data can be used to afford the electronegativity of the NSF_2 group. From the equation [4]

$\nu(PO) = 31.3\ \Sigma x_i + 1039$

one obtains the electronegativity $x_{NSF_2} = 3.3$. If one plots the mean PF frequency of the phosphoryl halides against the sum of the electronegativities, one obtains a linear dependence, whence the electronegativity of the NSF_2 group again appears as 3.3.

Compound *(4)* is a clear liquid of b.p. 72 °C and m.p. −70 °C and, as expected, is more stable than sulfur difluoride (fluorosulfonyl)imide. The compound was characterized by elemental analysis and by its IR, ^{19}F–NMR, and mass spectra.

The mass spectrum shows, besides the molecular ion at m/e = 183, the typical fragments M − F (164), FSO_2N (97), SOF_2 (86), FSO_2 (83), FSO (67), SF (51), and SO (48).

The ^{19}F–NMR spectrum shows a doublet at −45.4 and a triplet at −60.1 referred to CCl_3F as external standard; the coupling constant is J_{FF} = 8 Hz.

The IR spectrum (gas) in the NaCl region shows strong bands at 1475, 1450, 1245, 888, 821, 740, and 716 cm^{-1}, which are to be ascribed to stretching virations.

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[*] Prof. Dr. O. Glemser, Dr. H.W. Roesky, and Dipl.-Chem. P. R. Heinze
Anorganisch-Chemisches Institut der Universität
Hospitalstr. 8/9
34 Göttingen (Germany)

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[2] Cf. *O. Glemser, H. W. Roesky*, and *P. R. Heinze*, Angew. Chem. *79*, 153 (1967); Angew. Chem. internat. Edit. *6*, 179 (1967).

[3] vs = very strong, s = strong, m = medium.

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Preparation of Sulfur Oxide (Fluorosulfonyl)imide and Sulfur Dichloride (Fluorosulfonyl)imide [1]

By *H. W. Roesky* [*]

Fluorosulfonamide *(1)*, which can be prepared by hydrolysis of fluorosulfonyl isocyanate [2] by concentrated formic acid, reacts with thionyl chloride *(2)* to give sulfur oxide (fluorosulfonyl)imide *(3)*.

$$\underset{(1)}{FSO_2NH_2} + \underset{(2)}{SOCl_2} \rightarrow \underset{(3)}{FSO_2{-}N{=}S{=}O} + 2\,HCl$$

Thionyl chloride (0.75 mole) is added to the amide *(1)* (0.5 mole), and the whole is heated under reflux, with stirring, for 48 h, then distilled under vacuum (oil-pump). The product *(3)* is collected in a cold trap (−10 °C; ice/salt) and distilled [yield, 42 g (57 %); b.p. 20 °C/0.3 mm, 32 °C/15 mm]. Partial decomposition sets in at higher pressures.

Compound *(3)* is a yellow liquid that reacts explosively with water at room temperature. At −20 °C its reaction with water regenerates the amide and sulfur dioxide. The mass spectrum of *(3)* contains the molecular ion peak at m/e = 145 and peaks for the fragments FSO_2 (83), SO_2 (64), SO (48), and NS (46). The IR spectrum (capillary film) in the NaCl and KBr region shows bands at 1435, 1260, 1210, 1125, 830, 700, 628, 615, 595, 538, 482, and 460 cm^{-1}; these are provisionally allotted to the following vibrations: $\nu_{as}(SO)$ 1435, $\nu_s(SO)$, $\nu(SO)$, $\nu(N{=}S)$ 1260, 1210, 1125, $\nu(SF)$ 830, $\nu(SN)$ 700, and deformation vibrations.

Reaction of the imide *(3)* with phosphorus pentachloride gives sulfur dichloride (fluorosulfonyl)imide *(4)*.

$$\underset{(3)}{} + PCl_5 \rightarrow \underset{(4)}{FSO_2{-}N{=}SCl_2} + OPCl_3$$

Compound *(3)* is added dropwise to an excess of PCl_5 with stirring and with passage of dry nitrogen (molar ratio 1:1.2) at such a rate that the temperature does not rise above 50 °C. The mixture is then filtered under nitrogen from the excess of PCl_5 and fractionated in a vacuum (yield 70 %; b.p. 45 °C/0.4 mm).

Compound *(4)* can also be prepared, in an impure form, from *(1)* and sulfur dichloride.

The IR spectrum of *(4)* contains bands at 1425, 1210, 1125, 805, 712, 582, 537, 480, and 442 cm^{-1}, which are provisionally allotted to the following vibrations: $\nu_{as}(SO)$ 1425, $\nu_s(SO)$, $\nu(N{=}S)$ 1210, 1125, $\nu(SF)$ 805, $\nu(SN)$ 712, and $\nu(SCl)$ and deformation vibrations. The mass spectrum shows many fragments as well as the molecular ion at m/e = 199 and 201 (isotopic ratio).

Sulfur dichloride (fluorosulfonyl)imide *(4)* is a colorless liquid, that is hydrolysed immediately by water. It reacts with V2A steel at room temperature with decomposition.

	^{19}F–NMR [a]		^1H–NMR [a]	
	δ_F(ppm)	Multiplicity	δ_H (ppm)	J_{F-H} (Hz)
FSO_2NH_2 *(1)* [3]	−57.0	Triplet	6.1	6
$FSO_2N{=}S{=}O$ *(3)*	−59.2	Singlet	—	—
$FSO_2N{=}SCl_2$ *(4)*	−61.4	Singlet	—	—

[a] Referred to CCl_3F or $(CH_3)_4Si$ as external standard.

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[*] Dr. H.W. Roesky
Anorganisch-Chemisches Institut der Universität
Hospitalstr. 8/9
34 Göttingen (Germany)

[1] Part IV of Sulfur-Nitrogen Compounds. – Part III: *H. W. Roesky* and *A. Hoff*, Chem. Ber., in the press. – Part II: *O. Glemser, H. W. Roesky*, and *P. R. Heinze*, Angew. Chem. *79*, 153 (1967); Angew. Chem. internat. Edit. *6*, 179 (1967).

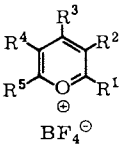
[2] I thank Farbwerke Hoechst for the supply of chlorosulfonyl isocyanate.

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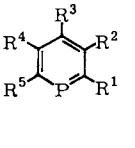
Determination, by ESR Spectroscopy, of the Constitution of the Phosphorus Radicals formed on Oxidation of Phosphorins

By *K. Dimroth, N. Greif, W. Städe*, and *F. W. Steuber* [*]

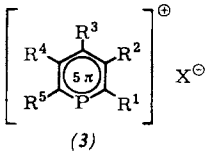
As part of a study of the radicals formed on oxidation of 2,4,6-triarylphosphorins [1] we have prepared the new phosphorins *(2)* listed in the table. These compounds, which were prepared by *Märkl*'s method [2] from the corresponding pyrylium salts *(1)*, were oxidized by 2,4,6-triarylphenoxyls, lead(IV) acetate or benzoate, mercury(II) acetate, or other oxidizing agents to the phosphorus radical cations *(3)*, which are very stable in solution.



(1)



(2)



(3)

(2)	R^1	R^2	R^3	R^4	R^5	M.p. (°C)	λ_{max} (nm) in n-hexane	$\varepsilon \times 10^{-4}$	Radical cation (3) a_P (gauss)
(a)	C_6D_5	H	C_6D_5	H	C_6D_5	168–171	278	5.2	23.2
(b)	C_6D_5	H	C_6H_5	H	C_6D_5	167	278	4.2	23.2
(c) [a]	C_6H_5	C_6H_5	C_6H_5	H	C_6H_5	188.5–189.5	271	3.7	24.8
(d) [a]	C_6H_5	C_6H_5	C_6H_5	C_6H_5	C_6H_5	216–217	264	3.13	26.0
(e)	p-Cl–C_6H_4	H	C_6H_5	H	C_6H_5	166–167	281	4.3	22.6
(f)	p-Cl–C_6H_4	H	p-Cl–C_6H_4	H	p-Cl–C_6H_4	181–182	285	5.4	22.4
(g) [a]	C_6H_5	H	p-CH_3O–C_6H_4	H	C_6H_5	110.5–112	283	3.7	21.6
(h)	p-CH_3O–C_6H_4	H	C_6H_5	H	C_6H_5	161.5–163	287	3.78	21.7
(i)	p-CH_3O–C_6H_4	H	p-CH_3O–C_6H_4	H	C_6H_5	134–136	291	3.78	21.6
(k) [a]	p-CH_3O–C_6H_4	H	C_6H_5	H	p-CH_3O–C_6H_4	132–133	291	3.78	22.3
(l)	p-CH_3–C_6H_4	H	C_6H_5	H	C_6H_5	155–156.5	281	3.75	
(m)	p-CH_3O–C_6H_4	H	p-C_6H_5–C_6H_4	H	C_6H_5	148–150.5	293	2.93	
(n)	α-$C_{10}H_7$	H	C_6H_5	H	C_6H_5	163–164	272	4.72	
(o)	C_6H_5	H	t-C_4H_9	H	C_6H_5	87.5–88.5	267	3.06	22.3
(p)	t-C_4H_9	H	C_6H_5	H	t-C_4H_9	104–105	288	1.8	23.7
(q)	t-C_4H_9	H	p-CH_3O–C_6H_4	H	t-C_4H_9	116–116.5	300	2.16	23.3
(r) [b]	t-C_4H_9	H	t-C_4H_9	H	t-C_4H_9	88	263	0.5	26.9

[a] These phosphorin derivatives were recently prepared by *G. Märkl et al.* [3] by another method. Material discrepancies in melting point occur only for *(2c)* and *(2d)*. These may be due, as for tetra- and penta-phenylbenzene derivatives, to formation of different crystal modifications.

[b] From 2, 4, 6-tri-t-butylpyrylium tetrafluoroborate, m. p. 216°C (*K. Dimroth* and *W. Mack*, unpublished).

The ESR spectra of all these radicals are very similar in type: They contain a doublet that is due to interaction of the free electron with the phosphorus. The phosphorus coupling constant a_P lies between 21.5 and 27 gauss (see table) according to the nature of the substituents. The doublet has hyperfine structure owing to coupling with the protons.

There are about 70 lines in the spectrum of the 2,4,6-triphenylphosphorin radical. However, if the three phenyl groups in 2-, 4-, and 6-position are replaced by pentadeuteriophenyl, then, exactly as with 2,4,6-tri(pentadeuteriophenyl)phenoxyl[4], the spectrum is greatly simplified by the small magnetic moment and the larger nuclear spin of the deuterium. Only the two protons in the central nucleus lead to resolution to hyperfine structure. One obtains a triplet 1:2:1, which, by phosphorus coupling ($|a_P|$=23.2 gauss) appears twice, (Fig. 1a). The hyperfine structure coupling constant $|a_H|$ amounts to about 2.4 gauss. In the NMR spectrum tris-(pentadeuteriophenyl)phosphorin *(2a)* gives signals only for the two protons in the central ring (doublet at $\delta = -8.12$ ppm, $J = 6$Hz).

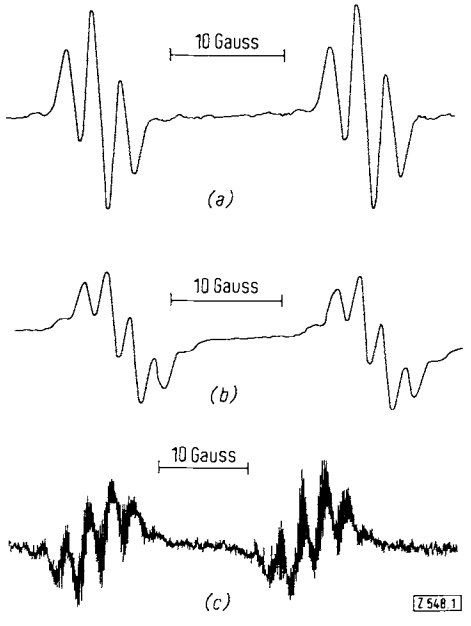


Fig. 1. ESR spectra of the cation radicals from (a) 2,4,6-tris(pentadeuteriophenyl)phosphorin *(2a)*, (b) 2,6-bis(pentadeuteriophenyl)-4-phenylphosphorin *(2b)*, and (c) 2,6-di-t-butyl-4-phenylphosphorin *(2p)*.

Every group of lines in the ESR spectrum of the oxidation product of 2,6-bis(pentadeuteriophenyl)-4-phenylphosphorin *(2b)* consists of a sextet with approximate intensities 1:5:10:10:5:1 (Fig. 1b), analogously to the spectrum of the correspondingly substituted phenoxyl[4]. The coupling constants of the protons in positions 3 and 5 of the central ring, and of the two *ortho*-protons and the *para*-proton of the phenyl group, are about equal in size (2.4 gauss), but the *meta*-protons on this phenyl ring have significantly lower coupling constants, so that no further resolution is observed. The spectrum can be unequivocally reconstructed.

It is thus proved that the new radicals retain the intact phosphorin ring. The same conclusion is reached on comproportionation of one molecule of the radical formed on oxidation and one of that formed on reduction of 2,4,6-triphenylphosphorin[5], which regenerates 2,4,6-triphenylphosphorin.

The phosphorins *(2o)* to *(2r)* are the first compounds of this type containing aliphatic groups. They too give very simple ESR spectra because the coupling constants of the t-butyl groups are small. Figure 1c shows the spectrum of 2,6-di-t-butyl-4-phenylphosphorin cation radical ($|a_P| = 23.7$ gauss, $|a_H| = 2.5$ gauss). For 2,6-di-t-butyl-4-(*p*-methoxyphenyl)-phosphorin cation radical the sextet of lines becomes a quintet, since here the coupling with the *para*-proton on the phenyl ring at C-4 is absent.

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[*] Prof. K. Dimroth, Dr. N. Greif,
Dipl.-Chem. W. Städe, and Dr. F.W. Steuber
Institut für Organische Chemie der Universität
Bahnhofstr. 7
355 Marburg (Germany)

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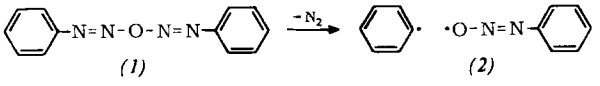
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Mechanism of the Gomberg Reaction and of Phenylation by *N*-Nitrosoacetanilide

By *Ch. Rüchardt* [*]

Phenylation of aromatic compounds by the Gomberg reaction and by *N*-nitrosoacetanilide can both be interpreted as formation and homolysis of diazoanhydrides *(1)* [1].



(1) *(2)*

The key hypothesis for understanding these reactions, namely, formation of relatively stable diazotate radicals *(2)*, is supported by chemical and physical evidence.

Polymerisation of styrene initiated by *N*-nitrosoacetanilide gives only a small amount of polymer (1 to 2 wt-%) containing nitrogen. The inhibiting action of stable diazotate radicals, which trap the growing chains, can explain this result. During the whole period of decomposition of *N*-nitrosoacetanilide in benzene an ESR spectrum is observable (g = 2.0055) that contains three groups of lines whose fine structure agrees with the structure of the diazotate radicals. By using ^{15}N-labeling the N coupling constant a_N = 11.61 gauss was assigned to the "outer" nitrogen atom and a_N = 1.67 gauss to the nitrogen attached to the aromatic group. The spectra of *p*-deuterio- and *p*-t-butyl-diazotate radicals can be best reproduced by assuming differing *ortho*-couplings, according to which diazotate radicals have a non-linear structure, as has been assumed also for diazotate anions.

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[*] Priv.-Doz. Dr. Ch. Rüchardt
Institut für Organische Chemie der Universität
Karlstr. 23
8 München (Germany)

[1] *Ch. Rüchardt*, Angew. Chem. 77, 974 (1965); Angew. Chem. internat. Edit. 4, 964 (1965).

The Viscosity of Liquid Aluminum Halides

By *K. H. Grothe* and *P. Kleinschmit* [*]

It is difficult to determine the viscosity of molten salts by the usual methods [1] if the substances are sensitive to air or have a high vapor pressure. Such substances include aluminum tribromide and triiodide. A method was therefore chosen in which a vessel suspended from a wire was made to execute torsional oscillations, the damping of the oscillations being measured and used to determine the viscosity. The salts were distilled into a cylindrical glass vessel of about 3 cm diameter and 4 cm height and the vessel was subsequently sealed in a vacuum. The vessel was hung on a torsion wire and made to oscillate about its vertical axis. The friction between the layer of liquid adhering to the inner wall and the liquid near the wall leads to damping of the oscillations.

$AlBr_3$					
T (°C)	100	150	200	250	
η (cP)	2.37	1.42	0.96	0.71	
AlI_3					
T (°C)	200	240	300	340	400
η (cP)	2.62	1.90	1.32	1.10	0.86

The values in the Table were found for the viscosity of $AlBr_3$ (m.p. 97.5 °C; b.p. 255 °C) and AlI_3 (m.p. 192 °C; b.p. 386 °C).

In both cases the exponential function $\eta = A \exp (E_\eta/RT)$ proposed by *Andrade* [2] was followed. For $AlBr_3$, $A = 34.5\times10^{-3}$ cP and E_η = 3.13 kcal mole^{-1}; for AlI_3, $A = 64.0\times10^{-3}$ cP and E_η = 3.46 kcal mole^{-1}.

The viscosities found also follow the equation given by *Batschinski* [3]: $v = B\varphi + b$, where v is the specific volume, $\varphi = 1/\eta$ the fluidity, b is the specific volume at zero fluidity, and B is a constant. The values of b extrapolated from this equation do not agree with the specific volumes of the solid aluminum halides at the melting point but are about 10 % greater.

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[*] Dr. K. H. Grothe und Dipl.-Chem. P. Kleinschmit
Institut für Anorganische Chemie
der Technischen Hochschule
Callinstr. 46
3 Hannover 1 (Germany)

[1] *E. Helmes* in: Ullmanns Encyklopädie der technischen Chemie. Urban und Schwarzenberg, München-Berlin 1961. Vol. 2/1, p. 777.

[2] *C. Andrade*, Nature (London) *125*, 309, 582 (1930).

[3] *A. J. Batschinski*, Z. physik. Chem. *84*, 643 (1913).

Measurement of Vapor-pressure Differences for Isotopic Compounds

By *H. Wolff* and *A. Höpfner* [*]

Replacement of H by D either decreases (normal effect) or increases (inverse effect) the vapor pressure (p) of a substance. Hydrocarbons show the inverse effect; alcohols and amines (including H_2O and NH_3) show a normal effect insofar as replacement is at the hydroxyl or amino group, but otherwise an inverse effect.

Study of the vapor-pressure isotope effect for the methylamines CH_3NH_2 *(1)*, CH_3ND_2 *(2)*, CD_3NH_2 *(3)*, and CD_3ND_2 *(4)* in relation to temperature and concentration (in mixtures with n-hexane) showed strong, temperature-dependent normal effects for the pairs *(1)/(2)* and *(3)/(4)*, that change to inverse effects at high dilution (molar fraction < 0.1). The inverse effects observed for *(1)/(3)* and *(2)/(4)* are only slightly dependent on temperature and independent of concentration.

It is concluded from the experimental results that appearance of the normal vapor-pressure isotope effect for the substances named is connected with the occurrence of association by hydrogen bonding. Quantitative interpretation seems to be possible by means of the hydrogen-bond vibrations to which the translational and rotational degrees of freedom of the free molecule correspond, though these vibrations are not readily accessible spectroscopically. For the ideal case of wholly independent harmonic vibrations the isotope effect of one degree of freedom is given by

$$\frac{p_D}{p_H} = \frac{\theta_H \sin \frac{\theta_D}{2T}}{\theta_D \sin \frac{\theta_H}{2T}}$$

This formula also explains why all substances show a normal effect at very low temperatures (< 70 °K), since, under these conditions, the lattice vibrations (whose characteristic temperatures mostly lie below 100 °K) may contribute to the

vapor pressure isotope effect whereas they are fully excited at room temperature and thus do not contribute.

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German version: Angew. Chem. 79, 728 (1967)

[*] Prof. Dr. H. Wolff and Dr. A. Höpfner
Physikalisch-Chemisches Institut der Universität
Tiergartenstr.
69 Heidelberg (Germany)

Developments of Fuel Cells

By *W. Vielstich* [*]

General Motors recently exhibited a bus (Electrovan) driven by a 32 kW H_2/O_2 battery (Union Carbide Inc.) operating an alternating current motor. Disadvantages of this experimental model are the tanks containing liquid hydrogen and liquid oxygen (danger of explosion) and the high cost of the noble metals in the hydrogen electrode. A 200 kW battery constructed by Firma ASEA, Sweden, for propulsion of a submarine, utilizes ammonia and liquid air; the ammonia is first cracked in a reformer and the hydrogen obtained is fed to skeleton nickel electrodes.

The triangular potential scan method is useful for study of the fundamental principles. In the region between initial H_2- and O_2-evolution, the electrode potential varies linearly with time in a periodic manner. In this way, the experimental electrode is reproducibly reactivated during measurement.

The nature of the intermediate product in the oxidation of formic acid is of particular interest. By comparing the charge needed for oxidation of the adsorbed intermediate with the amount of carbonate formed (determined by titration) it was shown that one electron is consumed per carbon atom. This result suggests that COOH radicals are the intermediates, rather than CO.

The composition and structure of the catalyst have a great effect on the dehydrogenation of methanol and formate in alkaline electrolytes. At the same electrode potential the anodic current densities for methanol (uncharged particles) and formate (charged particles) on various catalysts (*e.g.* Pt, Pd, and Pt/Pd alloys) differ by more than one order of magnitude.

Fuel cell batteries based on methanol/air and formate/air and incorporating these catalysts have already been tested as energy sources in signal installations and TV relay stations. Fuel monocells are superior to the usual dry batteries in respect of greater capacity, constant discharge potential, ease of recharging, and better storage life. Monocells are constructed on the following principles: The lid of the monocell is fitted with a cylindrical carbon diffusion electrode with an air inlet and a metal terminal. The cell also contains a cylindrical fuel electrode and fuel electrolyte (20 ml 4 M CH_3OH + 9 N KOH). After discharge (*e.g.* 50 mA, 0.6 V, 240 h, 12 Ah), the element can be regenerated simply by renewal of the electrolyte.

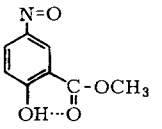
Lecture at Göttingen (Germany) on February 23rd, 1967 [VB 75 IE]
German version: Angew. Chem. 79, 726 (1967)

[*] Prof. Dr. W. Vielstich
Institut für physikalische Chemie der Universität
Wegelerstr. 12
53 Bonn (Germany)

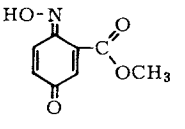
Intramolecular Hydrogen Bridges in Nitrosophenols

By *H. Uffmann* [*]

Tautomeric equilibria of the type *p*-nitrosophenol $\rightleftarrows$ 1,4-benzoquinone 4-monoxime are established *via* an intermediate mesomeric ion which can itself play a considerable part in the equilibrium [1]. Formation of the ion and achievement of the equilibrium are suppressed by internal hydrogen bridges. For instance, the 2-methoxycarbonyl compound *(1)* is a true nitrosophenol both in the solid state and in benzene or dioxane.



(1)



(2)

On the other hand, in the solid state the 3-methoxycarbonyl compound *(2)* is a quinone oxime with intermolecular hydrogen bridges. The oxime group is in the *anti*-position to the methoxycarbonyl group, as it is also in other quinone 4-oximes having a substituent on C-3 [2].

5-Methoxy-2-nitrosophenol exists in a brownish-green and in an orange form. *Burawoy* [3] concluded from the electronic spectra of this compound in various solvents that an equilibrium exists between the nitrosophenol with an internal bridge and a quinone oxime with an internal bridge. *Bartindale* [4] proved that the orange form in the solid state is a quinone oxime with intramolecular bridges and *anti*-relation of the oxime group to the quinone oxygen atom, which is in agreement with the behavior of 1,4-quinone oximes [2]. By means of IR and electron band spectra of the two solid forms and in various solvents, aided by the dependence of the spectra on the hydrogen ion concentration and on temperature, it has been found that, in carbon tetrachloride, there is an *o*-nitrosophenol with an internal bridge but that in polar solvents there is an equilibrium between the nitrosophenol with an internal bridge, the mesomeric ion, and the quinone oxime with intermolecular bridges (cf., however [5]).

A 1,2-quinone oxime with internal bridge is to be expected if a substituent in the second neighboring position to the oxime group prevents the movement of that group from the *syn*-position to the quinone oxygen, even though this type of substitution favors the quinone oxime structure. Such a case exists in 1,2-naphthoquinone 1-oxime; here also polar solvents lead to partial fission of the internal hydrogen bridge, so that the naphthoquinone with internal bridge is in equilibrium with the mesomeric ion and 1-nitroso-2-naphthol.

Lecture at Hanover (Germany) on February 23rd 1967 [VB 71 IE]
German version: Angew. Chem. 79, 692 (1967)

[*] Dr. H. Uffmann
Institut für Organische Chemie der Technischen Hochschule
Callinstr. 46
3 Hannover (Germany)

[1] *E. Havinga* and *A. Schors*, Rec. Trav. chim. Pays-Bas *69*, 457 (1950); *H. Uffmann*, Tetrahedron Letters *1966*, 4631.
[2] *H. Uffmann*, Z. Naturforsch., in press.
[3] *A. Burawoy et al.*, J. chem. Soc. (London) *1955*, 3727.
[4] *G. W. R. Bartindale et al.*, Acta crystallogr. *12*, 111 (1959).
[5] *C. Romers*, Acta crystallogr. *17*, 1287 (1964).

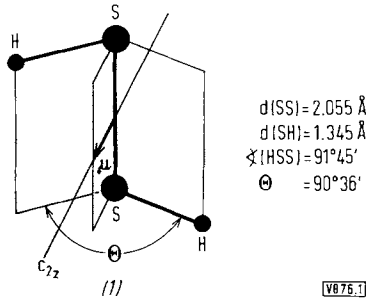
Investigation of Unstable Molecules and Free Radicals by Rotational Spectroscopy

By *M. Winnewisser* [*]

The millimeter and submillimeter region of the electromagnetic spectrum is a field of molecular spectroscopy that is rich but almost undeveloped. Because of their short wavelength [10 mm (30000 MHz) to 1 mm (300000 MHz) these waves can be collimated and focused by a combination of waveguides, horns, and Teflon lenses, which permits the use of large glass or quartz absorption cells for spectroscopy of unstable molecules and gaseous radicals [1]. The gases to be studied are contained in a cylindrical glass cell (diameter 10 cm, length 100 cm), which is placed in the path of the millimeter radiation. A system of gas discharge

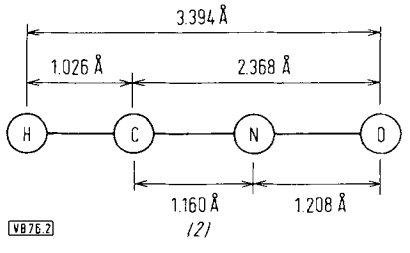
tubes, connected directly to the cell, serves for production of free radicals.

Using such a spectrometer, *Winnewisser, Sastry*, and *Gordy*[2] first obtained the millemeter spectrum of sulfur monoxide (electron ground state $^3\Sigma$) in the gas discharge products of SO_2 and studied the magnetic properties of the radical[3]. In the gas discharge product of H_2S the relatively unstable H_2S_2 is formed from the SH radical by secondary reactions[4], similarly to the production of H_2O_2 from OH radicals. Formation of disulfane was proved by the rotational spectrum in the millimeter region. The disulfane rotational spectrum is the first $\perp$-type spectrum of an almost symmetrical top with $\varkappa = -0.999985$. This shows that the dipole moment is perpendicular to the symmetry axis of the inertia tensor and parallel to the twofold symmetry axis, thus proving the chain structure of HSSH with C_2 symmetry. Analysis of the millimeter spectrum[5] and electron-diffraction measurements[6] yielded the preliminary structure *(1)* for disulfane.



(1) VB75.1

Fulminic acid is another unstable molecule whose structure in the free gaseous state was hitherto unknown. *Beck* and *Feldl*[7] proved that it has the nitrile oxide form by means of its IR spectrum. The microwave spectrum between 10000 and 50000 MHz indicates a linear molecule[8]. Measurement of the various isotope combinations showed the atomic bonding HCNO and the preliminary structural parameters indicated in formula *(2)*.



VB76.2 *(2)*

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German version: Angew. Chem. *79*, 727 (1967)

[*] Dr. M. Winnewisser
Technische Hochschule
Hertzstr. 16, Bau 35 II
75 Karlsruhe (Germany)

[1] *R. Kewley, K. V. L. N. Sastry, M. Winnewisser*, and *W. Gordy*, J. chem. Physics *39*, 2856 (1963).

[2] *M. Winnewisser, K. V. L. N. Sastry*, and *W. Gordy*, Bull. Amer. physic. Soc. *9*, 488 (1964).

[3] *M. Winnewisser, K. V. L. N. Sastry, R. L. Cook*, and *W. Gordy*, J. chem. Physics *41*, 1687 (1964).

[4] *G. Winnewisser, M. Winnewisser*, and *W. Gordy*, Bull. Amer. physic. Soc. *11*, 312 (1966).

[5] *G. Winnewisser, M. Winnewisser*, and *W. Gordy*, unpublished.

[6] *M. Winnewisser* and *J. Haase*, unpublished.

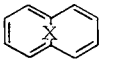
[7] *W. Beck* and *K. Feldl*, Angew. Chem. *78*, 746 (1966); Angew. Chem. internat. Edit. *5*, 722 (1966).

[8] *M. Winnewisser* and *H. K. Bodenseh*, unpublished.

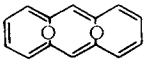
Electron Spin Resonance Studies of Bridged Annulenes

By *F. Gerson*[*]

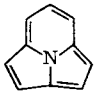
A model of a ten- or fourteen-membered π-electron perimeter can be used for interpretation of the ESR spectra of radical ions of the bridged annulenes *(1)* to *(4)*[1].



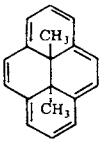
(1)
X = CH_2, O, NH



(2)



(3)



(4)

The lowest antibonding (ψ_a) and the highest bonding orbita (ψ_b) of the two perimeters are twofold degenerate. They can be classified as ψ_{a+} and ψ_{a-}, and as ψ_{b+} and ψ_{b-}, respectively. Here plus denotes symmetrical and minus antisymmetrical with respect to a plane that passes through two opposed centres in the perimeter and is perpendicular to the plane of the perimeter. Bridging of the system results in lifting of the degeneracy of ψ_{a+} and ψ_{a-} on the one hand and of ψ_{b+} and ψ_{b-} on the other.

In the radical anions of the bridged [10]annulenes *(1)* and *(3)* the unpaired electron occupies the antisymmetrical orbital ψ_{a-}, which thus lies lower than ψ_{a+}. However, in the radical anions of the bridged [14]annulenes *(2)* and *(4)* the unpaired electron is in the symmetrical orbital ψ_{a+}, which is here more stable than ψ_{a-}.

In the radical cation, which can also be prepared from compound *(4)*, there is an unpaired electron in the symmetrical ψ_{b+} orbital, which thus has a higher energy than ψ_{b-}.

These results permit conclusions to be drawn about the nature and direction of the effect exerted by the bridges on the π-electron systems in compounds *(1)* to *(4)*. Considered in conjunction with the geometry of the compounds, they lead to the following conclusions: In *(1)* and *(2)* the effect of CH_2, O, and N bridges is mainly inductive and electron-repelling. In *(4)*, however, this effect may perhaps be accompanied by hyperconjugation between the σ-electrons of the butane bridges and the π-electrons of the perimeter. Finally, in *(3)* the mesomeric and electron-donating effect of the central nitrogen atom plays the most important part.

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German version: Angew. Chem. *79*, 693 (1967)

[*] Doz. Dr. F. Gerson
Laboratorium für Organische Chemie
Universitätsstrasse 6
CH-8006 Zürich (Switzerland)

[1] Cf. also *F. Gerson, E. Heilbronner, N. Joop*, and *H. Zimmermann*, Helv. chim. Acta *46*, 1940 (1963); *F. Gerson* and *J. D. W. van Voorst, ibid. 46*, 2257 (1963); *F. Gerson, E. Heilbronner*, and *V. Boekelheide, ibid. 47*, 1123 (1964); *F. Gerson, E. Heilbronner, W. A. Böll*, and *E. Vogel, ibid. 48*, 1494 (1965); *F. Gerson*: Hochauflösende ESR-Spektroskopie, dargestellt anhand aromatischer Radikal-Ionen, Verlag Chemie, Weinheim 1967, in press, Chapter 2, Section 5.

Fixation of molecular nitrogen in a tris(triphenylphosphine)-cobalt complex *(1)* has been observed by *Y. Yamamoto, S. Kitazume, L. S. Pu,* and *S. Ikeda.* The complex was prepared under nitrogen as follows:

$$Co(acac)_3 + 3\ Al(C_2H_5)_2OC_2H_5 + 3\ P(C_6H_5)_3 + N_2 \rightarrow [\{(C_6H_5)_3P\}_3Co{\cdot}N_2]$$
(1)

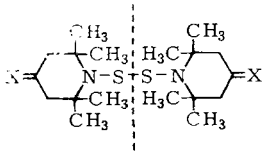
(1) forms yellow crystals, which can be recrystallized from toluene at low temperature, and is moderately stable under nitrogen. The nitrogen is released quantitatively at 80 °C. The IR spectrum of *(1)* contains a sharp band at 2088 cm^{-1}. / Chem. Commun. *1967*, 79 / –Kr. [Rd 656 IE]

Pahutoxin, the poison of the blue boxfish *(Ostracion lentiginosus)*, has been isolated in the crystalline form by *D. B. Boylan* and *P. J. Scheur.* The structure was established by alkaline and acidic hydrolysis and by synthesis. Approximately 60 mg of pahutoxin *(1)*, m.p. 74–75 °C, $[\alpha]_D^{22} = +3.05°$, was isolated per adult boxfish.

$$CH_3\text{-}(CH_2)_{12}\text{-}\underset{\underset{OCOCH_3}{|}}{CH}\text{-}CH_2\text{-}COO\text{-}(CH_2)_2\overset{\oplus}{N}(CH_3)_3Cl^{\ominus} \quad (1)$$

The fish emit *(1)*, together with mucus, on hard rubbing. Fish of other species are killed rapidly by the poison. / Science (Washington) *155*, 52 (1967) / –De. [Rd 655 IE]

New stable sulfur radicals, according to *J. E. Bennett, H. Sieper* and *P. Tavs*, are formed reversibly from the bis-(2,2,6,6-tetramethylpiperidino)disulfides *(1a)* and *(1b)* when they are heated to 90–150 °C and 140–200 °C respectively.



(1a), X = H_2
(1b), X = O

The three-line ESR spectrum shows a hyperfine splitting of about 11 oersted and a *g* factor of 2.0172. (Values for the corresponding nitroxyl radicals: about 15 oersted and *g* = 2.0061). *(1a)* (m.p. 84–85 °C; yield 66%) and *(1b)* (m.p. 145–147 °C; yield 81%) were prepared by treatment of the appropriately substituted pyridines with SCl_2 in dimethylformamide; S_2Cl_2 gives a chromatographically separable mixture of the di- and trisulfides. Tri-, tetra-, and pentasulfides are formed in nonpolar solvents (hexane, ether). / Tetrahedron *23*, 1697 (1967) / –Bu. [Rd 678 IE]

Thiolates of cobalt, nickel, copper, and zinc have been described by *D. C. Bradley* and *C. H. Marsh.* The cobalt and nickel thiolates are obtained by the addition of thiol (RSH) to $CoCl_2{\cdot}6H_2O$ and to $NiCl_2{\cdot}6H_2O$ or $Ni(NO_3)_2{\cdot}6H_2O$ in C_2H_5OH/NH_3 solution (molar ratio of reactants approx. 2:1) (R = C_2H_5, C_3H_7, i-C_3H_7, t-C_4H_9, C_5H_{11}, C_6H_5). Thiols with R = n-alkyl give mainly cobalt(III) thiolates (magnetic susceptibility!), while those with R = iso- or t-alkyl and phenyl give cobalt(II) thiolates. The brown to black nickel(II) thiolates mainly have degrees of polymerization of 4 to 6 in the primary stage, are stable up to about 180 °C, and undergo exchange with higher thiols.

The copper(I) thiolates, *e.g.* CuS-i-C_3H_7, CuS–C_5H_{11}, are pale yellow, diamagnetic solids, and are stable up to about 200 °C/0.1 mm Hg. The zinc thiolates, $Zn(S\text{-i-}C_3H_7)_2$, $Zn(SC_6H_5)_2{\cdot}2NH_3$, $Zn(SC_5H_{11})_2$, form white precipitates, and are stable up to about 190 °C/0.1 mm Hg. Coordination polymers occur in every case. It should be noted that these thiolates can be obtained in the presence of water, *i.e.* thiolates of $3d^6$ to $3d^{10}$ transition metal ions are resistant to hydrolysis. / Chem. and Ind. *1967*, 361 / –Jg. [Rd 692 IE]

The first carbonylmetal complexes of hydrogen isocyanide (HNC) have been obtained by *R. B. King* in the reaction of $Na[M(CO)_5CN]$ *(1)* with 4 N HCl.

$$Na[M(CO)_5CN] + HCl \rightarrow (HNC)M(CO)_5 + NaCl$$
(1) *(2)*

(2a), M = Cr; decomp. point 114–116 °C; the crystals are purified by sublimation at 60–90 °C/0.1 mm; yield 41%. *(2b)*, M = Mo; no decomposition point; sublimation at 70–80 °C/0.1 mm; yield 13%. *(2c)*, M = W; decomp. point > 105 °C; sublimation at 70–90 °C/0.1 mm; yield 32%. *(2b)* is very unstable; it turns brown within a few hours at room temperature. *(2c)* and *(2a)* are generally much more stable, but occasionally turn blue *(2c)* or yellow *(2a)*. The salts *(1)* are readily obtained from sodium bis(trimethylsilyl)amide and hexacarbonylmetal in benzene.

Their reaction with trimethylchlorostannane yields the colorless, crystalline trimethyltin isocyanide complexes $(CH_3)_3SnNCM(CO)_5$ (M = Cr, Mo, W). Spectroscopic investigations (IR and ^1H–NMR) clearly show that *(2)* contains an HNC ligand, which, in contrast to free HNC (rearrangement into HCN), is stabilized in this case by complex formation. / Inorg. Chem. *6*, 25 (1967) / –Sch. [Rd 661 IE]

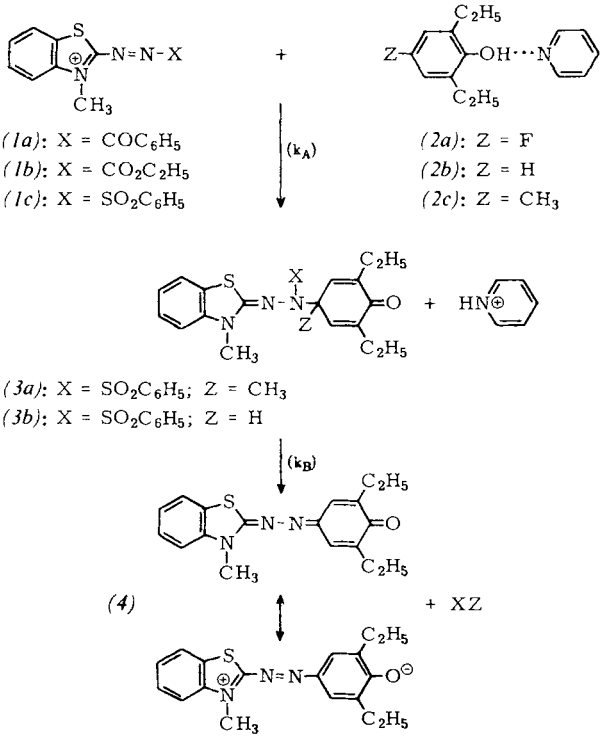
The mechanism of the Guerbet reaction was studied in the reaction of benzyl alcohol with potassium lactate to give α-hydroxy-γ-phenylbutyric acid (together with hydrogen and benzoic acid). According to *S. Veibel* and *J. I. Nielsen*, the reaction proceeds as follows: (a) Both hydroxy compounds are dehydrogenated to the carbonyl compounds, which (b) undergo aldol condensation followed by elimination of water. (c) Hydrogen is transferred to the resulting α,β-unsaturated ketones from the starting compounds, which are themselves reduced in this way (see step (a)) to carbonyl compounds. This leads to a chain reaction. The chain is terminated (d) by a Cannizzarro disproportionation of the benzaldehyde. The ratio of the rates of steps (a) to (c) to the rate of step (d) therefore determines the yield of α-hydroxy-γ-phenylbutyric acid. Raney nickel and Pd are effective catalysts for the dehydrogenation-hydrogenation reaction, though the reaction also takes place in their absence. If potassium benzylidenepyruvate is present at the beginning of the reaction, the latter can be carried out at 130 °C instead of at 160 °C (reaction (a), which is otherwise rate-determining, is thus avoided) and the liberation of hydrogen is greatly reduced. / Tetrahedron *23*, 1723 (1967) / –Bu. [Rd 675 IE]

Inactivation repression is the name given by *J. J. Ferguson, M. Boll,* and *H. Holzer* to a regulation phenomenon of yeast malate dehydrogenase (MDH, E.C. 1.1.1.37). When washed yeast cells grown on glucose are suspended in a nutrient medium that is 4×10^{-2} molar in acetate, a rapid increase in the MDH activity (doubled in about 30 min) takes place over 6 hours after an induction period of about 20 min. The num-

ber of cells increases by only about 10% during this time. The increase in the MDH activity is stopped by cooling and by the addition of cycloheximide ("Actidione" 1.78×10^{-5} M) and glucose (5.5×10^{-2} M). A rapid decrease in the MDH activity occurs some 5 min after the addition of glucose, and after about 60 min the MDH level has returned to its value before induction by acetate. It is interesting to note that this "repression" of MDH by glucose is prevented by cycloheximide (an inhibitor of protein biosynthesis) when this is added together with the glucose, but not when it is added 12 min later. Attempts to demonstrate the existence of an MDH inhibitor or of an MDH-inactivating protein or enzyme, *e.g.* by mixing extracts from acetate-induced and glucose-repressed cells, were unsuccessful. In the inactivation by glucose, no MDH is given up to the medium. MDH from induced cells is kinetically and physically (chromatography on DEAE cellulose) distinguishable from that from "repressed" cells. / Europ. J. Biochem. *1*, 21 (1967) / –Hö.

[Rd 679 IE]

The rare case of several possibilities in a two-step reaction ($k_1 \ll k_2$; $k_1 < k_2$; $k_1 \approx k_2$; $k_1 \gg k_2$) has been reported by *S. Hünig* and *G. Kaupp*. The kinetics of the formation of diazamerocyanine *(4)* from the azo-substituted benzothiazolium salts *(1)* and the phenols *(2)* point to the following reaction scheme:



(1a): X = COC_6H_5
(1b): X = $CO_2C_2H_5$
(1c): X = $SO_2C_6H_5$

(2a): Z = F
(2b): Z = H
(2c): Z = CH_3

(3a): X = $SO_2C_6H_5$; Z = CH_3
(3b): X = $SO_2C_6H_5$; Z = H

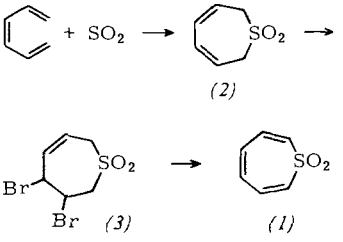
The rate of the addition step (k_A) remains roughly constant, while the rate of decomposition (k_B) varies over a range of four powers of ten. The marked difference between *(2a)* and

Substrates	k_A/k_B
(1a) + *(2a)*	1:70
(1b) + *(2a)*	1:12
(1c) + *(2a)*	1:1.5
(1c) + *(2b)*	230:1

(2b) is probably due to reversal of the electron displacement. Similarly, the reaction of *(1a)* and *(1b)* with *(2b)* could not be evaluated, since the groups X = COC_6H_5, $CO_2C_2H_5$ cannot leave nucleofugally. (However, these combinations give *(4)* in 20–35% yield by another reaction path.) When *(1c)* reacts with *(2c)*, the colorless adduct *(3a)* can be isolated, whereas *(3b)* can be obtained only in the tautomeric (phenolic) form; *(3b)* is the true intermediate since it forms *(4)* as rapidly as when *(1c)* and *(2b)* are chosen as starting materials. / Tetrahedron *23*, 1411 (1967) / –Bu.

[Rd 676 IE]

The synthesis of thiepin 1,1-dioxide *(1)* has been reported by *W. L. Mock*. Hitherto, only benzothiepin 1,1-dioxides have been obtainable. 1,6-Addition of SO_2 to *cis*-hexatriene in ether at room temperature yields 2,7-dihydrothiepin 1,1-dioxide *(2)*, m.p. 107–108 °C, which gives the hexahydro derivative, m.p. 70–71 °C, on hydrogenation. Bromination of *(2)* in chloroform leads to *cis*- or *trans*-3,4-dibromo-2,3,4,7-tetrahydrothiepin 1,1-dioxide *(3)*, m.p. 128–129 °C, which gives thiepin 1,1-dioxide *(1)*, m.p. 117–118 °C, on



(2)

(3) *(1)*

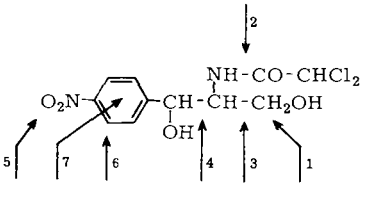
treatment with triethylamine in benzene at 25 °C. *(1)* decomposes at 100 °C into benzene and SO_2, probably *via* an intermediate episulfone. It is evidently nonplanar. / J. Amer. chem. Soc. *89*, 1281 (1967) / –Ma.

[Rd 700 IE]

The β-galactosidase repressor from *Escherichia coli* has been enriched and characterized by *W. Gilbert* and *B. Müller-Hill*. The test used was the bonding of the inductor isopropylthiogalactoside (IPTG, ^{14}C and ^{3}H) to the repressor on equilibrium dialysis. Accumulation from an i^t mutant, which synthesizes a repressor having a particularly high IPTG affinity (K_M approximately 7×10^{-7} as compared with 1.3×10^{-6} M), was achieved by precipitation with spermidine, ammonium sulfate fractionation, and chromatography on DEAE-Sephadex. The IPTG-binding fraction is sensitive to heat and proteinase, but insensitive to DNase and RNase; the molecular weight is 150000–200000 (7.6–8 S). The identity of the protein with the product of the galactosidase regulator gene (i-gene) is indicated by :1. The absence of the protein in i^-, i^s, and i deletion strains (no repressor formation, deficient repressor, and absence of the i-gene); 2. the higher affinity of the repressor from the i^t strain for IPTG than of the repressor from the wild strain, 3. the affinity of the protein for other galactosidase inductors such as thiomethylgalactoside (K_M = 2×10^{-6} M), *o*-nitrophenyl-β-D-galactopyranoside (2×10^{-5}), and galactose (5×10^{-4}, all values for i^t repressor), and 4. the correct correlation of these values with the concentrations of these substances required in the *in-vivo* induction. / Proc. nat. Acad. Sci. USA *56*, 1891 (1966) / –Hö.

[Rd 657 IE]

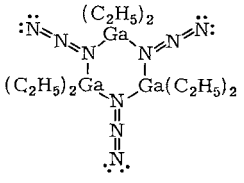
Chloramphenicol can be used as the only source of carbon and nitrogen by a strain of bacteria isolated from garden soil by *F. Lingens* and *O. Oltmanns*. The antibiotic chloramphenicol is effective against many gram-positive and gram-negative bacteria, as a result of inhibition of protein biosynthesis. The strain of bacteria in question is gram-negative, but despite detailed characterization, it has not yet been classified. Eleven



degradation products of chloramphenicol have been isolated from the culture medium. On the basis of these products, it has been possible to suggest a degradation path, the principal steps of which are indicated by arrows showing the presumed order. The reactions are: 1. oxidation, 2. hydrolysis, 3. decarboxylation and oxidation, 4. decarboxylation, 5. reduction and deamination, 6. hydroxylation, 7. oxidative cleavage. [Rd 658 IE]

Diethylgallium azide *(1)* has been obtained almost quantitatively by *J. Müller* and *K. Dehnicke* from the reaction of triethylgallium *(2)* with chlorine azide in benzene.

$$3\ Ga(C_2H_5)_3 + 3\ ClN_3 \rightarrow$$

(1)  $+ 3\ C_2H_5Cl$

(1) is a colorless, slightly hygroscopic, viscous liquid, which, unlike *(2)*, does not ignite spontaneously, and which distils at 86 °C/0.1 mm without decomposing. Cryoscopic measurement in benzene gives three times the expected molecular weight. In contrast to $(C_2H_5)_2AlN_3$, which decomposes explosively with water, *(1)* is not wetted by water. It is insensitive to mechanical treatment and to fast heating with an open flame. According to its vibration spectra (IR and Raman), diethylgallium azide forms a six-membered Ga–N ring open flame. According to its vibration spectra (IR and Raman), diethylgallium azide forms a six-membered Ga–N ring (D_{3h} symmetry). / J. organometallic Chem. 7, P1 (1967) / –Sch. [Rd 662 IE]

The mass-spectrometric detection of extremely small quantities of alkali metal is reported by *J. Kremer*. A small droplet (about 0.05 ml) of the test solution is placed on a strip of molybdenum and evaporated to dryness in the absence of dust. The strip is heated until thermal emission of alkali metal ions takes place, and the ion current is measured in a mass spectrometer adjusted to the mass of the nuclide to be detected. Measurement is continued until the ion source has given off all the alkali metal. A Geiger counter tube is used as the detector. The total number of pulses counted is then a measure of the quantity of the nuclide in question that was present in the sample. This method is only of theoretical interest for the detection of the lighter alkali metals up to and including Rb, since water cannot be sufficiently freed from alkali metals (the purest water examined contained about 10^{-10} g of K per ml). Only cesium is present in water in such small quantities that test solutions of definite concentration can be prepared. Cesium can be determined in concentrations of 10^{-14} g/ml. / Z. Physik *199*, 94 (1967) / –Hz. [Rd 663 IE]

Carbon trioxide CO_3 has been obtained by *N. G. Moll, D. R. Clutter*, and *W. E. Thompson* in three ways: (i) photolysis of solid CO_2 at 77 °K with vacuum UV from a xenon resonance lamp; (ii) photolysis of ozone in a matrix of solid CO_2 at 50–60 °K with the 2537 Å mercury line; (iii) radio-frequency discharge in gaseous CO_2 and freezing of the products at 50–70 °K. Spectroscopic studies, partly with isotope-enriched CO_2, indicate a planar molecule having symmetry C_{2v}, in which one oxygen is strongly bound to the carbon by a carbonyl-like bond, while the other two oxygen atoms are more weakly bound. There is probably also a covalent bond between the two equivalent oxygen atoms. CO_3 decomposes into CO_2 and atomic oxygen on photolysis with visible and ultraviolet light. / J. chem. Physics *45*, 4469 (1966) / –Hz. [Rd 664 IE]

BOOK REVIEWS

Ullmanns Encyklopädie der technischen Chemie. Band 16: Soja bis Terpentinöl (Ullmann's Encyclopedia of Industrial Chemistry. Vol. 16: Soya to Oil of Turpentine). Chief editor *W. Foerst*. Editor *Hertha Buchholz-Meisenheimer*. Verlag Urban & Schwarzenberg, München-Berlin 1965. 3rd fully revised Edit., 779 pages, 235 figures. Vol. 17: Terpentinöl bis Uran und -verbindungen (Oil of Turpentine to Uranium and its Compounds). 1966, xii, 789 pages, 240 figures, per volume DM 182.–. (obtainable only as the complete work).

With the publication of the present two volumes [*], this huge work draws slowly toward completion. The longer articles in Vol. 16 deal with steels (135 pages), spirits and alcoholic liquors (62 pages), explosives (54 pages), sulfonic acids (53 pages), tar and pitch (45 pages), starch (42 pages), coal (41 pages), synthesis gas (37 pages), sulfonamides (37 pages), and radiochemistry (30 pages). The shorter articles include sorbic acid, ice cream, injection molding masses, strontium and its compounds, sweeteners, superconductivity, tobacco, tall oil, tea, telomerization, and surfactants.

A large part of Vol. 17 deals with textile problems: textile bleaches (18 pages), textile printing (64 pages), textile processing aids (65 pages), and textile technology. Other long articles are concerned with the clay industry (132 pages), oil of turpentine products (64 pages), uranium and its compounds (50 pages), drying oils (44 pages), motor fuels (36 pages), and veterinary remedies (36 pages). This volume again contains a series of shorter articles dealing with, *e.g.* tetrahydrofuran, therapeutic acids, thiourea, toluene, peat, and driers. Not only do these later volumes present new material corresponding to the new entries, but an attempt is also made to include supplementary material on topics discussed earlier, so that the presentation is varied and stimulating. Thus the short article on injection molding masses follows on from Plastic Processing, Vol. 11, 1960, and describes the transition from piston-type injection molding machines to the screw type, as well as the associated material and processing problems. The article on steels follows on from the methods of steel production described under Iron, Vol. 6, 1955, but presents a very informative account of the progress and the present state of steel production. The article on coal is intended to supplement the discussion on coal and the upgrading of coal, which appeared in 1957 and 1958. Many more examples could be quoted. It has been possible in this way to bring the entire work (the first volume of which was published 13 years ago) up to date at the time of publication of the last volume.

The main emphasis in these two volumes is again placed on the industry. Of the 128 contributors, only 24 are employed at universities and public research establishments. The industrial contributors deal not only with problems of applied science, but also with basic research themes such as thermoelectricity, superconductivity, tellurium and its compounds, and veterinary remedies. One cannot quite escape the impression that the universities in Germany do not play any great part in the investigation of topics that are important in industry, even when these topics lie in the field of pure science and theory.

The article on steel is by *I. Class*, who has for some time been manager of the BASF Materials Division. The aim of the

article is "to describe the relationships between the composition and history of a steel and its properties and to offer the chemist or chemical engineer a guide to the selection of a steel suitable for a special application." Theory and practical experience are skilfully blended in this well-founded discussion. It would have been better if the use of different type sizes and faces (bold, italic, spaced) to indicate main sections and subsections had been more consistent throughout the work. The article on the clay industry is a joint contribution by 12 authors, with a very good introduction by *U. Hofmann*, Heidelberg. It gives an all-round detailed picture of the perfusion of this, the oldest industry in the world, with modern technology.

The articles on textile bleaches, textile printing, textile processing aids, and textile technology show how important textile problems have become in the chemical industry. The bleaches are discussed by two former colleagues at Degussa. Current developments in this field are marked by an increase in the importance of peroxy compounds. A detailed description of textile printing is given by two authors from Farbenfabriken Bayer, and textile processing aids are discussed in similar detail by two colleagues from Böhme Fettchemie. The Deutsche Forschungsinstitut für Textilindustrie and the Staatliche Ingenieurschule für Textilwesen, both in Reutlingen, are largely responsible for the article on textile technology. Since this chapter is intended for those who do not work in this field, short explanations of technical terms would have been useful. Thus it is difficult for the layman to distinguish between "Wirkerei" and "Strickerei". Similarly, the "degree of pilling" is described as ranging from pill-free to "verpillt" (literally "completely pilled"), but these terms are not explained, nor is the reader told where to find explanations. In pressing forward into the textile field, chemistry has not only gained a large new production sector, but it has also come into very close contact with the consumer with its new products. This field is scientifically and technically very interesting; however, it is not an easy field to work in, since it is not the chemical composition of the products that is of primary importance, but some rather intangible technological properties. Moreover, the chemist and the physicist are forced to match their products to many old-established processing methods. The discussion is very instructive to anyone concerned with this cooperation. The chapter on textile technology is particularly instructive to the chemist.

The article on synthesis gas can be read in conjunction with the earlier articles on ammonia, the hydrogenation of carbon monoxide, the synthesis of methanol, and the oxo synthesis, and presents a concentrated progress report and an account of the present situation with respect to the production of synthesis gas. This situation is characterized by the increased importance of the production of synthesis gas from liquid and gaseous raw materials in relation to the classical gasification of solids. The number of synthesis gas processes is now so large that it is to the author's credit that he managed to compress the essentials into 37 pages. In no other process does the choice of procedure depend so strongly on the point of view and on the manner of insertion into the rest of the production program. The article also contains a comparison of the cost of production of synthesis gas by pressure gasification of coal, by reaction of natural gas at normal pressure, and by partial combustion of oxygen under pressure, the costs for all these processes being given as a function of the cost of the raw material and the size of the processing units.

The article on tobacco deals with the botany, the production, and the chemistry of tobacco. The pharmacological and toxicological aspects are discussed authoritatively and impartially by a pathologist and a clinical physician. The article on uranium, uranium alloys, and uranium compounds (including processing of spent fuel elements and fuel material) was written by three authors from Nuklear-Chemie und Metallurgie, GmbH, Hanau. It presents a good picture of the intensive technological investigation and the spirited efforts that have been devoted to this important problem. The rapid technical development is reflected in the changes in the price of the products. The article on spirits, which is confined to ethyl alcohol, is somewhat rambling in many places. The short section on sulfite spirit is good. The State Monopoly's term "Primasprit" (refined spirit), as can be seen from the legal section, is not entirely rational; on the one hand the spirit must be produced from agrarian raw materials, while on the other it must be so highly purified that its source is no longer recognizable. The section on physiology and toxicology presents a gloomy picture of the unpleasant effects of the consumption of alcohol on behavior, judgement, self-criticism, and finer psychic coordination.

In the article on veterinary remedies, two colleagues from Farbenfabriken Bayer present the essential viewpoints and methods of veterinary medicine. We learn that useful animals and pets are two fundamentally different groups of patients. The veterinary medicine of useful animals is mainly concerned with the prevention and cure of herd diseases, whereas pet therapy is very much more like human medicine, since treatment is individual. The article deals mainly with the fight against parasite and bacterial infection.

Lack of space prevents us from evaluating any more of the articles. In Ullmann, chemistry is treated from the point of view of its practical importance. Consequently, many problems of every-day life are also discussed. These practical problems are often theoretically very complex, so that one often tends not to discuss them scientifically. However, modern physical and chemical methods and the progress of analysis are constantly winning over traditionally empirical fields to the systematic, scientific approach. Ullmann goes into both the practical and the theoretical sides of this problem, and so presents a piece of research that is of interest outside the boundaries of industrial chemistry.

H. Sachsse [NB 595 IE]

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[*] Cf. Angew. Chem. *78*, 652 (1966); Angew. Chem. internat. Edit. *5*, 618 (1966).

Chemie photographischer Prozesse. (Chemistry of Photographic Processes.) By *H.-M. Barchet*. Wissenschaftliche Taschenbücher, Volume 31. Akademie Verlag, Berlin 1965. 1st Edit., 167 pp., DM 8.–.

The author of this little book gives a lucid explanation, from the viewpoint of an organic chemist, of the reactions that are of importance in the formation of photographic images. The division of the subject matter is excellent: Descriptions of substances incorporated in photographic materials and involved in their processing are followed in each case by a discussion of the corresponding chemical reactions and in some cases by a detailed account of their syntheses.

Physicochemical and purely physical aspects are dealt with only so far as is necessary in order to indorporate the purely chemical processes into the photographic process as a whole. Understandably, color photography occupies an important place in the book. Processes not involving siver halides are only mentioned briefly

The book thus provides a general review of the many problems associated with the chemistry of photographic processes, with reference to specialized literature; this information will hardly be encountered elsewhere in such a concise form.

E. Klein [NB 578 IE]

Anorganische und allgemeine Chemie in flüssigem Ammoniak (Inorganic and General Chemistry in Liquid Ammonia). By *J. Jander*. Chemie in nichtwäßrigen ionisierenden Lösungsmitteln (Chemistry in non-aqueous ionizing solvents), edited by *G. Jander*, *H. Spandau*, and *C. C. Addison*, Vol. I, Part 1. Friedr. Vieweg & Sohn, Braunschweig – Interscience Publishers, a Division of John Wiley & Sons, Inc., New York-London 1966. 1st Edit., xxiv, 561 pages, 75 figures, 213 tables, DM 110.–; subscription price DM 96.–.

This series of monographs, which was started by *G. Jander* and *H. Spandau* and is being carried on by *H. Spandau* and *C. C. Addison*, is to consist of eight volumes on chemistry in non-aqueous inorganic and organic solvents. The inorganic solvents discussed include ammonia, sulfur dioxide, dinitrogen tetroxide, a few halides and oxyhalides, and a number of salt melts, while the organic solvents include the lower fatty acids and their derivatives, nitrogen bases, alcohols, ethers, and esters.

The first part of the first volume deals with inorganic and general chemistry in liquid ammonia. The author has taken great pains to cover all the literature on inorganic and physical chemistry in liquid ammonia. The resulting article covers 500 printed pages, including a 42-page list of about 2000 references (from 1826) and more than 200 tables, the longest of which occupies 32 pages.

This passion for completeness is not always to the reader's advantage, since all the published values for one quantitative measurement are often presented on an equal footing and without discussion, and the reader has to decide which value is correct. This is not troublesome *e.g.* in the case of the boiling point and the melting point of pure ammonia or its critical temperature, since the numerous values differ by less than 1 deg, and the best values can be found in suitable tables anyway. However, the inclusion of all the values *e.g.* for solubilities (Table 86) is confusing. For example, the following values are given for the solubility of NaCl between −76.9 and −74.9 °C: 0.232, 0.074, 0.28, 0.123, and 0.306 g/100 g and 0.203 g/100 ml. A similar situation is found *e.g.* in Table 152 (phase separation in metal-NH_3 solutions): the existence of a miscibility gap in Li−NH_3 solutions is given as "not detectable", "uncertain", and "certain" and in K−NH_3 solutions as 'not detectable" and "uncertain' (in fact both systems have a miscibility gap with an accurately known critical temperature). Similar lack of clarity is found in the subsequent tables on the metal adducts.

References to other parts of the book are given, not as a page number containing up to three digits, which would be easy to remember and could be found quickly, but as a key number for the section in question, which may contain up to seven digits, *e.g.* 2.9.2.2.2.1.6. (Oxidation of ammonium azide with exclusion of solvent molecules as reactants). The key numbers in the supplementary chapter, in which the latest literature is collected do not agree with those of the principal chapters.

Apart from these and similar failings, however, the book probably fulfils the purpose expressed in the Preface, *i.e.* to be of use to all chemists in the laboratory and in practice. Owing to its completeness, it can replace all past volumes of Chemical Abstracts or of Chemisches Zentralblatt for the chemist who is working with liquid ammonia.

U. Schindewolf [NB 598 IE]

Molecular Photochemistry. By *N. J. Turro*. W. A. Benjamin, Inc., New York-Amsterdam 1965. 1st Edit., xiii, 286 pages, numerous figures, DM 55.−.

Photochemistry. By *J. Calvert* and *J. N. Pitts jr.* John Wiley and Sons, Inc., New York-London-Sydney 1966. 1st Edit., xvii, 899 pages, numerous figures, DM 84.−.

The reviewer can recall the earnest discussions only 10 years ago on whether a light-induced reaction in the course of a total synthesis made such a synthesis doubtful as structural evidence. Photochemistry has now been emancipated, and chapters on this field are now no longer found only in textbooks of physical chemistry, but have recently also earned a firm place in textbooks of organic chemistry. The preparative chemist now values light as a cheap reagent; the MO theory, which should already have been met in basic chemistry reading, provides a structural model that is partly based on consideration of the primary photophysical processes, and that offers an explanation of the primary photochemical processes. The further development of photochemistry will open up new preparative routes; it will add to and improve the model concepts of the structure and structural changes of molecules. Accordingly, a steadily growing number of workers will wish to enter this field and to take part in its development. The two monographs reviewed here may help them to do this.

Both books are recommended to a wide circle of readers. Their aim is to provide information required in order to understand current publications on photochemical investigations, and hence to provide the newcomer with a foundation on which to base his own investigations.

In the book by *Turro*, an eight-page introduction is followed by four chapters on photophysical processes and problems (electronic excitation, 11 pages; electronic spectra and electronic excitation states, 48 pages), and the transfer of electronic energy, 45 pages). Four further chapters deal with photochemical processes and problems (photoreductions and related reactions, 25 pages; photo-rearrangements and photoisomerization, 32 pages; photo-cycloadditions 30 pages; photofragmentation and related processes, 21 pages), and a final chapter (11 pages) touches on a number of experimental aspects. This book is based on a lecture manuscript, and is naturally selective in character. The fact that the author belongs to one of the leading schools of photochemistry guarantees the significance of the material.

Calvert and *Pitts* have succeeded in producing *the* standard work on photochemistry. Every conceivable field apart from photoblology and photography is covered. The first four chapters (lightand the laws of photochemistry, 22 pages; the action of light on atoms and reactions photosensitized by atoms, 90 pages; the action of light on simple molecules and their photochemistry, 100 pages; the primary photophysical processes of polyatomic molecules, 112 pages) provide a fundamental description of photophysical principles. The fifth chapter (190 pages) presents a colorful review of the photochemistry of polyatomic molecules, which systematically embraces all the known classes of photoreactive substances. Two further chapters (determination of the mechanism of a photochemical reaction, 83 pages; the experimental methods of photochemistry, 111 pages) deal with the fundamental methods used in the study of reaction mechanisms and with the detailed procedures used.

The book contains a comprehensive author and subject index and more than 1500 references.

To those who wish to buy only one of these books, the reviewer would recommend that by *Calvert* and *Pitts*.

G. Quinkert [NB 607 IE]

Encyclopedia of Chemical Technology. By *R. E. Kirk* and *D. F. Othmer*. Edited by *A. Standen*. Vol. 9: Ferroelectrics to Foams. Interscience Publishers, a Division of John Wilev & Sons, Inc., New York-London-Sydney 1966. 2nd Edit., xvi, 901 pages, numerous illustrations, bound 338s; subscription price 260s.

Volume 9 of Kirk-Othmer[*] contains 22 articles having an average length of 41 pages, including fluorine chemistry (341 pages), fertilizers (126 pages), fluidization (47 pages), flavors and spices (44 pages), fluid mechanics (38 pages), foamed plastics (37pages), and ferroelectrics (25 pages), as well as fibers, films, filtration, fish, fire prevention, fluorescent pigments, and foams. The second edition is largely rewritten, mainly by new authors (of the 60 contributors to this volume, only 10 were connected with the first edition). The volume has increased in size to about 900 pages, as opposed to 445 pages in the edition published 15 years ago. The detailed coverage of new developments is very pleasing, though the increase in the quantity of material to be included forces the editorial staff to abbreviate and compress in order that the required information may still be quickly accessible.

The particularly marked growth of fluorine chemistry in the past few years can be seen in the article: Fluorine (21 pages); Fluorine Compounds, Inorganic (159 pages); and Fluorine Compounds, Organic (161 pages). It is clear that the rapid development of this field has been largely due to two important applications, *i.e.* the use of fluorochlorocarbons as refrigerants and the use of uranium hexafluoride for the separation of the isotopes of uranium. The discussion of the subject is the work of 37 authors from no fewer than 16 firms, Purdue University, and the US Naval Research Laboratory.

The article on elementary fluorine presents a clear picture of properties, occurrence, production, storage, and dispatch. In plants producing several tons per year, the costs can be as low as about $ 1 per lb. In the following article, the inorganic fluorine compounds are described alphabetically in 27 subsections by several authors. Since no reviews of a general nature are included, the article gives the impression of being somewhat lacking in coherence. On the other hand, the article on organic fluorine compounds, has a good introduction (18 pages) and a very good section on the surface chemistry of fluorine compounds (32 pages). All the sections are provided with full lists of references.

The article on fertilizers has also been rewritten, and has expanded in the process from 76 to 126 pages. However, this chapter could have been appreciably shortened or its content increased. The section on the nutrient function of chemicals presents a general account, and even contains historical reminiscences, but no numerical data. It does not go into the laws of plant metabolism or into crop yields; for example, the antagonism of potassium and calcium with respect to the water balance is not mentioned. The arrangement of the article as a whole is not very good. The author deals with questions on the structure of the industry, mixed fertilizers, production, costs, and locations before discussing the properties of the main products. Consequently, repetitions cannot be avoided. The author mentions several times that the fertilizer industry has changed more since 1950 than ever before; however, he does not specify the changes, but simply states that products of minor importance have become more important, the industry has become more reserch-conscious, *etc.* More information could have been presented in a smaller space if the arrangement had been better and the discussion more concrete.

The well-written article on filtration has been substantially retained from the first edition. In spite of additions to the content, it has been possible to compress the article from 24 pages to 22, mainly by the omission of photographs were diagrams were sufficient. A full and well-executed treatment is given to flavors and spices. Flavors are those components of foods that can be detected by their taste and smell. They have acquired great economic importance, since next to appearance they determine the sale of foods.

The article on flavor characterization describes the use of modern analytic methods such as gas chromatography and IR and mass spectroscopy for the recognition of the active substances. The aim of a complete analysis is now very much nearer; thus 93 "aromaphores" have been detected in and isolated from a few ml of oil of orange. The food industry makes wide use, not only of natural and synthetic flavors, but also of flavor precursors (some enzyme-based) and flavor potentiators. The chapter also contains recipes. The section on spices contains a very instructive historical survey of the spice trade, describes quality control, and then proceeds to discuss the individual spices. The term "spice" is reserved for flavorings of exclusively natural origin.

The article on fluidization has been largely taken over from the first supplement to the first edition, with revision and inclusion of additional material, but with no appreciable increase in size. The main new feature is the description of the material exchange between the gas bubbles ascending in the fluidized bed and their surroundings. The article is comprehensive and instructive, but is largely confined to the situation in America. A table is given with 101 examples of the use of fluidized bed processes, of which there are only one each from England, India, Belgium, Czechoslovakia, and Yugoslavia, and five from Germany. No mention is made of *Fritz Winkler*, the inventor of the fluidized bed process, or of the fluidized bed process for the roasting of pyrites developed by BASF after the war and now used internationally on the large scale.

The present volume also contains other contributions, but these cannot all be reviewed individually. In view of the rate of industrial expansion, any attempt to present a survey is very welcome. Though Kirk-Othmer is mainly confined to the situation in the USA, it is also useful to the German reader, since it is backed by the largest and most diversified chemical industry in the world. It is to be hoped that the publication will have much success in the future.

H. Sachsse [NB 594 IE]

[*] Cf. Angew. Chem. *77*, 359 (1965); Angew. Chem. internat. Edit. *4*, 378 (1965).

Experimental Organic Chemistry. By *J. Baldwin.* McGraw-Hill Book Company, New York - St. Louis - San Francisco-Toronto-London-Sydney 1965. 2nd Edit., 183 pages, numerous figures, paper 52s.

The present volume, which is presented in brochure form, follows an unconventional path for a practical textbook. It begins with the isolation of caffeine from tea, explaining some of the elementary operations such as extraction, filtration, and sublimation. This is followed by a section on the purification of hydrocarbons, in which chromatography is used and discussed. IR and NMR spectra are used as early as Chapter 6 for the characterization and identification of preparations, and are subsequently used repeatedly throughout the book (with illustrations).

The experiments are grouped according to reaction mechanisms, such as nucleophilic substitution, nucleophilic addition, electrophilic addition and substitution and molecular rearrangements. Experiments on stereoselective reactions and on structure and equilibrium, which are often ignored in practical textbooks, are not forgotten.

Further chapters are devoted to heterocyclic compounds (synthesis of 1,2-diphenyl-5-nitrobenzimidazole), the synthesis of peptides, and ion-exchange chromatography. Each chapter closes with a selection of questions and problems.

The experiments and preparations are so chosen that the student has a sense of tackling current problems and that the time required is relatively short. The appendix contains the IR and NMR spectra of about 40 compounds mentioned in the book. These are accompanied only by the empirical formulae, so that the student has ample opportunity for practice in the interpretation of spectra.

The book by *Baldwin* is full of suggestions both for the demonstrator and for the student. Unfortunately, the presentation is not very suitable for bench-use. However, a copy of "Practical Organic Chemistry" should be available in every laboratory. Demonstrators are recommended to use various preparations from the book as a change from the "hackneyed" standard preparations.

H. J. Bestmann [NB 593 IE]

Atomic Absorption Spectroscopy. By *J. W. Robinson.* Marcel Dekker, Inc., New York 1966. 1st Edit. xi, 204 pp., 40 illustrations, many tables, $ 9.75.

Authors of monographs about rapidly developing subjects suffer from the fact that many parts of their books are out of date when they appear; the author of the present book about atomic absorption spectroscopy is no exception. He is aware of the fact that his presentation is merely a momentary aspect of a rapidly changing overall picture. For this reason he has placed the greatest emphasis on the chapters headed "Instrumental Equipment" and "Analytical Parameters".

On the other hand, the chapter about analytical applications, which is arranged according to elements and which contains a subsection on commercially available equipment, will appear too short for many analytical chemists who are interested in this new technique. In spite of the closing chapter about subjects which are closely connected with atomic absorption, for example, oscillator strength, vacuum UV, and fluorescence effects, the book leaves many questions open because of its somewhat oversimplified style. For instance, the discussion of burner types makes no mention of important possible interferences such as light scattering effects and variations in flame profiles. In the section on applications, the characteristics of various flame types are given incompletely. The reader misses a critical comparison between turbulent and laminar flames. The acetylene-nitrous oxide flame is mentioned only very briefly, this being a field of study in which great improvements in sensitivity have been made in the last two years. The literature is covered up to the beginning of 1965. With more than 100 papers being published each year, it is no mean feat to provide a review which represents something more than an interim report.

Such limitations, however, tend to mask the achievement of the author, who has after all succeeded in presenting a comprehensible introduction to atomic absorption to all who are interested in this topic which has proved very useful in many branches of applied analytical chemistry. Nevertheless, before wishing the book a wide readership, the reviewer would recommend a thorough revision of the work.

J. Ringhardtz [NB 625 IE]

Applications of Statistical Mechanics. By *W. A. Guggenheim*, Clarendon Press/Clarendon University Press, London 1966. 1st Edit., 211 pp., numerous illustrations, 55 s.

This book is an extended reproduction of the author's "Baker Lectures" at Cornell University in 1963, and may be regarded as a modern appendix to "Statistical Thermodynamics" by *Fowler* and *Guggenheim*. The eleven chapters deal with:

"Absolute activities and grand partition functions", "Crystalline argon", "Corresponding states", "Argon at the triple point and equations of state for liquid argon and gases at high densities", "Sodium and potassium chlorides and the repulsion between their ions", "Symmetrical mixtures", "Athermic mixtures and solutions of macromolecules", "Ion distribution in dilute aqueous solutions", "Aqueous solutions of simple electrolytes", "Aqueous solutions of several electrolytes", and "Adsorption of gases in single and multiple layers".

This new book by *Guggenheim* is again a model of correctness and clarity. It presents a good survey of recent developments in the fields mentioned, with special reference to recent work by the author. However owing to the small size of the book and the lecture style of the presentation, a number of interesting recent developments have not been included, *e.g.* work on ions in concentrated electrolyte solutions or on the salt lattice under high hydrostatic pressure. Nevertheless, this informative and comprehensible book is warmly recommended.

E. U. Franck [NB 590 IE]

Dictionary of Organic Compounds. Edited by *R. Stevens*. 2nd Supplement Eyre & Spottiswoode Publishers Ltd. E. & F. N. Spoon Ltd., London 1966. 4th Edit., 216 pp., cloth £ 10.00.

It is normally unnecessary to review a supplement. If the main work[1] is good, then one assumes (correctly, in the present instance) that the same will be true of the supplement; if the main work is bad (which this dictionary is not), then supplements are rarely of much help.

The second supplement to the "Dictionary of Organic Compounds", however, deserves mention in that some minor changes are introduced (spelling of systematic names, alphabetical order of elements in empirical formulae, quoting abbreviated Christian names in literature references), which bring the text more into line with international usage and make it easier to follow. Additions to entries in the main work are indicated by an asterisk. Whenever the additions are particularly extensive, the entire entry is repeated, collating all the information. Literature up to the end of 1965 is included. With the two supplements, the Dictionary provides a handy reference tool giving all the information that may be required on the compounds listed. It is, moreover, exceptionally up-to-date; further supplements are to be published to ensure that it remains so.

H. Grünewald [NB 580 IE]

[1] Cf. Angew. Chem. *78*, 724 (1966); Angew. Chem. internat. Edit. *5*, 688 (1966).

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A Topological Approach to the Problem of Ring Structures

BY R. FUGMANN, U. DÖLLING, AND H. NICKELSEN [*]

In the mechanized documentation of chemical literature, the definition of structural concepts is very important. The usual definitions for ring structures are inadequate. Essential ring structures are sometimes not recognized on the basis of these definitions and are therefore missed in a literature search. This is particularly true of bridged ring systems. The ring concept and ring condensation types are now redefined on a topological basis in the closest possible analogy to the intuitive approach of the chemist. In complicated molecular structures, these "fundamental rings" can be easily determined, either manually or by means of a programmed computer. The concept of the "ring complex" is defined and suggested as a preliminary screen in literature searches for ring structures. This will save machine time, and so reduce the cost of searches.

1. Introduction

A great deal of chemical research is concerned with studies on characteristic ring structures. These rings often impart certain characteristic properties to the substances in question, or they may have acquired considerable importance in the theory of the chemical bond. The literature in this field is very extensive.

In undertaking a search for literature in which molecules having a given ring structure are described, one is faced with inherent difficulties that can mainly be traced to two causes. On the one hand, the formula may be projected in such a way that the desired ring is difficult to recognize. On the other, the conventions used in the common filing systems to recognize a ring structure in a molecule do not always coincide with the ideas of the chemist who is making the search.

1.1. The Influence of the Projection Plane on the Recognizability of a Ring Structure

If a three-dimensional molecule is to be represented by a structural formula, it must be projected on a plane. The resulting projection can vary considerably according to the plane selected, so that a given ring structure in the structural formula may be obvious in one projection yet not apparent in another. For example, A and B are different projections of the same molecule.



A B

Projection A ("side view") shows a six-membered ring and a five-membered ring, while a second five-membered ring remains hidden. Conversely, projection B ("top view") clearly shows two five-membered rings, while the six-membered ring is hidden. To eliminate the arbitrariness associated with the adoption of a given projection plane, the three ring structures (two five-membered and one six-membered rings) must be treated as being of equal importance.

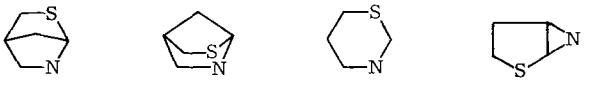
Great demands are occasionally made on the imagination and patience if one is to recognize all the ring structures present from an arbitrarily chosen projection of a molecule, and there is always a danger that essential rings may be overlooked.

1.2. The Influence of the Filing Principle on the Retrieval of Literature on Ring Structures

Provided that the chemist confines his search to perusal of the recent literature, his intuitive judgment as to whether the desired ring system is or is not present in a

[*] Dr. R. Fugmann, Dr. U. Dölling, and Dr. H. Nickelsen
Farbwerke Hoechst AG., vormals Meister Lucius & Brüning
623 Frankfurt/Main-Höchst (Germany)

structural formula is sufficient. However, this is not so when he wishes to make use of the earlier literature, since he must then consult an index or file, in which a specific subject heading exists for the desired ring. In this case the searcher is wholly dependent on the principles by which the ring structures are defined in the index in question. Whether the expected references will in fact be found under a given subject heading depends on whether its definition in the index agrees with the searcher's views.

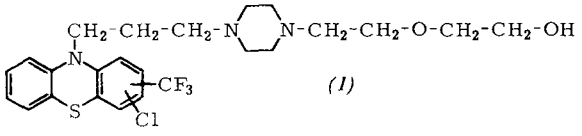


C 1 C 2 D E

For example, in an index in which structure C is regarded only as a system of two condensed five-membered rings (C1), so that the six-membered ring structure (C2) is not taken into account, references to structure C will not be found in a search for six-membered rings with nitrogen and sulfur in the ring (D) (1,3-thiazine derivatives). On the other hand, if the structure E is purely formally regarded in the index as a six-membered ring, the searcher will also be directed to articles on E, which will be of no interest. These two phenomena, loss of relevant information and retrieval of irrelevant information, are the unmistakable signs of the disorder which is inevitably caused by an expressly formal index principle.

The procedure normally used to determine the number of ring structures in a molecule is also formal. According to *Frèrejacque's* rule[1], the number of rings in a molecule is equal to the number of cuts required to obtain a coherent open-chain structure. Thus structure C would have only two rings, and one must decide which of the three rings that are undeniably present is to be regarded as non-existent. Similarly, a cubic structure such as occurs in the cubanes, which clearly contains six four-membered rings, would be presented as having only five. This procedure has been criticized by various authors[2], but no satisfactory alternative has yet been suggested.

Thus all the common indexing principles can give misleading results when used to determine the number and nature of the ring structures in a molecule. This is true no matter what technical assistance is ultimately available for the literature search, whether a manual punched card system, a mechanical punched card system, or the magnetic-tape file of a programmed computer. No technique, however sophisticated, can overcome the obstacles resulting from an excessively formal classification system. Moreover, in the case of an index in the form of a book or a vertical card file, technical inadequacy is added to conceptual obstacles. Thus for purely technical reasons, it is impossible in such systems to cite literature under every heading that might apply. This is due to the necessarily linear, "one-dimensional" arrangement[3] in an index. In particular, it is impossible to give a structural formula under each relevant heading in the index or card file.



(1)

For example, compound *(1)* is a phenothiazine as well as a propylenediamine, a piperazine, an ethanolamine, an ethylene glycol, a condensed 1,4-thiazine, a condensed trifluoromethylated and chlorinated benzene, *etc.* However, the compound cannot be given in the index under all these headings. In the extreme case, an order of precedence of the various headings is established on a purely formal basis, and a compound is entered only under one single heading, namely under that having the highest precedence.

Thus in a generic literature search for related compounds having *e.g.* the same substructure in common, the difficulties encountered in a one-dimensional file are not all of a conceptual nature. The technical peculiarities of these systems are also partly responsible. It has been shown that in an otherwise excellently organized subject index, some 30 % of all the relevant articles are not cited under the heading "phenothiazines", though they are in fact included in the index[3a].

One-dimensional aids and conventional indexing principles can give satisfactory results only in a search for literature on an individual compound. The fact that related compounds are scattered more or less randomly in the index is not detrimental in this case. An individual compound can always be reliably located in the conventional one-dimensional file.

It is an inherent feature of "multidimensional" documentation techniques (punched cards, electronic computers) that a structure can in principle be found under any relevant heading, and particularly under any combination of headings. If these headings are the designations of substructures, there is no hindrance to a generic search for substructures, as far as purely technical aspects are concerned.

However, multidimensional aids can be effective only if the conditions for a generic search are also satisfied from the conceptual viewpoint. No indexing principle is justified in a mechanized, i.e. multidimensional documentation, if this principle had been originally designed for one-dimensional locating of individual compounds. Its use should strictly be limited to a simple one-dimensional index or card file, or else the efficiency of the multidimensional searching device will be seriously impaired. No conventional documentation can really be "modernized" by mere transition from a one-dimensional technique to a mechanized technique without establishing the respective conceptual preconditions in the indexing principle.

[1] *M. Frèrejacque*, Bull. Soc. chim. France *6*, 1008 (1939). However, *Frèrejacque* was interested in other objectives when he formulated his rule, and limitations were imposed regarding its application to non-planar structures.

[2] *W. E. Cossum* and *G. M. Dyson*, American Documentation Institute, Washington, Annual meeting 1963, Short papers 15-18.

[3] In a "one-dimensional" file, a selection can only be made using a single heading, *i.e.* a combination of headings cannot be used in machine selection. The selected references must then be examined intellectually to determine whether they contain the desired combination of headings.

[3a] *B. Loev*, J. chem. Documentation *1961*, 27.

To permit a generic inquiry concerning the presence of a ring as a substructure in various molecular structures, the indexing principle must be capable *e.g.* of showing the relationship between the two structures F and G, *i.e.* that they both contain a nine-membered ring (shaded).



F G

After any change in the structure F that does not affect any of the atoms of the nine-membered ring, the indexing principle should still recognize the nine-membered ring. Otherwise this would point to some vestige of formalism, to random scattering of closely related information, to limited ability of the indexing principle to deal with generic inquiries, and hence, finally, to limited suitability for mechanization.

2. The Fundamental Rings and their Aggregations with One Another

None of the ring-indexing principles known at present satisfies the requirements illustrated in the above example. In an attempt to eliminate this shortcoming, we propose a new definition of the ring concept that is closer to the chemist's idea than the existing formal approach (cf. Section 2.1.). According to this definition, a ring structure is always reliably recognized, even if it occurs as a substructure in any higher system of condensed rings. To find a ring structure by this principle, it is immaterial whether one starts with the three-dimensional model of the molecule or from any of its projections. The same rings and the same number of rings are always recognized. This ring concept will be referred to in future as the "fundamental ring". In establishing this ring concept, mathematical methods, particularly topological methods, were applied.

Two ring structures can be condensed in various ways, at least one ring atom always being shared by at least two rings. The literature contains various definitions of the condensation types of ring structures, some of which are contradictory, and which are again unsatisfactory because of their formal character. We therefore propose new definitions for the condensation types of pairs of ring structures. These definitions are also based on topology.

Ring structures can combine with one another in many ways to give higher aggregates. The mode of aggregation of ring structures is an extremely characteristic feature of a molecule, and can therefore be used as a very effective screen in a mechanized search. With the aid of such a screen, irrelevant structures can be very quickly recognized and rejected in the mechanized scrutiny of a file. Methods of this type for shortening a mechanical selection are particularly desirable in a purely topological search, since the machine time required, and hence the cost of the search, can otherwise become considerable. Topological methods can also be used for handling these aggregations of ring structures, as will be shown later.

Furthermore, in order to enable the chemist to recognize fundamental rings reliably, even in complicated structures, a manual procedure was designed.

Finally, this procedure was used to develop an algorithm by means of which a programmed computer would be able to determine the nature and number of all the fundamental rings present in a given structural formula. This technique is particularly interesting in connection with modern methods for the topological documentation of structural formulae. Thus if a file already contains a topological representation of a structural formula, the machine can relieve man of the work of analysing a structure to find the rings present.

It should be realized that even with the conventional indexing principles, it is not always easy to name a polycyclic structure correctly. A surprising number of errors can occur, despite the greatest care. This recently became clear when an electronic computer was programmed for the von Baeyer nomenclature[4], the names given by the machine then being compared with those found purely intellectually by application of the rules[5].

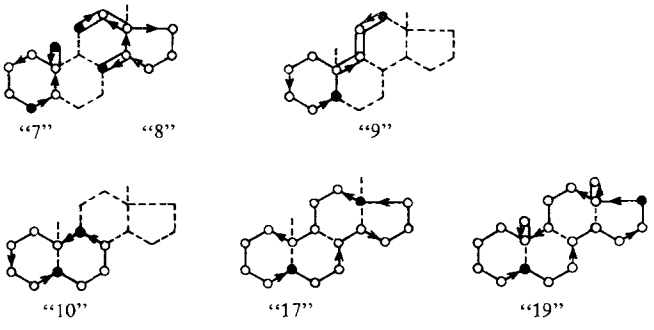
2.1. Definition of the "Fundamental Ring"

"*Cycle*"

A cycle[6] exists in a molecule if it is possible to proceed from one atom to another along the interatomic linkages by two different routes. The cycle is formed by combination of the two routes between the two atoms in question ("•" in Scheme 1). In other words, a cycle is a coherent, closed sequence of lines of the "graph" of the molecule. However, such a definition of a cycle would not agree with the chemist's intuitive idea of ring structures.

"*Fundamental path*" and "*Fundamental ring*"

Cycles that satisfy the above definition cannot all be recognized as ring structures from the chemical point of view. This would lead to devious results in many



Scheme 1. Cycles formed by combination of two different routes between two atoms (•) in the steroid skeleton, with numbers of ring atoms.

[4] IUPAC: Nomenclature of Organic Chemistry, Sections A & B. 2nd Edit., Butterworths, London 1966, p. 32.

[5] *K. Conrow*, Chem. Engng. News *44*, No. 51, p. 84 (1966).

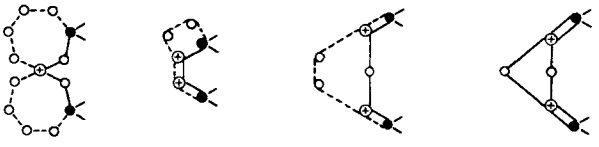
[6] Cf. *C. Berge*: The Theory of Graphs. John Wiley and Son, New York (General Definitions, p. 9).

cases. The steroid skeleton, for example, contains "cycles" of every size from five-membered to nineteen-membered (see Scheme 1).

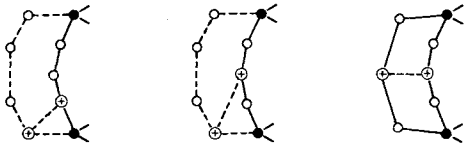
To obtain an answer that agrees with the view of every chemist, namely that the steroid skeleton contains only one five-membered ring and three six-membered rings, cycles with "double points" [7] and with pairs of "neighboring points" [8] must be excluded. Thus it must be stipulated that the routes are combined only in accordance with rules a and b.

a) Routes that are "coupled" with a shorter route cannot be used for combination. The remaining paths are named "fundamental paths".

Two routes between two given atoms are "coupled", α) if they pass through at least one common atom (⊕) (α coupling):



or β) if two atoms (⊕) on different routes are directly joined by a linkage that does not form part of either of the two routes (β coupling):



In the examples, the fundamental paths between the atoms in question are represented by a continuous line. The coupled longer route is indicated by a broken line. When a route is coupled only with another route of the same length, both are fundamental paths (see the last example in each case).

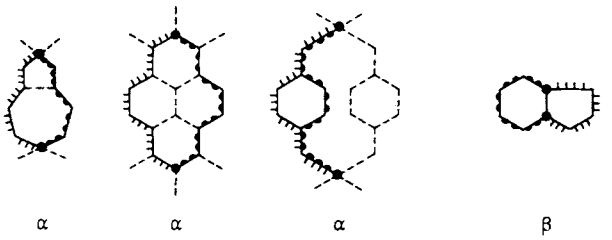
b) To find the fundamental rings for two given atoms, the fundamental paths are combined in pairs. However, all possible combinations of two fundamental paths between these two atoms are not necessarily permissible. In particular, combinations of fundamental paths that would give a cycle containing a double point or a pair of neighboring points are not admissible. The combination of fundamental paths must be in accordance with (i) and (ii) (see Scheme 2).

[7] A double point in a cycle is one that is passed through at least twice when the ring is traced out.

[8] If in tracing out a cycle one passes through two points that are directly connected (neighboring), and if the direct connection between these points is not a part of that cycle, this ring contains a pair of neighboring points.



Cycle with a double point (⊕) cycle with a pair of neighboring points (⊕ ··· ⊕) in the steroid skeleton.



α α α β

Scheme 2. Examples of fundamental paths that cannot be paired to give fundamental rings (⎯⎯ and ⏑ ⏑ ⏑).

i) If two atoms are joined by a number of fundamental paths of equal length, such that one can pass over from any one of these fundamental paths to all the others by simply proceeding *via* a coupled fundamental path, these fundamental paths form a class of their own. The combination of fundamental paths from the same class to form a fundamental ring is not permitted.

ii) If the two atoms are directly linked, the remaining fundamental paths between these two atoms also form a class of their own. Fundamental rings again cannot be formed by combination of fundamental paths from the same class, but only by combination of each fundamental path of such a class with the direct linkage between the two atoms in question.

2.2. Relationships between Two Fundamental Rings (Definitions)

"Isolated fundamental ring"

If a fundamental ring has no ring atom in common with another fundamental ring, it is named "isolated".

"Condensed fundamental ring"

If a fundamental ring has at least one ring atom in common with another fundamental ring, it is said to be "condensed" with this other ring.

"Condensation types"

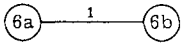
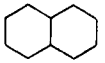
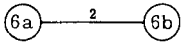
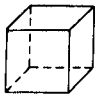
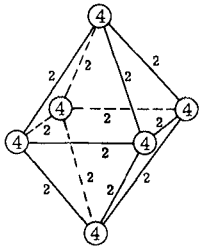
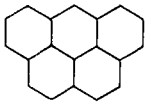
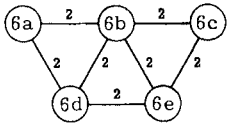
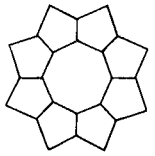
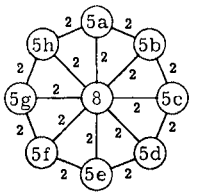
If two fundamental rings are condensed, the system contains a sequence of atoms, consisting of at least one atom, that is common to both fundamental rings. Such a sequence constitutes a "condensation zone" for these two fundamental rings.

A monatomic condensation zone is characteristic of two spiro-condensed fundamental rings [9].

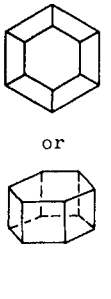
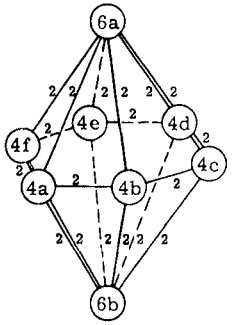
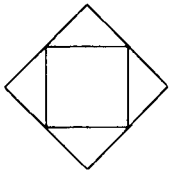
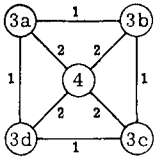
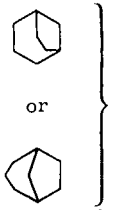
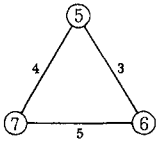
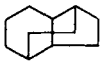
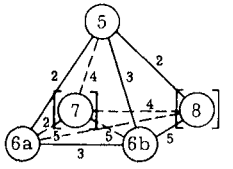
A diatomic condensation zone is characteristic of two ortho-condensed fundamental rings (corresponding to "ortho-fused") [10].

[9] The usual definition ("only one atom is common to two ring structures") does not allow for the possibility that two large ring structures may be spiro-condensed at two points, so that they have more than one ring atom in common.

[10] In the IUPAC nomenclature, for example, there is no consistent designation for the condensation type of two condensed rings. Depending on whether a ring contains the "maximum number of noncumulative double bonds" or not, it is referred to as "fused" or "bridged". "Fused" is always preferred for saturated six-membered rings.

No.	Structure	Fundamental ring	Ring complex
1.		1 six-membered ring	
2.		2 six-membered rings	
3.		2 six-membered rings no ten-membered ring	
4.		6 four-membered rings not 5 four-membered rings	
5.		5 six-membered rings no ten-membered ring no fourteen-membered ring and so on	
6.		1 eight-membered ring 8 five-membered rings no sixteen-membered ring no fifteen-membered ring and so on	

Scheme 3. Fundamental rings and ring complexes for selected structures.

No.	Structure	Fundamental ring	Ring complex
7.		2 six-membered rings 6 four-membered rings no eight-membered ring	
8.		1 four-membered ring 4 three-membered rings no eight-membered ring and so on	
9.		1 five-membered ring 1 six-membered ring 1 seven-membered ring	
10.		1 five-membered ring 2 six-membered rings [1 seven-membered ring 1 eight-membered ring][*]	

[*] Cf. page 729.

A condensation zone containing more than two atoms is characteristic of two "bridged" fundamental rings [10].

"*Degree of condensation of two fundamental rings*"

The numerical value of the degree of condensation gives the number of ring atoms that are common to both rings.

"*Condensation point*"

A condensation point is an atom of a fundamental ring that is linked with at least three other atoms, provided that these atoms are themselves members of fundamental rings [11].

2.3. Aggregation of Fundamental Rings

To permit the topological definition of the types of aggregation of fundamental rings, we have introduced the concept of the "ring complex". The ring complex is a graph that systematically represents the rings and their condensations in a molecule. It does not embody any familiar chemical concept that might be expected to be used by the chemist in a literature search, but is in fact a topological figure, which, if necessary, is automatically constructed and further processed by a computer. The object of this process is merely to facilitate the search by the machine for a system of condensed ring structures.

To construct the ring complex, each fundamental ring in the molecule is assigned a point such that each ring uniquely corresponds to one point and each point uniquely represents one ring. To each linkage of two fundamental rings by condensation is assigned a line in the ring complex. Each of these lines is given a positive integer equal to the degree of condensation of the pair of fundamental rings in question. Each point in the ring complex, and hence each fundamental ring, is given a symbolic name. In the examples in Scheme 3, the number and nature of the fundamental rings present are indicated. The fundamental rings are represented in the ring complexes by circles, in which is shown the symbolic name of the fundamental ring, starting with a figure giving the ring size.

Another topological method for the treatment of condensed ring systems was developed by *Lederberg*. The aim of this method is to permit the mechanical establishment of a notation for systems of condensed rings for which a planar representation is possible, as well as the mechanical deduction and cataloging of every conceivable type of such systems. Unlike the "fundamental ring" concept, however, it is not intended to display relationships between condensed ring systems that are based on the nature, number, and mode of condensation of their constituent rings.

[11] The condensation points correspond to the "vertices" referred to by *Lederberg*; DENDRAL-64. A System for Computer Construction, Enumeration and Notation of Organic Molecules as Tree Structures and Cyclic Graphs, Part II. Topology of Cyclic Graphs. Interim Report to the National Aeronautics and Space Administration. Grant NsG 81–60, December 15, 1965.

2.4. Procedure for the Determination of the Fundamental Rings

Since the definition of the fundamental ring closely follows the chemist's intuitive approach, the fundamental rings in a molecular structure can generally be distinguished by direct inspection, without the need for any special instructions. A number of characteristic ring systems are given in Scheme 3 as examples.

The situation is least favorable in ring systems in which the bridged condensation type occurs together with other condensation types. The fundamental rings are then less obvious on projection on only one plane. To permit the recognition of all the fundamental rings in these cases, irrespective of the projection, a detailed general procedure is given, together with an example (see Scheme 4).

a) Find all the condensation points. Rings that contain only one condensation point or none at all are already fundamental rings.

b) In any order, number the ring atoms of the cycles containing at least two condensation points.

c) Form all possible combinations of two condensation points and mark those in which the condensation points are directly linked.

d) Determine all the possible routes between a selected pair of condensation points and mark those that are coupled in accordance with α or β (cf. Section 2.1.a). The shortest of a set of coupled routes is a fundamental path between the selected pair of condensation points. All other routes are shown in brackets in Scheme 4.

The α-coupling of two paths is recognized by the fact that at least one of the linking atoms is common to both routes (cf. Section 2.1.a)α).

For β-coupling of two routes, the structure must contain at least one pair of directly linked condensation points. One of the condensation points of this pair must lie on one of the two routes and the other condensation point on the other route (cf. Section 2.1.a)β).

e) Form all possible pairs of fundamental paths between the selected condensation points, with the exception of pairs consisting of fundamental paths of the same class (see Section 2.1.b). The rings formed when the fundamental paths are combined in this way are fundamental rings.

f) Arrange the ring atoms named in each fundamental ring in a numerical order. This makes it easy to recognize a fundamental ring when it recurs for another pair of condensation points.

g) Repeat steps d to f for all the other pairs of condensation points.

h) Eliminate repetitions of the same fundamental ring.

i) Add the fundamental rings found in step a.

This procedure gives the nature and number of all the fundamental rings in the structure.

In the fundamental rings resulting from this procedure the intuitive approach of the chemist is very closely approximated. However, application of this procedure sometimes results in the quoting of special kinds of fundamental rings, which a chemist would hardly recognize as acceptable ring structures. To take remedial measures, one can again differentiate special groups among the fundamental rings. The members of each group are characterized by the fact that they correspond to each other in a definite manner, and

only the smallest fundamental ring of such a group of corresponding fundamental rings is finally recognized.

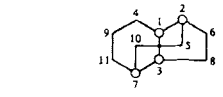
The other fundamental rings are eliminated. It is, for example, the result of such an elimination, at present still manually performed, that in Figure 7 in Scheme 3 eight-membered rings are suppressed. These rings would extend over "bottom" and "top" of the six-cornered column.

The same correspondence principle would lead to the elimination of the seven-membered and of the eight-membered fundamental ring in Figure 10 in Scheme 3 (fundamental rings D and E in Scheme 4). The reader himself may judge whether or not he would intuitively state these ring structures as being present.

Fundamental rings can also be recognized by applying a slightly modified procedure: In order to find the fundamental paths, one can combine a condensation point only with one of its neighboring condensation points at a time. Among the routes found between two of these condensation points those which are coupled with a shorter fundamental path are eliminated. Since this procedure has not yet been programmed for the computer we shall not describe it in detail here.

One might be inclined to look out for definitions of ring structures which are simpler to handle than the proposed concept of the fundamental rings. One could, for example, drastically cut short the procedure of ring recognition by considering only neighboring condensation points and by restricting oneself to the combinations of the two shortest routes between these condensation points in order to recognize ring structures with them as members. However, this would result *e.g.* in the failure to recognize the four-membered central ring in Figure 8 in Scheme 3.

There are many other possible ways of defining ring structures in a simpler manner than proposed, but they are all more or less formal, as was already pointed out for the conventional definitions. This inevitably



a) 1; 2; 3; 7

c) 1,2; 1,3; 1,7; 2,3; 2,7; 3,7

d1) 1,2:

1 2

1 3 {(7 10 5 2)
{ 8 6 2

(1 4 9 11 7 { 3 8 6 2)
{10 5 2)

belonging to the same class.

e1) 1,2,6,8,3

f1) 1 2 3 6 8 A

d2) 1,3:

1 3

1 2 {(5 10 7 3)
{ 6 8 3

1 4 9 11 7 { 3
{(10 5 2 6 8 3)

belonging to the same class.

e2) 1,3,8,6,2

f2) 1 2 3 6 8 A

e2) 1,3,7,11,9,4

f2) 1 3 4 7 9 11 B

d5) 2,7:

2 1 { 3 7
{(4 9 11 7)

2 5 10 7

(2 6 8 3 { (7)
{1 4 9 11 7)

e5) 2,1,3,7,10,5

f5) 1 2 3 5 7 10 C

d6) 3,7:

3 7

3 1 {2 5 10 7
{4 9 11 7

(3 8 6 2 {1 4 9 11 7)
{5 10 7)

belonging to the same class.

e6) 3,7,10,5,2,1

f6) 1 2 3 5 7 10 C

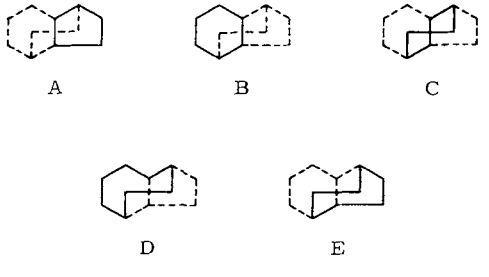
e6) 3,7,11,9,4,1

f6) 1 3 4 7 9 11 B

Furthermore resulting from the pairs 1,7 und 2,3:

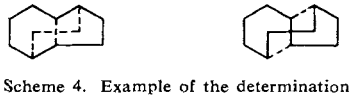
1 2 4 5 7 9 10 11 D

2 3 5 6 7 8 10 E



A B C D E

Cycles that are not fundamental rings:



Scheme 4. Example of the determination of the fundamental rings in a given structure.

leads to results that frequently are far distant from the intuitive ring concept of the chemist, which, however, has proved much too complicated to be satisfactorily represented by a simple formal definition. If one aims at such an approximation of the chemist's point of view, as has been achieved in the fundamental ring concept, a certain amount of effort is required in defining ring structures. At present extensive investigations are being undertaken to economize the recognition of fundamental rings.

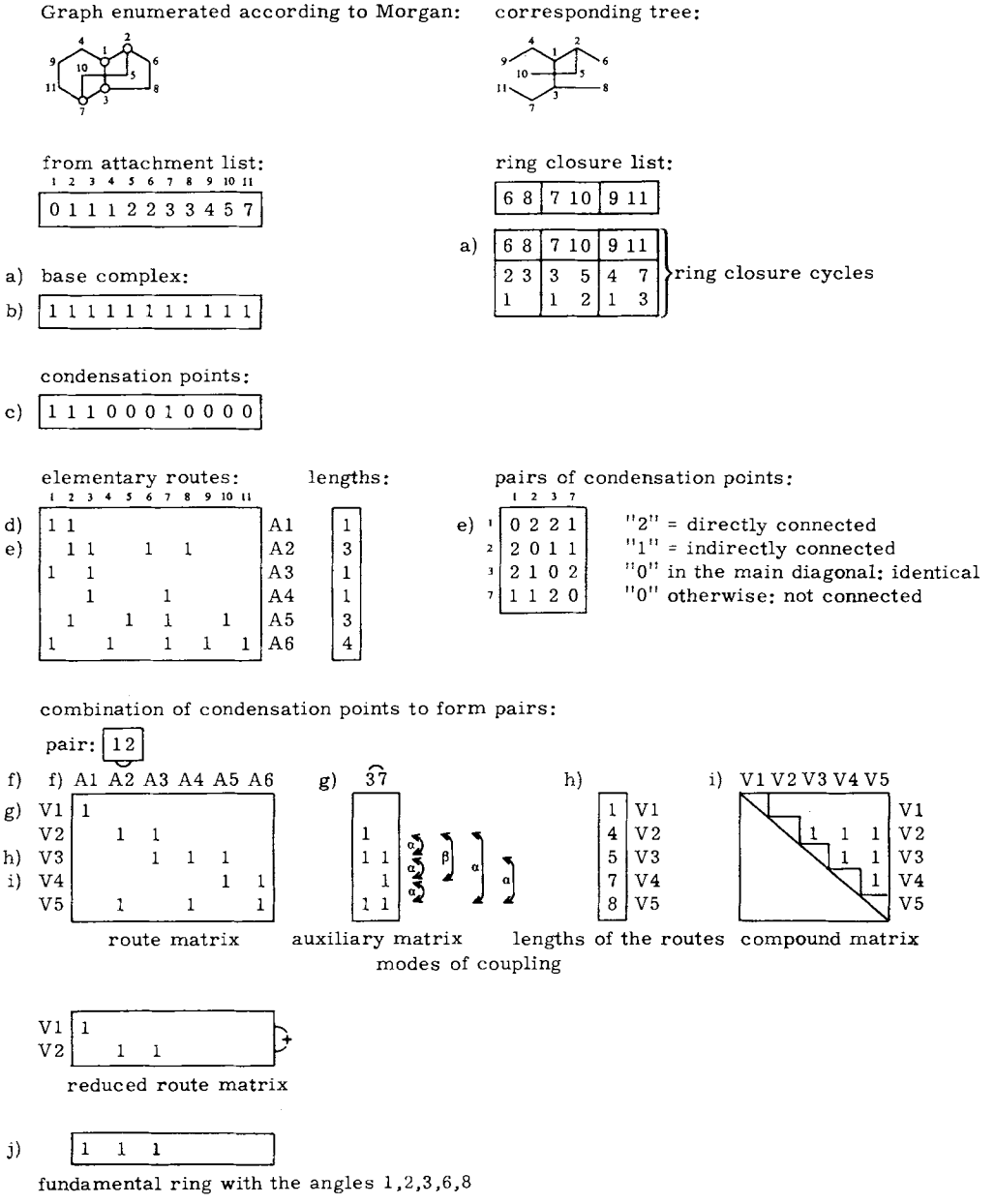
If the structural formula satisfies certain requirements, the process can be considerably shortened by the use of simplifications. In the majority of cases the fundamental rings can be recognized by direct inspection of the structural formula, particularly if no bridged structures are present. For example, it can be easily shown that the only fundamental rings present in condensed aromatic hydrocarbons are the obvious benzene rings, so that analysis by the above procedure is unnecessary. However, this will not be discussed further here.

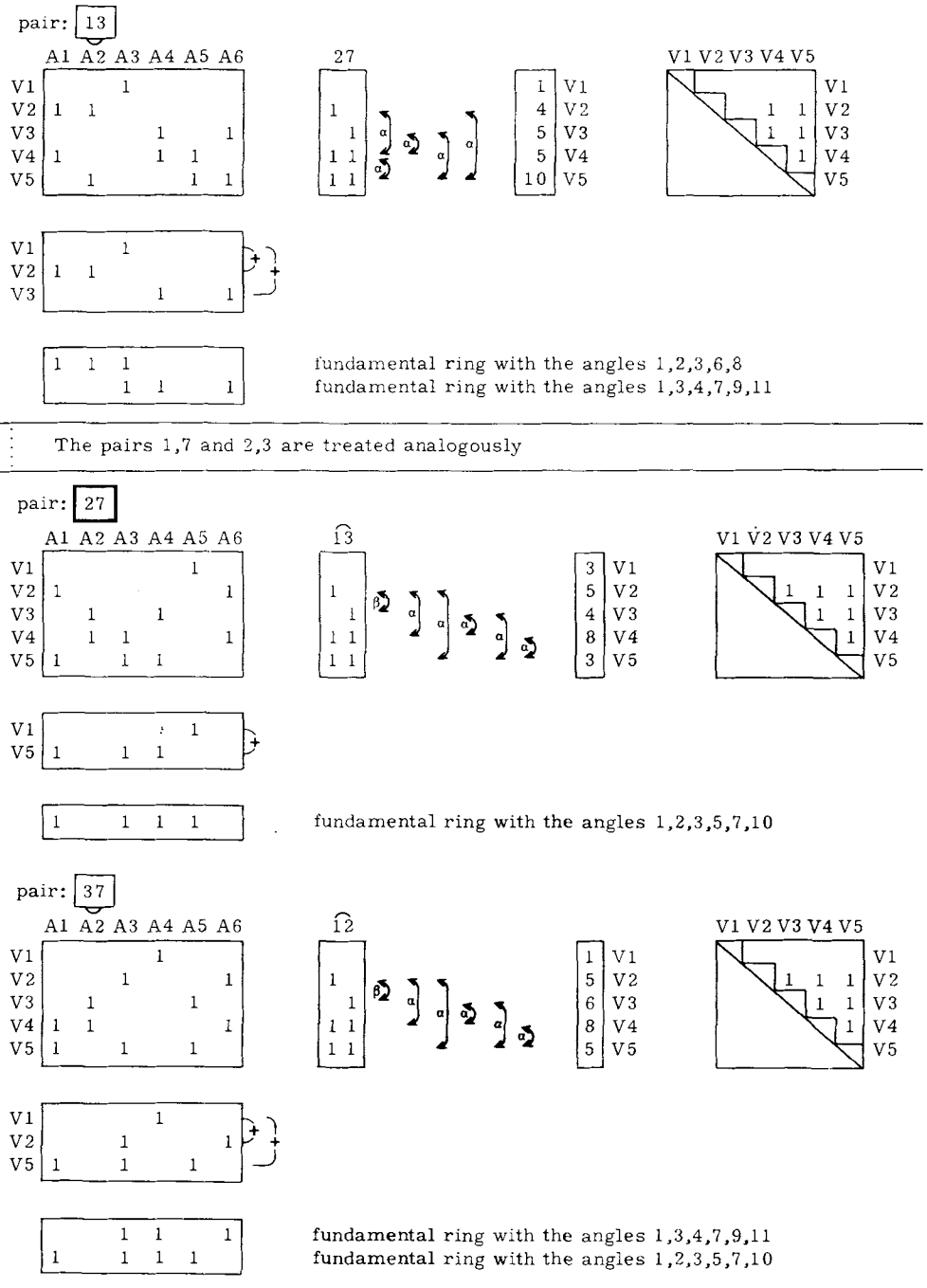
3. An Algorithm for the Mechanical Determination of Fundamental Rings

If the atoms of a structural formula are represented by points ("angles") and the bonds by "lines", one obtains a graph corresponding to the structural formula. In the determination of the fundamental rings present by means of an algorithm, the hydrogen atoms may be ignored, as can the nature of the skeletal atoms and the details of their bonding (*e.g.* multiple bonds).

Such a graph can also be completely represented in a numerical form by enumerating all its angles and listing the connections between them. For example, in a procedure given by *H. L. Morgan*[12], a "from attachment list" gives for each angle one of the directly connected angles ("ligands"), the particular ligand given being the one with the lowest number out of all the ligands of this angle.

[12] *H. L. Morgan*, J. chem. Documentation *1965*, 107.





Scheme 5. Mechanical determination of fundamental rings.

All the lines represented in the list in this way combine to form a tree that contains all the angles of this graph. This list cannot contain lines that would lead to ring closures in the graph. These are given in an additional "ring closure list". All these lists can be readily compiled by hand for a given structural formula. However, they can also be produced by a programmed electronic computer[7] from a suitable representation of the formula.

To find the fundamental rings from a numerical representation of the graph, the computer must carry out the following steps (see Scheme 5).

a) The cycle corresponding to each ring closure in the "ring closure list" is constructed. To do this, the two ends of the ring closure line are joined by the sequence of lines in the tree. This sequence of lines, together with the ring-closure line, makes up the cycle.

b) Every cycle present in the graph, and hence all the fundamental rings, can be found from these "ring-closure cycles". Thus the fundamental rings can be found by analysis of the sub-graph consisting of the ring-closure cycles, *i.e.* the "base complex".

c) All the condensation points in the structure are then determined. These are the angles in the graph having more than two ligands in the base complex. If a ring-closure cycle contains only one condensation point or none at all, this cycle is already a fundamental ring.

d) If a ring-closure cycle has more than one condensation point, "elementary routes" are formed to find fundamental rings. An elementary route runs between two condensation points in the base complex. It contains no double points, and has no condensation points except at its ends.

These elementary routes are then combined to form the fundamental paths, which will give the desired fundamental rings on combination with other fundamental paths. The elementary routes are marked in a matrix of the type (number

of angles, number of elementary routes). A 1 is inserted in position (i,k) if the i-th angle occurs in the k-th elementary route A_k. All the other matrix elements have the value zero. The length of any elementary route A_k is equal to one less than the number of angles.

e) The next step is the formation of all possible combinations of two condensation points that are joined in the base complex. In a matrix of the type (number of condensation points, number of condensation points), a 2 is inserted in position (i,k) if the i-th condensation point is directly linked to the k-th. A 1 is inserted in this position if the condensation points are only indirectly linked. Otherwise a 0 is inserted.

A pair (l,m) of directly linked condensation points is selected from all these points, provided it is present.

f) All routes V_i between l and m that do not contain double points are now expressed by elementary routes. This is done in the route matrix of the type (number of routes, number of elementary routes). A 1 is inserted in position (i,k) if A_k occurs in the i-th route V_i. All the other elements are equal to zero.

g) Coupled routes are now found by means of an auxiliary matrix. Since two routes can be coupled only by condensation points, a check is made to determine whether route V_i contains any condensation points other than those at its ends. This is indicated by a 1 in the column of the condensation point in question.

α) Coupling of two routes by a common angle is shown by the occurrence of this angle on both paths.

β) Coupling of two routes by the direct linkage of two angles, each of which lies on a different path, is recognized as follows.

If one checks only the columns in the auxiliary matrix that are assigned to two directly linked condensation points l' and m' the occurrence of this type of coupling is shown by a characteristic arrangement of the elements 0 and 1 at the positions assigned to the routes in question, V_o and V_p, *i.e.* either:

	l'	m'	or:		l'	m'
V_o	0	1		V_o	1	0
V_p	1	0		V_p	0	1

If one of these criteria shows that two routes are coupled, the longer of the two routes is not considered further.

h) To establish this, a V-membered vector is formed for the individual route lengths. Its i-th element is equal to the scalar product of the i-th row vector of the route matrix and the elementary route-length vector.

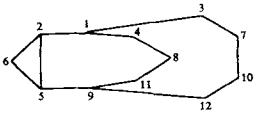
i) The coupling of two routes is marked in a compound matrix of the type (V,V). A 1 is inserted in position (i,k) if the i-th route is coupled with the k-th route. All the other matrix elements are equal to zero. With the aid of this compound matrix and the route-length vector, the longer of two coupled routes is eliminated from the route matrix. The resulting simplified route matrix only contains all the fundamental paths between the pair of condensation points in question.

j) To form the fundamental rings from the fundamental paths, the row vector representing the direct linkage of a pair of condensation points is added modulo two to each of the other row vectors.

All the other pairs of directly linked condensation points are treated in the same way.

The fundamental paths between pairs of indirectly linked condensation points are determined in a similar manner. In this case, however, the fundamental paths must be combined mainly in pairs, *i.e.* each with every other, to form rings. "Mainly" is intended to indicate that care must be taken in the program to ensure that fundamental paths of the same class (cf. Section 2.1.) are not combined with one another.

This procedure finally gives all the fundamental rings that can be found by considering pairs of condensation points. The total number of rings in the graph is then found by adding this number to the number of fundamental rings, obtained by consideration of the base rings with a maximum of one condensation point.

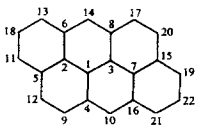


RING SIZE

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RING MEMBERS

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5	11	5	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9	8	9	6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
11	4	12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8	1	10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4	3	7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
1	7	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0	10	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0	12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
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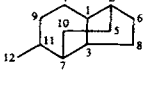


RING SIZE

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RING MEMBERS

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1	3	3	2	8	7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4	8	7	5	17	15	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
9	14	16	11	20	19	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
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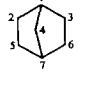


RING SIZE

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RING MEMBERS

1	3	1	1	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	1	2	2	6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
6	4	5	5	8	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
8	9	10	10	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
3	11	7	7	7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0	7	11	3	10	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0	0	9	0	5	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0	0	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
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0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0



RING SIZE

5 6 5 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0 0

RING MEMBERS

1	1	7	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
2	2	4	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
5	5	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
7	7	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
4	6	6	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0	3	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
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0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Scheme 6. Some results of the recognition of fundamental rings by machine.

The machine program for the determination of fundamental rings is written in the problem-oriented FORTRAN language. It has already been tested on the IBM® 7010, 7090, and 360 Model 40 machines (the last with a 64 K core memory). A series of different structural-formula graphs with up to 12 condensation points were fed into the machine in the short topological form described by *Morgan*[*], and the fundamental rings present in each were determined by computer. The results were expressed in the form of a list: a heading line that can accommodate up to 24 two-digit numbers gives the various ring sizes. Under these, in a fourteen line matrix, the individual ring members are given in the order of their occurrence in the ring (cf. Scheme 6).

[*] Cf. Section 3, [12].

It may happen that in a highly complicated molecule so many condensation points and fundamental rings exist that the available space in the memory of the computer does not suffice for all steps of the complete ring-recognition process. Then the machine prints a message showing which of the condensation points it was unable to consider. After that the result can easily be completed by intellectually completing the algorithm. These limitations can be overcome, if necessary, by using a computer with a larger memory or by writing the program in a machine-oriented language instead of FORTRAN.

The authors would like to thank W. Schwier and M. Wildgrube for substantial mathematical contributions.

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New Methods of Preparative Organic Chemistry[**]

Transfer of Diazo Groups[1]

BY M. REGITZ[*]

BASED ON WORK CARRIED OUT WITH D. STADLER, H. SCHWALL, A. LIEDHEGENER, H. J. GEELHAAR, F. MENZ, J. HOCKER, J. RÜTER, AND W. ANSCHÜTZ

When an arenesulfonyl azide, particularly p-toluenesulfonyl azide, reacts, in the presence of a base, with a compound containing an active methylene group, the two hydrogen atoms of the active methylene group are replaced by a diazo group to form a diazo compound and an arenesulfonamide. The method may be used for the synthesis of the diazo derivatives of cyclopentadienes, cyclohexadienes, 1,3-dicarbonyl, 1,3-disulfonyl, and 1,3-ketosulfonyl compounds, ketones, carbonic acid esters, and β-iminoketones. Secondary reactions can lead to azo compounds and heterocycles such as 1,2,3-triazoles, 1,2,3-thiadiazoles, and pyrazolin-4-ones. Azidinium salts react in the same way, but in this case an acidic reaction medium is necessary, a fact that is sometimes advantageous.

I. Introduction

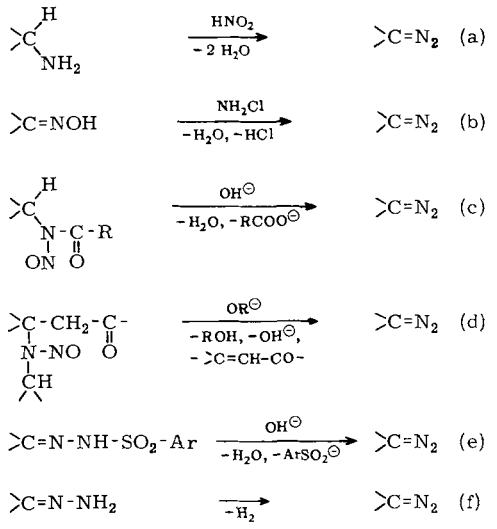
Two main routes have been used so far for the synthesis of aliphatic diazo compounds. In one case, compounds in which the future diazo C atom already carries a substituent containing nitrogen are converted into diazo compounds by condensations, *e.g.* by diazotization of amines in accordance with eq. (a) or by the Forster reaction (b). The starting materials for the second route are substances in which the future diazo C atom carries a functional group with two adjacent N atoms. Some important examples are the deacylation (c) of the *N*-acyl-*N*-nitrosoalkylamines, the cleavage (d) and (e) of β-(*N*-alkyl-*N*-nitrosoamino)-ketones and arenesulfonyl hydrazones by alkali, and the dehydrogenation (f) of hydrazones[2].

[*] Doz. Dr. M. Regitz
Institut für Organische Chemie der Universität
66 Saarbrücken 15 (Germany)

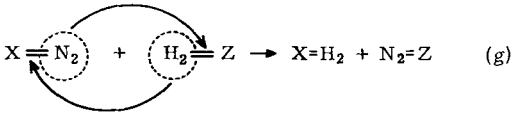
[**] The articles in this series have been published in five volumes by Verlag Chemie, Weinheim/Bergstrasse. An English edition has also been published. The present article, together with procedures will appear in Volume VI of the series.

[1] XIIIth report on reactions of compounds containing active methylene groups with azides. From the Habilitation Thesis of *M. Regitz*, Universität des Saarlandes, Saarbrücken, 1965; supplemented by more recent work.

[2] For individual methods, see *B. Eistert* in: Neuere Methoden der präparativen organischen Chemie. 3rd Edit., Verlag Chemie GmbH., Weinheim/Bergstr. 1949, Vol. I, p. 359; *R. Huisgen*, Angew. Chem. *67*, 439 (1955); *F. Weygand* and *H. J. Bestmann*, Angew. Chem. *72*, 535 (1960).



In contrast to these methods, the transfer of the diazo groups in accordance with reaction (g) involves the transfer of an existing N_2 group from a donor to an acceptor in exchange for two H atoms, with formation of a new diazo compound.

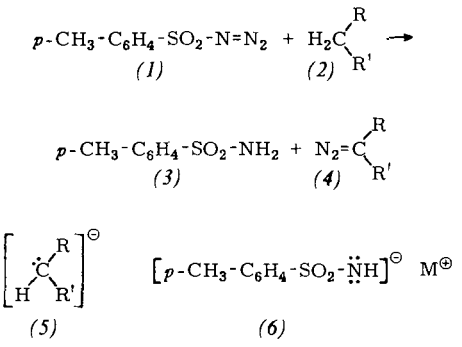


The first compounds that come to mind as donors might be the aliphatic diazo compounds. However, these can be ruled out on two grounds. Firstly, they react in accordance with eq. (g) only in special cases[1,3]; secondly they would have to be prepared by one of the conventional methods (reactions (a) to (f)), so that any advantage of the present method is lost.

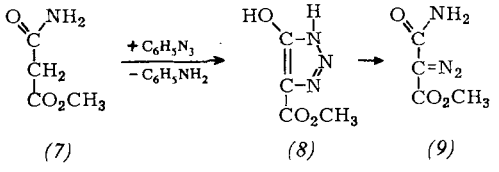
II. Transfer of Diazo Groups from Sulfonyl Azides

Sulfonyl azides, which can be readily obtained from sulfonyl chlorides by halogen-azide exchange, do not suffer from the above disadvantage. The surprising discovery that azides transfer N_2 groups is plausible since they are isoelectronic with diazo compounds, so that *e.g.* sulfonyl azides may be regarded as sulfonyl diazoamides. Azides and diazo compounds also exhibit pronounced similarities in reactivity, as is seen *e.g.* in the Curtius degradation of carboxylic acid azides as a counterpart of the Wolff rearrangement, the formation of imenes and carbenes, or even the 1,3-dipolar cycloadditions of both classes of compounds.

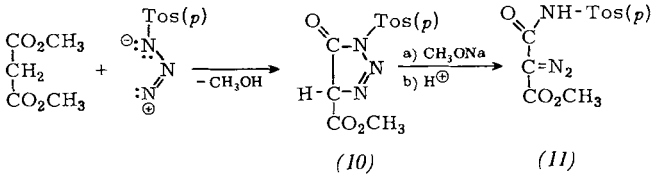
The N_2 group of *p*-toluenesulfonyl azide *(1)*, which is the azide component used in almost every case, is exchanged in a one-step reaction for two H atoms of an active methylene compound *(2)*, with formation of *p*-toluenesulfonamide *(3)* and the diazo compound *(4)*. The transfer of the diazo group is carried out in the presence of a base whose strength corresponds to the proton activity of *(2)*, since the carbanion *(5)* is the actual reacting species. The acidic *p*-toluenesulfonamide *(3)* is generally separated from *(4)* as a salt *(6)*.



The preparation of a diazo compound from an azide (phenyl azide) was first carried out by *O. Dimroth*[4] in 1910. The reaction with the malonic ester amide *(7)* led *via* the triazole *(8)* to the diazomalonic ester amide *(9)*.



Curtius and *Klavehn*[5] later prepared methyl diazomalonate amide *(11)* from dimethyl malonate and *p*-toluenesulfonyl azide, the triazolone *(10)* being assumed to occur as an intermediate.



More recently, *Doering* and *De Puy*[6] synthesized diazocyclopentadiene *(14)* (see Section A.1), evidently with no knowledge of the above-mentioned work. This synthesis provided the incentive for our own investigations in this field, which, along with other investigations, are reported below.

A. Synthesis of Diazo Compounds

1. Diazocyclopentadienes

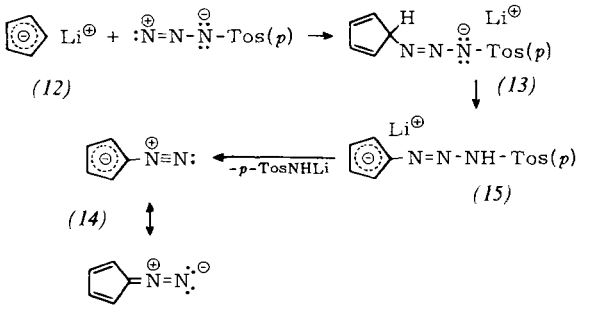
Cyclopentadienyl-lithium *(12)*, which can be obtained from cyclopentadiene and phenyl-lithium, reacts with *p*-toluenesulfonyl azide in ether to form diazocyclopentadiene *(14)*[6]. The "azo coupling product" *(13)* and the triazene *(15)* are regarded as hypothetical intermediates, the decomposition of which yields

[3] *D. G. Farnum* and *P. Yates*, Proc. chem. Soc. (London) *1960*, 224.

[4] *O. Dimroth*, Liebigs Ann. Chem. *373*, 356 (1910).

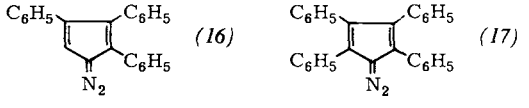
[5] *Th. Curtius* and *W. Klavehn*, J. prakt. Chem. [2] *112*, 76 (1926).

[6] *W. v. E. Doering* and *C. H. De Puy*, J. Amer. chem. Soc. *75*, 5955 (1953).

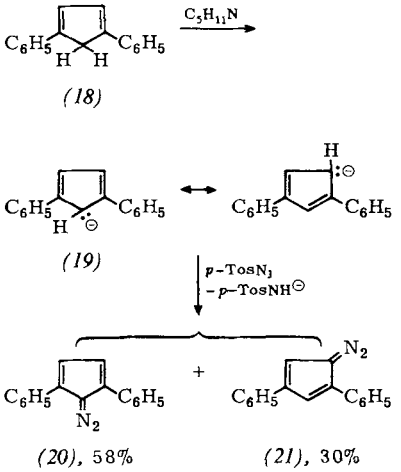


lithium *p*-toluenesulfonamide and diazocyclopentadiene *(14)*.

The use of the rather expensive phenyl-lithium as the base can be avoided by carrying out the reaction in the presence of diethylamine without a solvent [7], or even better, in acetonitrile (yield of *(14)* 84 %) [8]. The analogous synthesis of 1-diazo-2,3,4-triphenylcyclopentadiene *(16)* (yield 97 %) and 1-diazo-2,3,4,5-tetraphenylcyclopentadiene *(17)* (yield 95 %) in acetonitrile/piperidine [8] is superior to the transfer of diazo groups with phenyl-lithium [9,10] and with diethylamine [11]. 2,5-Diphenylcyclopentadiene *(18)* gives the



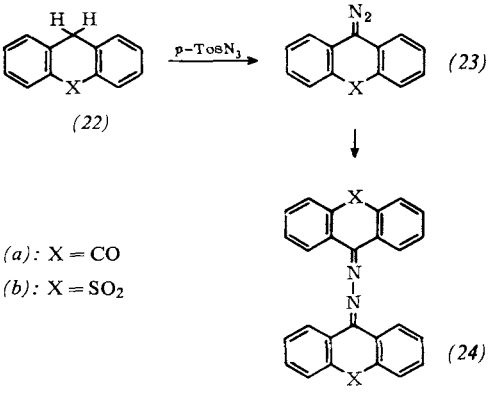
two isomeric diphenyldiazocyclopentadienes *(20)* and *(21)* [8]. The formation of these products is readily explained as involving the mesomeric carbanion *(19)*, formed from *(18)* and piperidine, which contains two nucleophilic centers.



(20), 58% *(21)*, 30%

2. Diazocyclohexadienes

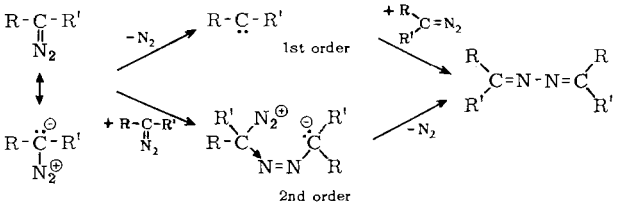
The only dibenzocyclohexa-1,4-diene derivatives *(22)* that have been used so far for diazo group transfers are those in which the CH_2 group is further activated by



an additional CO or SO_2 group in the meso position (vinylogy principle).

Diazoanthrone *(23a)* is obtained in this way in 94 % yield from anthrone *(22a)* and *p*-toluenesulfonyl azide in ethanol/piperidine [12]. A compound to which the same structure was assigned, and which was formed from *(22a)* and methylsulfonyl azide in pyridine/piperidine [13], was found to be a mixture of 66 % of anthraquinone azine *(24a)* and 27 % of 9-diazoanthrone *(23a)* [12]. This conversion of a methylene component into an azine is generally possible only if the initially formed diazo compound is unstable to bases, and if the reaction conditions for the diazo group transfer coincide with those required for the decomposition of the diazo compound.

Base-catalysed decompositions of diazo compounds into azines and nitrogen are known. Compound *(23)* also decomposes to give *(24)* when treated with pyridine/piperidine. Consequently, it is very doubtful that *Pelz* [13] isolated a compound *(23)*, since this is not stable under the reaction conditions used. The two mechanistically possible paths A (first order) and B (second order) were not studied kinetically.

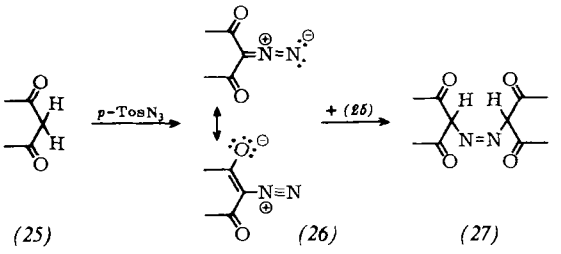


Since the proton-activating action of the arenesulfonyl group is weaker than that of the carbonyl group [14], the transfer of a diazo group onto thioxanthene *S,S*-dioxide *(22b)* requires the use of potassium ethoxide as the base, but it then gives a 98 % yield of *(23b)* [12]. However, if the addition of azide is carried out over a relatively long period (*ca.* 30 min), the 9-diazothioxanthene *S,S*-dioxide *(23b)* that is formed undergoes $C_2H_5O^{\ominus}$ - catalysed decomposition into nitrogen and 10,10'-azinobis(thioxanthene *S,S*-dioxide) *(24b)*. The reaction of *(22b)* with *p*-toluenesulfonyl azide in ether/tetrahydrofuran gives only 45 % of *(23b)* [10].

[7] *Th. Weil* and *M. Cais*, J. org. Chemistry *28*, 2472 (1963).
[8] *M. Regitz* and *A. Liedhegener*, Tetrahedron *23*, 2701 (1967).
[9] *P. L. Pauson* and *B. J. Williams*, J. chem. Soc. (London) *1961*, 4153.
[10] *F. Klages* and *K. Bott*, Chem. Ber. *97*, 735 (1964).
[11] *D. Lloyd* and *F. J. Wasson*, J. chem. Soc. (London) *1966*, 408.
[12] *M. Regitz*, Chem. Ber. *97*, 2742 (1964).
[13] *W. Pelz*, US.-Pat. 2950273 (August 23, 1960), Agfa AG.
[14] *S. Hünig* and *O. Boes*, Liebigs Ann. Chem. *579*, 28 (1953).

3. 2-Diazo-1,3-dioxo Compounds

2-Diazo-1,3-dioxo compounds *(26)* are usually synthesized by diazotization of suitable amines. Since these amines are generally prepared from the β-dicarbonyl compounds *(25)*, the synthesis is considerably shortened by the transfer of diazo groups onto *(25)*.

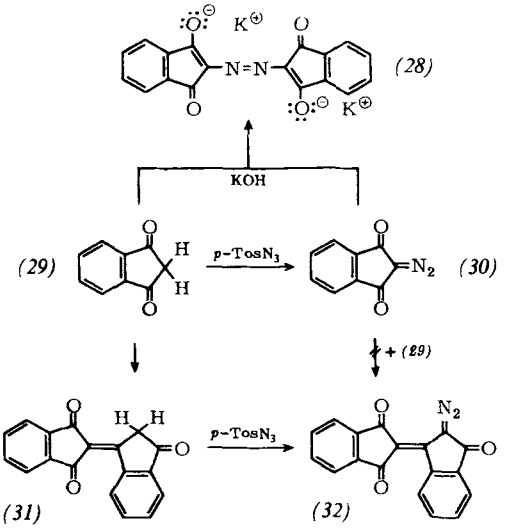


The possibility of keto-enol tautomerism in the β-diketones is of no importance to the transfer reaction, since the keto form and the enol form react with bases to give the same mesomeric anion, which reacts with the sulfonyl azide. Owing to the high CH or OH (enol) acidity of *(25)*, even weak bases such as piperidine or triethylamine can cause anion formation. Whenever possible the use of such weak bases is preferred to the use of alkali metal hydroxides or alkoxides since side reactions can often be avoided and higher yields can be obtained. Cyclic β-dicarbonyl compounds fixed in the *trans* configuration occasionally also give azo compounds *(27)* or tautomers as secondary products of the diazo synthesis, which will be discussed more fully in Section II.B.

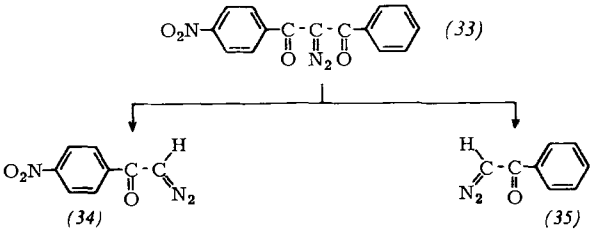
a) 2-Diazo-1,3-diketones

Investigations on the structure of hydrindantin [15] led to the synthesis of 2-diazoindan-1,3-dione *(30)* by diazo group transfer. The reaction was found to proceed satisfactorily, not only in ethanol/potassium ethoxide [16,17] but also in ethanol/triethylamine [15], which gives *(30)* in 85 % yield; in aqueous-ethanolic potassium hydroxide solution, on the other hand, the reaction leads to 2-diazo-1',3,3'-trioxo-1,2'-bisindanylidene *(32)* [16].

The transfer of diazo groups onto *(31)* is preceded by autocondensation of the indan-1,3-dione in the presence of KOH (*(29)* → *(31)*). Since *(29)* couples with *(30)* to give the dipotassium salt *(28)*, the formation of *(32)* *via* 2-diazoindan-1,3-dione *(30)* may be ruled out.



Diazo group transfers onto β-diketones of the benzoylacetone or dibenzoylmethane type are best carried out in methylene chloride/piperidine. In contrast to the usual high yields (see Table 1), *p*-nitrodibenzoyldiazomethane *(33)* is formed in a yield of only 29 %. This is mainly due to deacylation of *(33)* in both of the



possible directions to give *p*-nitrobenzoyldiazomethane *(34)* and benzoyldiazomethane *(35)* [18]. This cleavage is prevented by reaction of *p*-nitrodibenzoylmethane with *p*-toluenesulfonyl azide in ethanol in the presence

Table 1. 2-Diazo-1,3-diketones synthesized.

	Solvent, base	Yield (%)	M.p. (°C)	IR Diazo band (KBr) (cm^{-1})	Ref.
2-Diazo-5,5-dimethylcyclohexane-1,3-dione	Ethanol/triethylamine	73	108	2257	[19]
	Ether/triethylamine	78		2193	[20]
				2146	
2-Diazo-4,5-benzoindan-1,3-dione	Ethanol/triethylamine	91	149—150	2141	[15]
5-Diazobarbituric acid	Ethanol-water/potassium hydroxide	67	276—279	2193	[21]
3-Diazo-1,2,3,4-tetrahydroquinoline-2,4-dione	Dimethylformamide/triethylamine	86	226	2155	[19]
Dibenzoyldiazomethane	Ethanol/piperidine	81	107	2119	[18]
	Ether/triethylamine	82		2137	
	Methylene chloride/piperidine	70			
Benzoyl-2-pyridylcarbonyldiazomethane	Methylene chloride/piperidine	76	87	2174	[18]
				2137	
				2119	
Acetylbenzoyldiazomethane	Ethanol/triethylamine	71	63—64	2273	[18]
				2212	
				2114	

[15] *M. Regitz, H. Schwall, G. Heck, B. Eistert,* and *G. Bock,* Liebigs Ann. Chem. *690*, 125 (1965).

[16] *M. Regitz* and *G. Heck,* Chem. Ber. *97*, 1482 (1964).

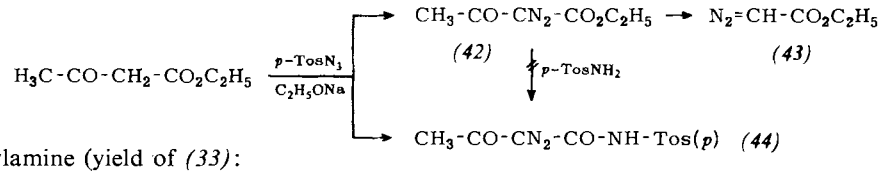
[17] *A. Schönberg* and *K. Junghans,* Chem. Ber. *98*, 820 (1965), use methanol/sodium methoxide.

[18] *M. Regitz* and *A. Liedhegener,* Chem. Ber. *99*, 3128 (1966).

[19] *M. Regitz* and *D. Stadler,* Liebigs Ann. Chem. *687*, 214 (1965).

[20] *M. Rosenberger, P. Yates, J. B. Hendrickson,* and *W. Wolf,* Tetrahedron Letters *1964*, 2285.

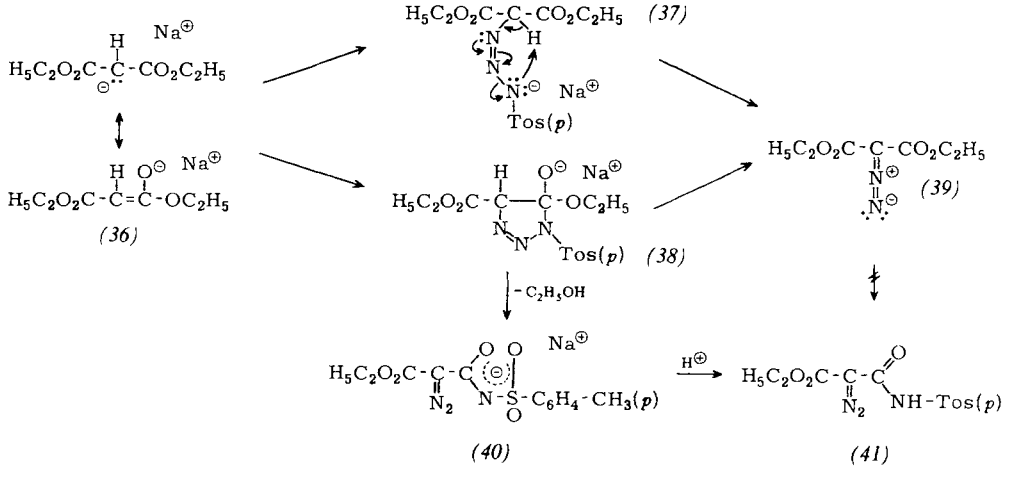
[21] *M. Regitz,* Liebigs Ann. Chem. *676*, 101 (1964).



of catalytic quantities of triethylamine (yield of *(33)*: 80 %)[18]. The versatility of the reaction for the synthesis of 2-diazo-1,3-diketones can be judged from Table 1.

b) Diazomalonic Ester and α-Diazo-β-oxocarboxylic Esters

Diethyl diazomalonate *(39)* can be obtained by diazo transfer in ether/diethylamine (yield 75 %)[20] or in acetonitrile/triethylamine (yield 95 %)[18], the resulting product being almost pure. It can be purified by low-temperature recrystallization (distillation is sometimes dangerous) from ether, a process that is very useful for the purification of liquid diazo compounds [18,42]. The rate of the triethylamine-catalysed transfer reaction decreases with decreasing polarity of the solvent, *i.e.* in the order acetonitrile > methylene chloride > ether.



Diethyl diazomalonate *(39)* is formed only in traces (3 %) from diethyl sodiomalonate *(36)* and *p*-toluenesulfonyl azide; the main product (97 % yield) is the sodium salt of ethyl *N*-(*p*-toluenesulfonyl)diazomalonamide *(40)*, which is formed by displacement of an ethoxy group, and which gives *(41)* on acidification[18,21].

The reaction cannot proceed *via* diethyl diazomalonate *(39)*, which does not react with sodium *p*-toluenesulfonamide to give *(41)* under the conditions used. A cyclic intermediate, the triazoline *(38)* must be involved, *(40)* being formed by ring cleavage between the azo and sulfonamide nitrogens with elimination of ethanol[22]. The formation of traces of diethyl diazomalonate *(39)* can be explained in a similar manner, but with elimination of sodium *p*-toluenesulfonamide; however, *(39)* could also be formed by a mechanism involving the triazene *(37)*[18,23].

Ethyl acetoacetate reacts with *p*-toluenesulfonyl azide in ethanol/sodium ethoxide to give only 31 % of α-diazo-*N*-(*p*-toluenesulfonyl)acetoacetamide *(44)*, together with a considerable quantity of ethyl α-diazoacetoacetate *(42)*, which is contaminated with ethyl diazoacetate *(43)*[18,21]. *(43)* is evidently formed by deacylation of *(42)*.

A mechanistic argument similar to that outlined for diethyl malonate also applies to the formation of *(42)* and *(44)*, particularly since *(42)* does not react with sodium *p*-toluenesulfonamide to give the diazo derivative *(44)*. Further evidence of the cyclic intermediate in the displacement reaction (triazoline formation in accordance with *(36)* → *(38)*; $CO-CH_3$ instead of $CO_2C_2H_5$) is provided by the fact that the reaction of t-butyl acetoacetate yields only traces of *(44)*, clearly because of steric hindrance to triazoline formation.

On the other hand, the synthesis of α-diazo-β-oxocarboxylic esters *(45)* under the conditions given for the malonic ester, *i.e.* with acetonitrile/triethylamine, proceeds without side reactions. Some examples are listed in Table 2[18,24].

Table 2. Esters *(45)* of α-Diazo-β-oxocarboxylic acids $CH_3-CO-CN_2-CO_2R$.

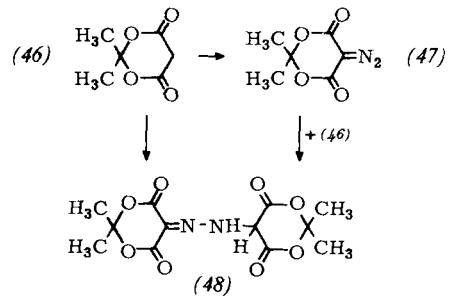
R	Yield (%)	IR Diazo band (Film) (cm^{-1})
Ethyl	84	2217, 2141
i-Propyl	90	2222, 2137
n-Butyl	92	2212, 2132
t-Butyl	92	2212, 2132
Phenyl	92	2132

The transfer of diazo groups onto a cyclic malonic ester, *i.e.* 2,2-dimethyl-1,3-dioxane-4,6-dione ("Meldrum's acid") *(46)* in ethanol/triethylamine leads, not only to the expected diazo derivative *(47)* (53 %), but also to its azo-coupling product with *(46)*, this product

[22] Concerning the base-catalysed ring cleavage of triazolines, see *R. Huisgen, G. Szeimies,* and *L. Möbius,* Chem. Ber. *99*, 475 (1966).

[23] *M. Regitz,* Angew. Chem. *78*, 684 (1966); Angew. Chem. internat. Edit. *5*, 681 (1966).

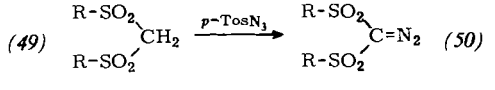
[24] *J. Hocker,* Diploma Thesis, Universität Saarbrücken, 1966.



being in the tautomeric hydrazone form *(48)* (20%) [19]. This secondary reaction, which greatly reduces the yield of *(47)* is mainly due to the nucleophilic nature of the carbanion of *(46)*.

4. Diazomethylene Disulfones

The methylene disulfones *(49)* are sufficiently acidic for conversion into diazo derivatives *(50)* with *p*-toluenesulfonyl azide, even in aqueous-ethanolic potassium hydroxide solution; however, the less acidic diamide *(49f)* must be converted into its lithium compound by treatment with methyl-lithium in ether before it will react in the usual manner to give diazomethionic bis(ethylanilide) *(50f)* [10]. A number of data are given in Table 3.



(a): R = C_6H_5 *(d)*: R = $C_6H_3F_2$-(2,4)
(b): R = C_6H_4-CH_3(*p*) *(e)*: R = C_2H_5
(c): R = $C_6H_3(CH_3)_2$-(2,4) *(f)*: R = $N(C_2H_5)C_6H_5$

Table 3. Diazomethylene sulfones synthesized.

	M.p. (°C)	Color	Yield (%)	IR Diazo band (KBr) (cm^{-1})
(50a)	99	pale yellow	70	2130
(50b)	121–122	yellowish green	75	2117
(50c)	135–136	yellowish green	85	2109
(50d)	164	almost colorless	84	2145
(50e)	88–90	almost colorless	46	2135
(50f)	97	yellowish green	50	2118

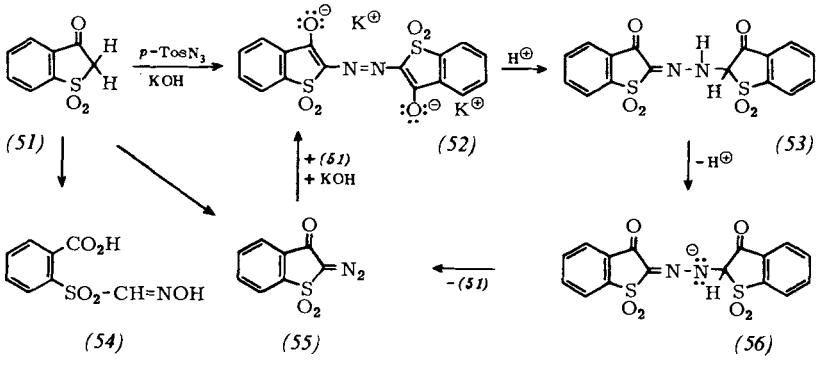
Attempts to synthesize the α-diazo sulfones R-SO_2-CN_2-R', which have only recently become obtainable by another route [25], we e unsuccessful in the case of (2,4-dinitrobenzyl)-*p*-toluene sulfone [26, 27].

5. α-Diazo-β-oxo Sulfonyl Compounds

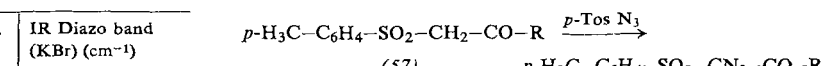
Until recently, the α-diazo-β-oxo sulfones were an unknown class of compounds, and it is only by the use of diazo group transfers that they have become available. Attempts to synthesize the sulfonyl analogue *(55)* of 2-diazoindan-1,3-dione *(30)* by the Forster reaction (eq. b) were unsuccessful, since the β-oxo sulfone gave *(54)* on oxidation (*(51)* → *(54)*). Compound *(51)* was therefore treated with *p*-toluenesulfonyl azide in ethanolic potassium hydroxide solution.

As in the case of "Meldrum's acid" (see Section II.A.3.b), the initially formed diazo compound *(55)* immediately couples with the starting material *(51)* to form the dipotassium salt of 3,3'-dihydroxy-2,2'-azothionaphthene 1,1,1',1'-tetroxide *(52)* [28], which is converted into the hydrazone *(53)* on acidification.

The experiments would probably have stopped at this point, had their continuation not been made possible by a completely unexpected reaction. When attempts were made to recrystallize the hydrazone *(53)* (which is sparingly soluble in the usual solvents) from ethylene glycol or dimethylformamide, "decoupling" [29] took place to give the β-oxo sulfone *(51)* and the desired α-diazo derivative *(55)*. The reaction probably proceeds *via* an anionic intermediate *(56)*, the polar solvent acting as a proton-transfer agent. This assumption is supported by the fact that the reaction does not take place in tetralin, even at 200 °C [28].



On the other hand, open-chain β-oxo sulfones such as *p*-toluenesulfonylacetone *(57a)* or *p*-toluenesulfonylacetophenone *(57b)* react smoothly with *p*-toluenesulfonyl azide in ethanol/water/triethylamine to give the diazo derivatives *(58a)* and *(58b)* [27]. Ethyl *p*-



(a): R = CH_3 (70%)
(b): R = C_6H_5 (60%)

[25] *J. Strating* and *A. M. van Leusen*, Recueil Trav. chim. Pays-Bas *81*, 966 (1962).

[26] *M. Regitz*, unpublished, Saarbrücken 1964.

[27] *A. M. van Leusen, P. M. Smid*, and *J. Strating*, Tetrahedron Letters *1965*, 337.

[28] *M Regitz*, Chem. Ber. *98*, 36 (1965).

[29] *B. Eistert* and *K. Schank*, Chem. Ber. *96*, 2304 (1963).

toluenesulfonylacetate *(59a)* and ethyl (1,1-dimethylethanesulfonyl)acetate undergo diazo transfer only in the presence of sodium ethoxide in ethanol/ether, but the reaction then leads to the displacement of the alkoxy group to give the sodium salts *(60a)* and *(60b)* of *N*-(*p*-toluenesulfonyl)-α-diazo-α-sulfonylcarboxylic amides [27] (for the analogous reaction of the esters of β-oxo acids, see Section II.A.3.b).

$$R{-}SO_2{-}CH_2{-}CO{-}OC_2H_5 \xrightarrow[C_2H_5ONa]{p\text{-Tos } N_3} R{-}SO_2{-}CN_2{-}CO{-}\ddot{N}{-}Tos(p)$$

(59) *(60)*

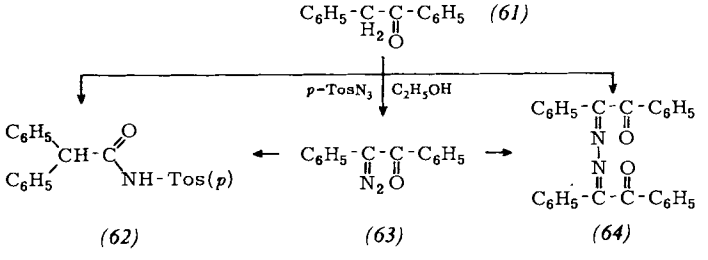
(a): R = $C_6H_4{-}CH_3$ (*p*) (70 %)
(b): R = $C(CH_3)_3$ (60 %)

Na⊕

6. α-Diazocarbonyl Compounds

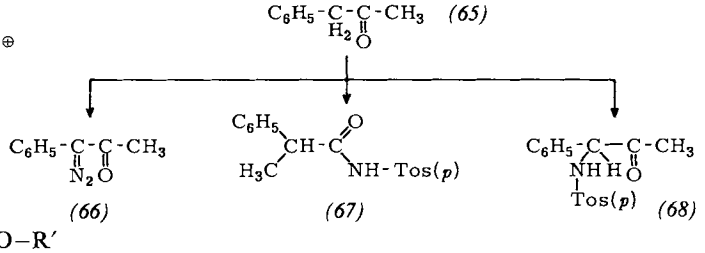
a) From Arylmethyl Ketones

Carbonyl compounds of the type $R{-}CH_2{-}CO{-}R'$ react with sulfonyl azides in the desired manner only when their CH_2 group is additionally activated by an aromatic residue [14]. Desoxybenzoin *(61)* reacts with *p*-toluenesulfonyl azide in ethanol/potassium ethoxide



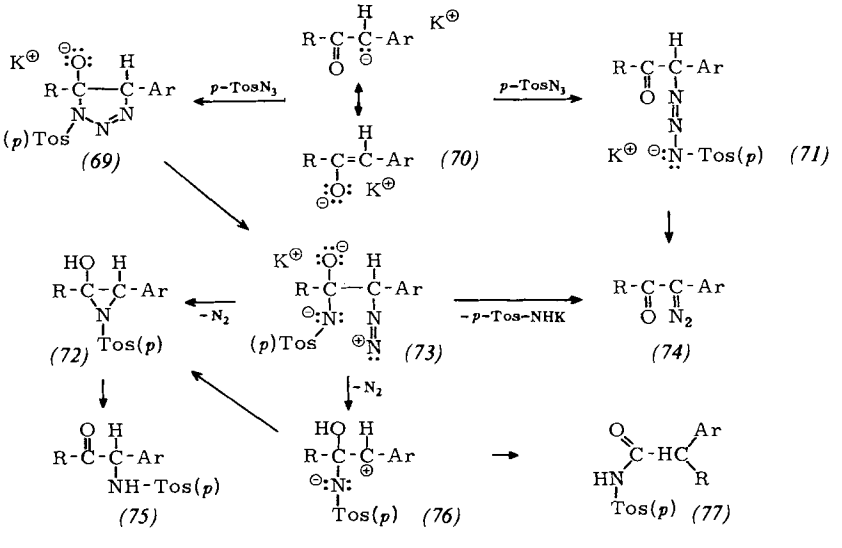
at 5 to 10 °C to give 23 % of benzoylphenyldiazomethane ("azibenzil") *(63)*, together with its decomposition product benzil monoazine *(64)* (24 %) and *N*-(*p*-toluenesulfonyl)diphenylacetamide *(62)* (25 %). Compound *(62)* is formally a Wolff rearrangement product of *(63)* with *p*-toluenesulfonamide; however, it was only partly obtained from *(63)* [30, 31].

Both side reactions can be avoided by the use of a short reaction time at 0 to 5 °C. The initially formed unstable adduct of *p*-toluenesulfonyl azide and the anion of *(61)*, which probably has the structure *(69)* (R = Ar = phenyl), decomposes on addition of a second equivalent of base to give the desired "azibenzil" *(63)* (70 %) and potassium *p*-toluenesulfonamide [22]. Decomposition by acids, on the other hand, leads to elimination of N_2 and formation of *N*-(*p*-toluenesulfonyl)diphenylacetamide *(62)* in 80 % yield. Similar behavior is observed with benzyl α-naphthyl



and β-naphthyl ketones, which give phenyl-α(or β)-naphthoyldiazomethane and *N*-(*p*-toluenesulfonyl)-α-(or β)-naphthylphenylacetamide [30, 31]. The "diazo-synthesis" proceeds normally with phenylacetone *(65)* to give *(66)*, whereas acid hydrolysis of the reaction mixture yields *N*-(*p*-toluenesulfonyl)-α-phenylpropionamide *(67)* and α-(*p*-toluenesulfonyl)amino-α-phenylacetone *(68)*.

One mechanistic interpretation of these results is as follows. Two isomeric structures *(69)* and *(71)* are conceivable for the $TosN_3$ adducts with the mesomeric anion *(70)*. Structure *(71)* can be ruled out simply because it does not explain the formation of the rearrangement product. The 1,2,3-triazoline salt *(69)*, on the other hand, can undergo ring cleavage with formation of α-diazo ketones *(74)* *via* the hypothetical diazonium betaine *(73)* (with elimination of potassium



p-toluenesulfonamide), or alternatively N_2-elimination to form the carbonium ion *(76)* may be followed by anionotropic rearrangement to give the *N*-(*p*-toluenesulfonyl)carboxylic amide *(77)*. The formation of the amino ketone *(68)* could result from a "short circuit

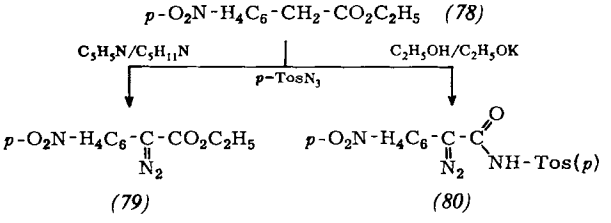
[30] *M. Regitz*, Tetrahedron Letters *1964*, 1403.
[31] *M. Regitz*, Chem. Ber. *98*, 1210 (1965).

mechanism" leading *via (72)* to the isomer *(75)*, R = CH_3, Ar = C_6H_5 [31].

A number of substituted "azibenzils" were synthesized under the above conditions, except that in the case of 4-nitrophenylbenzoyldiazomethane (yield 80 %), triethylamine was used instead of potassium ethoxide [32].

b) From Esters of Arylacetic Acids

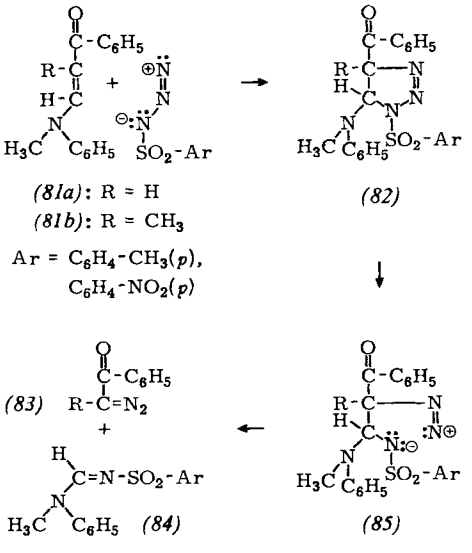
The diazo transfer onto ethyl *p*-nitrophenylacetate *(78)* confirms the observations made on β-oxo esters and malonic esters (see Section II.A.3.b). In ethanol/potassium ethoxide, displacement of the ethoxy residue gives *N*-(*p*-toluenesulfonyl)-diazo-(*p*-nitrophenyl)acetamide *(80)* (yield 61 %), while reaction in pyridine/piperidine leads to the diazo ester *(79)* (yield 72 %); methyl diazo-(2,4-dinitrophenyl)acetate is synthesized in a similar manner (yield 88 %) [31].



The product obtained from *(78)* and methylsulfonyl azide in methanol/potassium hydroxide, which was thought to be *(79)* [13], is in fact *N*-(methylsulfonyl)-diazo-(*p*-nitrophenyl)acetamide (*(80)* with CH_3SO_2 instead of *p*-Tos) [31].

c) From α-En-β-amino Ketones

α-En-β-amino ketones of the type *(81)*, which can be obtained from benzoyl-acetaldehydes and *N*-methylaniline, form α-diazo ketones *(83)* and formamidines *(84)* when heated with sulfonyl azides in chloroform [33]. The formation of these products points to

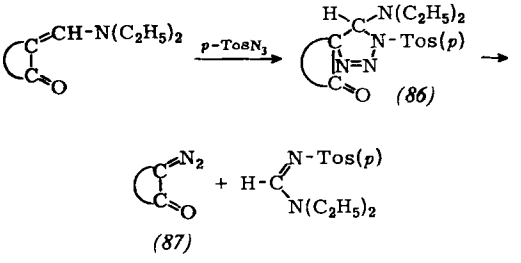


[32] *W. Jugelt*, Z. Chem. *5*, 455 (1965).

[33] *R. Fusco, G. Bianchetti, D. Pocar*, and *R. Ugo*, Chem. Ber. *96*, 802 (1963).

the intermediate occurrence of a 1,2,3-triazoline *(82)* [34], which isomerizes with ring cleavage to give the diazonium betaine *(85)*.

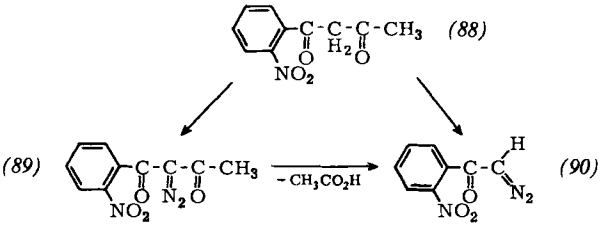
This principle can be used for the synthesis of α-diazocycloalkanones *(87)* (diazocyclohexanone and diazocamphor); the decomposition of the triazoline adduct *(86)* has been formulated somewhat differently [20].



The same principle has also been used for the synthesis of α-diazobutyraldehyde from α-ethyl-β-dimethylaminoacrolein [35].

d) From 1,3-Diketones or β-Oxo Aldehydes

The transfer of diazo groups onto *o*-nitrobenzoylacetone *(88)* can be directed in such a way as to yield acetyl-*o*-nitrobenzoyldiazomethane *(89)* (methylene chloride/piperidine) or with additional deacetylation to give *o*-nitrobenzoyldiazomethane *(90)* (ethanol/water/piperidine) [18].



This principle may be used for the synthesis of α-diazo carbonyl compounds from methylene components whose proton activities are too low for N_2-transfer from sulfonyl azides. However, the reaction proceeds satisfactorily and uniformly only when the reactivities of the two acyl groups are very different (for non-specific cleavage, see Section II.A.3.a). Thus the cleavage of arylcarbonylacetyldiazomethanes (cf. Section II.A.3.a) with aqueous potassium hydroxide leads mainly, but not exclusively, to arylcarbonyldiazomethanes [23, 36]. The deacetylation of α-diazoacetoacetic esters *(45)* (for synthesis see Section II.A.3.b) under solvolytic conditions that leave the ester group intact (see Table 4) leads to very high yields of diazo-

$$CH_3{-}CO{-}CN_2{-}CO_2R \rightarrow N_2{=}CH{-}CO_2R$$
(45) *(91)*

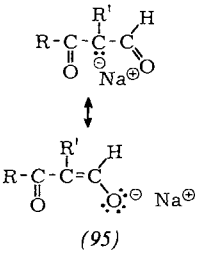
[34] The orientation of the addition to azides is similar to that of the addition to enol ethers. See *R. Huisgen, L. Möbius*, and *G. Szeimies*, Chem. Ber. *98*, 1138 (1965); *R. Huisgen* and *G. Szeimies*, Chem. Ber. *98*, 1153 (1965).

[35] *J. Kucera* and *Z. Arnold*, Tetrahedron Letters *1966*, 1109.

[36] *M. Regitz* and *Liedhegener*, unpublished, Saarbrücken 1966.

Table 4. Diazoacetates N_2CH-CO_2R *(91)* prepared by deacetylation of 2-diazoacetoacetates.

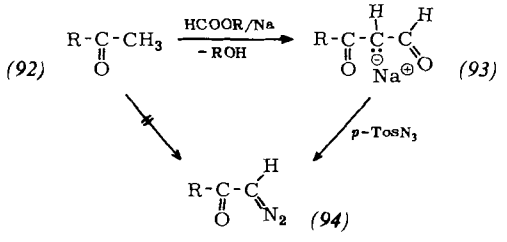
R	Reaction conditions	Yield (%)
Ethyl	Acetonitrile/water/potassium hydroxide; 2 h	61
Propyl	Methanol/sodium methoxide; 1 min	55
i-Propyl	Methanol/sodium methoxide; 1 min	55
t-Butyl	Acetonitrile/water/potassium hydroxide; 4 h	68
	Methanol/sodium methoxide; 30 min	69



(95)

acetic esters *(91)*, and can compete with the usual diazotization of amines [24]. In the case of t-butyl diazoacetate [37] it is actually superior to the conventional syntheses [38, 39].

β-Oxo aldehydes are more suitable for use in the α-diazo ketone synthesis. The formyl group has a stronger proton-activating effect in the diazo transfer reaction [14], and can also be more readily removed by solvolysis than acetyl or arylcarbonyl groups. Thus the sodium salts *(93)* react with *p*-toluenesulfonyl azide in



(92) *(93)* *(94)*

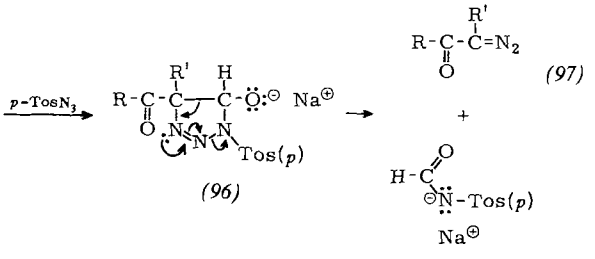
ethanol to give α-diazo carbonyl compounds *(94)*. Methylcarbonyl compounds *(92)* that do not undergo diazo transfer directly (see Section II.A.6.a) can be smoothly converted into their diazo derivatives *(94)*

Table 5. Diazomethyl carbonyl compounds $R-CO-CH=N_2$ *(94)* obtained by diazo transfer with deformylation.

R	*(94)* Yield (%)	M.p. (°C) or b.p. (°C/mm)	IR Diazo band (KBr, Film) (cm^{-1})
Ethoxy	69	45/12	2114
i-Propyl	52	72–73/19	2198, 2105
t-Butyl	83	69/15	2227, 2110
Phenyl	73	48–49	2105
4-Methoxyphenyl	75	90–91	2179, 2105
4-Nitrophenyl	58	114–115	2165, 2110
2-Furyl	53	68/0.1	2114
2-Thienyl	69	64–66	2110
3-Pyridyl	34	71–73	2112
Ferrocenyl	84	68	2110

after introduction of a formyl group by Claisen condensation [40–42]. The scope of this principle can be seen from Table 5.

While the diazo transfer with deformylation has so far been used only for the synthesis of diazomethylcarbonyl compounds *(94)*, the analogous reaction of the sodium salt of α-alkyl-α-acylacetaldehydes *(95)* can be used for the synthesis of compounds of the type *(97)* [41].



(96) *(97)*

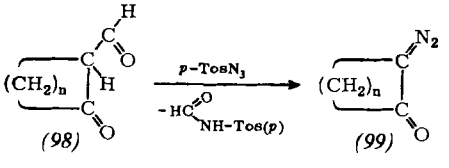
The cycloadduct *(96)* is assumed to occur as an intermediate, since the decomposition of this adduct would explain the formation of the sodium salt of *N*-(*p*-toluenesulfonyl)formamide together with *(97)*. Some examples of this type of reaction are given in Table 6.

Table 6. 2-Diazo ketones $R-CO-CN_2-R'$ *(97)* obtained by diazo transfer with deformylation.

R	R'	*(97)* Yield (%)	B.p. (°C/mm)	IR Diazo band (film) (cm^{-1})
Methyl	Methyl	60	56–59/25	2128, 2075
Ethyl	Methyl	75	[*]	2128
n-Propyl	Ethyl	65	81–82/22	2075
n-Butyl	n-Propyl	68	102/12	2075
			58/0.4	
Ethoxy	Methyl	87	68/41	2083
Phenyl	Methyl	77	[*]	2075, 2169

[*] The liquid diazo compounds were recrystallized from ether at −70 °C.

α-Formylcycloalkanones *(98)*, which have the same structural characteristics as *(95)* (*i.e.* free α-alkyl-α-acylacetaldehydes), evidently react by the same mechanism to give α-diazocycloalkanones *(99)*; triethylamine/methylene chloride has been found suitable as the reaction medium [42,43]. The reaction is closely related to the reaction of enamines discussed in Section II.A.6.c.



(98) *(99)*

(a): n = 3 (98%) *(d)*: n = 6 (87%)
(b): n = 4 (80%) *(e)*: n = 9 (94%)
(c): n = 5 (89%) *(f)*: n = 10 (40%)

[37] *M. Regitz, J. Hocker*, and *A. Liedhegener*, Org. Syntheses, in press.

[38] *H. Reimlinger* and *L. Skatteböl*, Chem. Ber. *93*, 2162 (1960).

[39] *E. Müller* and *H. Huber-Emden*, Liebigs Ann. Chem. *660*, 54 (1962).

[40] *F. Menz*, Diploma Thesis, Universität Saarbrücken, 1966.

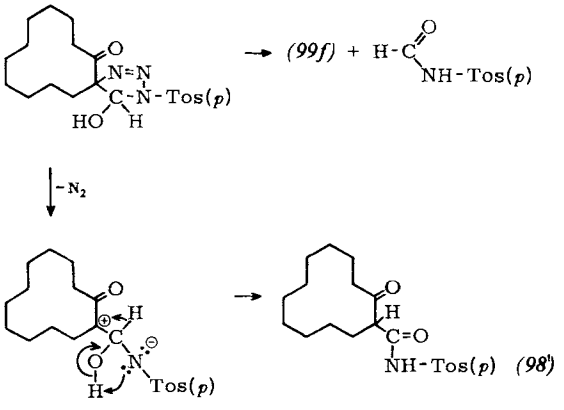
[41] *F. Menz*, Dissertation, Universität Saarbrücken.

[42] *M. Regitz, F. Menz*, and *J. Rüter*, Tetrahedron Letters *1966*, 739.

[43] *J. Rüter*, Diploma Thesis, Universität Saarbrücken, 1966.

Condensation of the α-formylcycloalkanones with diethylamine to form enamines, which precedes the addition of azide to form the triazoline *(86)*, is impossible in this case on grounds of constitution.

Further evidence of the occurrence of a triazoline in the reaction *(98)* → *(99)* is provided by the fact that about 50 % of cyclododecanone-α-carboxylic *p*-toluenesulfonamide (98′) is also formed in the synthesis of 2-diazo-cyclododecan-1-one *(99f)*. One scheme that appears plausible is a competitive

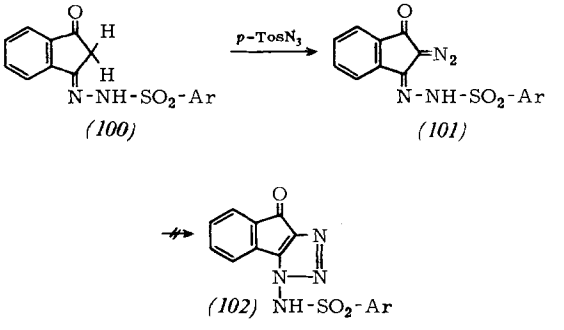


decomposition of the adduct by two routes, one leading to the formation of the diazo ketone *(99f)*, while the other leads to elimination of N_2 to form a carbonium ion, which then forms the β-keto amide by hydride shift. The same reaction branching has been observed, though to a smaller extent, in the synthesis of 2-diazocyclohexanone *(99b)* [43].

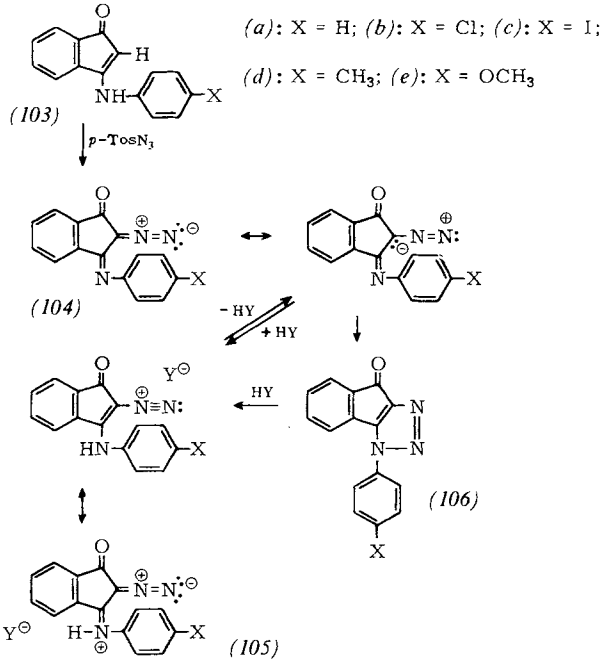
7. α-Diazo Imines and α-Diazo Imonium Salts

α-Diazo imines are generally regarded as nonexistent since *L. Wolff* [44] obtained, not α-diazo-β-imino ketones, but their cyclic isomers, 1,2,3-triazoles, from acyclic α-diazo-β-diketones and ammonia or primary amines.

True α-diazo imines, *i.e.* 3-(arenesulfonylhydrazono)-2-diazoindan-1-ones *(101)*, which show no tendency toward cyclization to give *(102)*, have been obtained by diazo group transfer onto 3-(arenesulfonylhydrazono)indan-1-ones *(100)* [16].



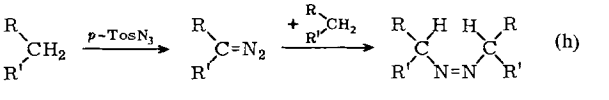
Under the same conditions (ethanol/potassium ethoxide), the 3-aminoindenones *(103a)* and *(103b)* also react to give stable diazo compounds *(104a)* and *(104b)*, whereas *(103c)* to *(103e)* are converted directly into 1-aryl-4-oxoindeno[2,3-*d*]triazoles *(106c)* to *(106e)* [45]. The triazole formation becomes understandable if the ring closure in the diazo imine is considered from the point of view of the 1,3-dipolar cycloaddition of the $C{=}N_2$ dipole across the azomethine bond, since substituents having a -E effect undoubtedly increase the nucleophilic strength of the imino N atom.



The diazo imines *(104a)* and *(104b)* and the triazoles *(106c)* to *(106e)* add on mineral acids such as HCl, HBr, $HClO_4$ (the addition of HX is accompanied by ring cleavage in the case of *(106c)*–*(106e)*) to give salts of the 3-arylimino-2-diazoindan-1-ones *(105a)* to *(105e)*. On deprotonation with aqueous potassium hydroxide, the diazo compounds *(104c)* and *(104e)* can also be isolated, whereas *(104d)* immediately cyclizes to form the triazole *(106d)*.

B. Synthesis of Azo Compounds or Their Tautomers

Though the combination of two molecules having active methylene groups by reaction with *p*-toluenesulfonyl azide is a one-step preparation, it is actually a two-step reaction (both steps requiring a basic medium) involving transfer of a diazo group followed by azo coupling (eq. h).

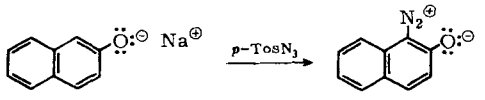


The azo synthesis from the methylene components naturally requires only a half equivalent of sulfonyl azide. For the second step, *i.e.* the actual azo coupling, the diazo component must be strongly electrophilic; this condition is generally satisfied when the N_2 group is flanked by strongly electron-attracting substituents.

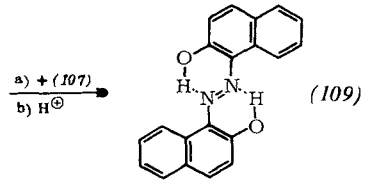
[44] *L. Wolff*, Liebigs Ann. Chem. *325*, 129 (1902); *394*, 23 (1912).

[45] *M. Regitz*, Tetrahedron Letters *1965*, 3287; Angew. Chem. *77*, 735 (1965); Angew. Chem. internat. Edit. *4*, 710 (1965).

Sodium β-naphthoxide *(107)* reacts with a half equivalent of *p*-toluenesulfonyl azide in ether to give 2,2'-dihydroxy-1,1'-azonaphthalene *(109)* together with a small amount of *(108)* [46].

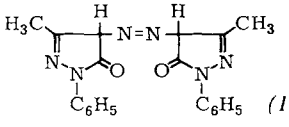


(107) *(108)*



(109)

Even when an excess of *p*-toluenesulfonyl azide is used, the diazo compound *(108)* is formed in a yield of only 9 %, together with *(109)*. A number of other examples are known, such as the synthesis of 3,3'-dimethyl-1,1'-diphenyl-4,4'-azopyrazol-5-one *(110)* using phenyl azide/piperidine [13].

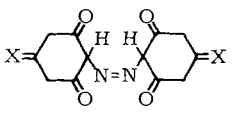


(110)

β-Dicarbonyl compounds fixed in the *trans* configuration, which satisfy the conditions given in Section II.A.3.b for the diazo synthesis, can be readily converted into α,α'-azo compounds [19,47]. Thus the 2,2'-azocyclohexane-1,3-diones *(111a)* to *(111c)* were obtained when the β-diketones were heated with *p*-toluenesulfonyl azide in ethanol/piperidine, *i.e.* under conditions that appear remarkable for azo coupling.

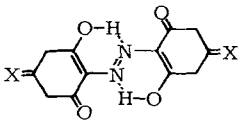
The azo compounds *(111)* and *(113)* exist as dienol chelates *(112)*, at least in methylene chloride and chloroform [19,48]. They exhibit a high absorption in the visible region (for *(111b)*: $\lambda_{max} = 425$ mμ, $\varepsilon = 18650$, CH_2Cl_2), and their NMR spectra in $CDCl_3$ contain no signal corresponding to the proton between the two carbonyl groups. Instead, they show singlets at very low fields for the OH protons chelated in accordance with *(112)* (for *(111b)*: $\delta = 12.44$ ppm) the ratio of the areas of the signals corresponding to that of the other protons present in the molecule.

3,3'-Azo-(2,4-dioxo-1,8,8-trimethylbicyclo[3.2.1]-octane) *(113)* is formed under the same conditions. Azo compounds containing heterocycles, such as 4,4'-dihydroxy-6,6'-dimethyl-3,3'-azo-2-pyrone *(114)* or the hydrazones *(115b)* and *(115c)*, are obtained by the same principle. Compounds *(115b)* and *(115c)* are derived from unenolized β-dicarbonyl compounds [49]; it is therefore understandable that the high-energy unconjugated azo form *(111)* is by-passed. (Further examples may be found in Sections II A.5 and II D.)

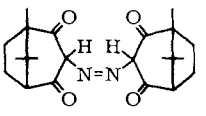


(111)

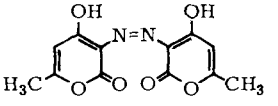
(a): X = H_2 (70 %)
(b): X = $(CH_3)_2$ (70 %)
(c): X = $(CH_2)_5$ (74 %)



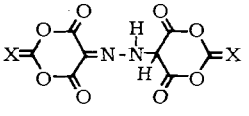
(112)



(113)



(114)

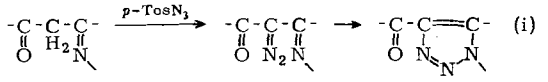


(115b), (115c)

C. Synthesis of Heterocycles

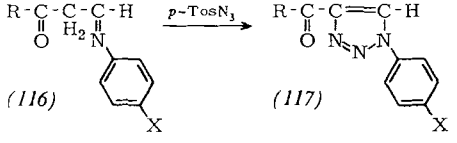
1. 1,2,3-Triazoles

Diazo transfers onto β-imino ketones generally lead directly to 1,2,3-triazoles (eq. (i)).



(i)

Apart from the exceptions in the indan system (Section II.A.7), the anils of *trans*-fixed β-diketones such as cyclohexane-1,3-dione, 5,5-dimethyl-cyclohexane-1,3-dione, and 5,5-pentamethylenecyclohexane-1,3-dione follow scheme (i) [50]. Only some triazoles are contaminated with small quantities of the diazo isomer, as can be seen from the presence of weak diazo bands in the IR spectrum of the crude products. The anils of open-chain β-dicarbonyl compounds can also be cyclized to 1,2,3-triazoles by diazo group transfer in ethanol/potassium ethoxide. Thus benzoyl (or



(116) *(117)*

(a): R = C_6H_5; *(b)*: R = CH_3
X = H, CH_3, Cl, I, OCH_3, NO_2

acetyl) acetaldehyde anils *(116a)* and *(116b)* give high yields (60–90 %) of 1-aryl-4-benzoyl-(or acetyl-)1,2,3-triazoles *(117a)* and *(117b)* [40].

Dehydrogenation of α-pyridinealdehyde hydrazone *(118)* yields, not α-pyridyldiazomethane *(119)*, but

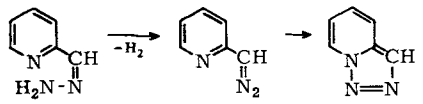
[46] *J. M. Tedder* and *B. Webster*, J. chem. Soc. (London) *1960*, 4417, and further examples given there.

[47] *M. Regitz* and *D. Stadler*, Angew. Chem. *76*, 920 (1964); Angew. Chem. internat. Edit. *3*, 748 (1964).

[48] *D. Stadler*, Dissertation, Universität Saarbrücken, 1966.

[49] *B. Eistert* and *F. Geiss*, Tetrahedron *7*, 1 (1959).

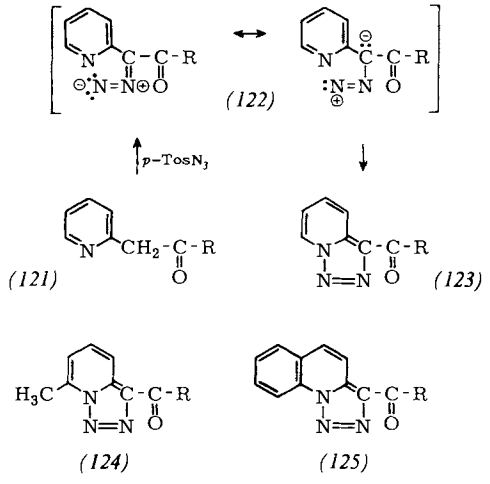
[50] *M. Regitz*, Angew. Chem. *77*, 428 (1965); Angew. Chem. internat. Edit. *4*, 431 (1965).



(118) (119) (120)

the cyclic isomer 1,2,3-triazolo[3,4-*a*]pyridine *(120)* [51,52].

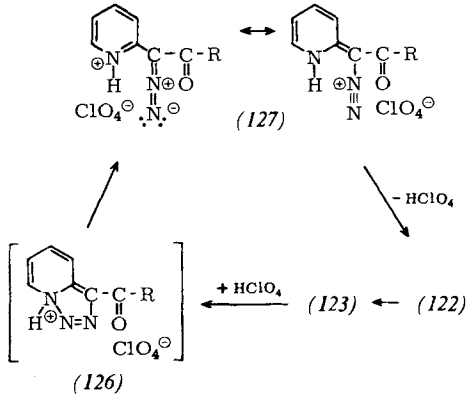
A similar ring closure was observed in diazo group transfers onto alkyl and aryl (2-pyridyl)methyl ketones *(121)* in ethanol/potassium ethoxide [50,53]. The diazo stage *(122)* could not be isolated, but high yields of



(121) (122) (123) (124) (125)

3-acyl-[1,2,3]triazolo[3,4-*a*]pyridines *(123)*, their 7-methyl derivatives *(124)*, and 3-acyl-[1,2,3]triazolo-[3,4-*a*]quinolines *(125)* were obtained. Some examples are given in Table 7.

The ring cleavage of indeno[1,2-*d*][1,2,3]triazoles with mineral acids to give salts of the isomeric diazo imines was mentioned in Section II.A.7. This ring cleavage also takes place on treatment of the 1-acyl-[1,2,3]triazolo[3,4-*a*]pyridines *(123)* with perchloric acid in dioxane, and leads *via* the hypothetical compound *(126)* to the yellow-orange perchlorates *(127)* of the diazo stage *(122)*, which could not be isolated during the diazo transfer onto *(121)* [53]. This is



(126) (127)

[51] *J. H. Boyer, R. Borgers,* and *L. T. Wolford,* J. Amer. chem. Soc. *79*, 678 (1957).

[52] *J. D. Bower* and *G. R. Ramage,* J. chem. Soc. (London) *1957*, 4506.

[53] *M. Regitz* and *A. Liedhegener,* Chem. Ber. *99*, 2918 (1966).

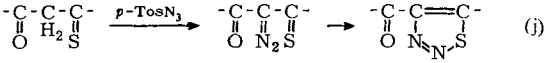
Table 7. 3-Acyl-[1,2,3]triazolo[3,4-*a*]pyridines and -quinolines prepared.

	R	Yield (%)	M.p. (°C)	UV-Absorption (methanol) $\lambda_{max}(m\mu)$ ($\varepsilon \times 10^{-3}$)
(123)	Methyl	50	157–158	247 (3.8) shoulder; 254 (4.4); 287 (11.2); 305 (13.65)
	t-Butyl	90	95–96	248 (3.75) shoulder; 256 (4.35); 288 (10.95); 307 (13.3)
	2-Furyl	94	215	222 (15.0); 282 (9.15); 292 (10.0); 332 (25.1)
	Phenyl	88	111–112	217 (17.7); 256 (8.85); 29? (10.65) shoulder; 319 (19.25)
(124)	Methyl	84	147–148	219 (16.6); 245 (2.2); 252 (2.5); 309 (17.15)
	2-Furyl	77	183	226 (13.1); 281 (10.05); 291 (9.95); 339 (26.0)
	3-Pyridyl	75	160	227 (15.35); 269 (5.4); 278 (5.35); 291 (6.4); 329 (21.6)
(125)	Propyl	88	137–138	229 (15.1); 253 (17.0); 26? (11.25) shoulder; 281 (7.35) shoulder; 291(11.95); 302 (15.25); 323 (16.3); 336(13.85)
	2-Thienyl	85	213	301 (10.0) shoulder; 314(14.85); 337 (32.1); 353 (29.95)
	3-Pyridyl	65	213	239 (23.95); 296 (9.3) shoulder; 309 (14.35) shoulder; 332 (26.15); 344 (22.85)
	Phenyl	85	167–168	249 (22.1); 295 (11.7) shoulder; 307 (15.75); 330 (23.45); 340 (19.9) shoulder

understable in that the salts *(127)* are cyclized by loss of $HClO_4$, even in ethanol, with regeneration of the triazoles *(123)*, and the diazo compounds *(122)* expected initially cannot be isolated.

2. 1,2,3-Thiadiazoles

Diazo group transfer and intramolecular cycloaddition can be used in accordance with equation (j) for the synthesis of 1,2,3-thiadiazoles. As has been known



(j)

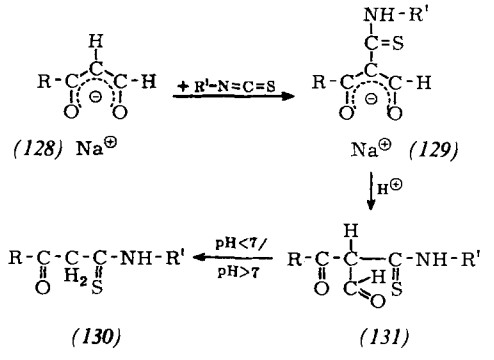
for some time, this ring closure also takes place when 2-diazo-1,3-dioxo compounds are treated with hydrogen sulfide/ammonium hydrogen sulfide [54].

β-Thioxo carbonyl compounds *(130)* have recently been described [55,56]. A variant of this process, *i.e.* the reaction of the sodium salts of β-oxo aldehydes *(128)* (instead of the sodium salts of 1,3-diketones) with isothiocyanates in acetonitrile leads *via* the sodium salt *(129)* to high yields of formylacylthioacetamides *(131)*.

[54] *H. Wieland* and *S. Bloch,* Ber. dtsch. chem. Ges. *39*, 1488 (1906); *H. Staudinger, J. Becker,* and *H. Hirzel,* Ber. dtsch.chem. Ges. *49*, 1978 (1916).

[55] *G. Barnikow, H. Kunzek,* and *D. Richter,* Liebigs Ann. Chem. *695*, 49 (1966).

[56] *G. Barnikow,* Z. Chem. *6*, 109 (1966); J. prakt. Chem. [4] *32*, 259 (1966).



(128) $Na^{\oplus}$ $Na^{\oplus}$ (129)

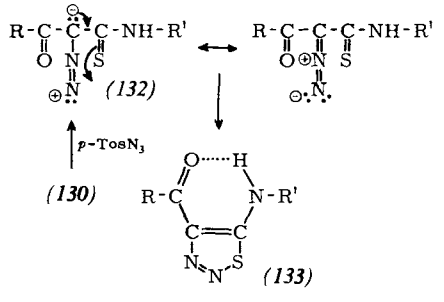
(130) (131)

Table 8. 4-Acyl-5-alkyl(or aryl)amino-1,2,3-thiadiazoles synthesized.

R	R′	Variant A (%)	Variant B (%)	Variant C (%)	M.p. (°C)	UV-Absorption (CH_2Cl_2) λ_{max} (mμ) (ε × 10^{-3})
C_6H_5	C_6H_5	93	77	82	189–190	248 (13.6); 348 (17.4)
2-Thienyl	C_6H_5	90	89	80	128	242 (10.8); 282 (8.5) shoulder; 319 (12.8) shoulder); 361 (20.3)
CH_3	C_6H_5	87	–	43	117–118	327 (17.5)
CH_3	C_6H_4–OCH_3(*p*)	76	–	50	109–111	332 (14.7)
C_6H_5	C_6H_5–CH_2	–	–	61	88–90	249 (9.4); 297 (11.8); 318 (12.9)
OC_2H_5	C_6H_5	68	58	–	90–92	282 (8.8) shoulder; 317 (17.1)
OC_2H_5	C_6H_4–CH_3(*o*)	85	91	–	108–109	282 (9.0) shoulder; 320 (15.3)
OC_2H_5	C_6H_4–OCH_3(*o*)	98	98	–	132–134	282 (7.1); 330 (19.4)
OC_2H_5	C_6H_4–NO_2(*p*)	82	–	–	172–174	272 (5.6); 354 (26.8)

These can be used directly or after deformylation to give *(133)* by diazo-group transfer [57].

Diazo transfer from *p*-toluenesulfonyl azide onto acylthioacetamides *(130)* takes place in ethanol (variant A) or in methylene chloride/triethylamine (variant B) and gives high yields of 4-acyl-5-aryl(or alkyl)amino-1,2,3-thiadiazoles *(133)* [57] (for examples see Table 8). In a few cases the same thiadiazoles were obtained by 1,3-dipolar cycloaddition of diazo carbonyl compounds to isothiocyanates, though only



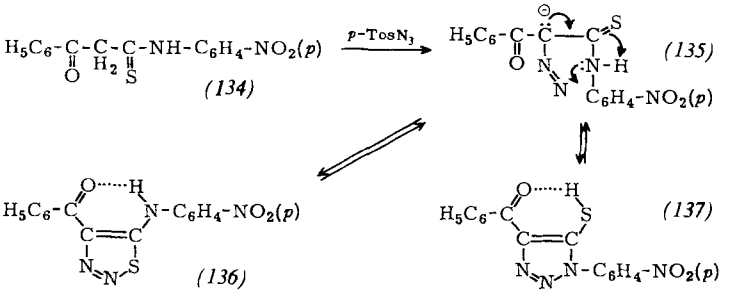
(132) (130) (133)

in moderate yields [58]. The diazo isomer *(132)* could not be isolated, since the cycloaddition *(132)* → *(133)* is evidently faster than the transfer reaction *(130)* → *(132)*.

The formylated acylthioacetamides *(131)* also give thiadiazoles *(133)* on diazo transfer in acetonitrile/diethylamine (variant C!) (see also Section A.6.c and d).

However, the formyl group is split off as diethylformamide (*(131)* → *(130)*) before the transfer reaction takes place [57].

The transfer of diazo groups onto *N*-(4-nitrophenyl)benzoylthiaocetamide *(134)* in ethanol gave 55 % of thiadiazole *(136)* together with 21 % of isomeric 1-(4-nitrophenyl)-4-benzoyl-5-mercapto-1,2,3-triazole *(137)*, which isomerizes at its melting point, probably *via* the diazo isomer *(135)*, to the



(134) (135) (136) (137)

thiadiazole *(136)*. It is concluded from the experiments carried out so far that *(135)* can cyclize by two routes, the very high yield of *(137)* in the present case being due to a particularly high NH activity (NO_2 group in the *p* position). However, it has also been shown that *(136)* isomerizes *via* *(135)* to the triazole *(137)* under the conditions of the diazo transfer (ethanol/triethylamine), though only to a very small extent [57]. Thus the thiadiazole and the isomeric triazole are evidently interconvertible by a Dimroth rearrangement [59] *via* a diazo isomer.

3. 3,5-Diacylpyrazolin-4-ones and 2,4-Bisdiazo-1,3,5-triketones

Diazo-transfer reactions of 1,3,5-tricarbonyl compounds *(138)* in ethanol/potassium ethoxide yield neither monodiazo compounds *(139)* nor 2,4-bisdiazo-1,3,5-triketones *(140)*, but give cyclic isomers of *(139)*; these are the 3,5-diacylpyrazolin-4-ones *(141)* [60], a class of compounds that had previously been unknown.

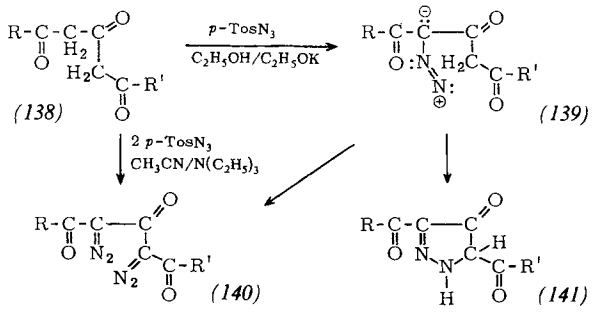
Their formation can be interpreted as follows. The initially formed *(139)* cyclizes by intramolecular azo

[57] *M. Regitz* and *A. Liedhegener*, Liebigs Ann. Chem., in press. The keto-enol equilibrium of benzoylthioacetanilide *(130)*, R=R′=C_6H_5, is also discussed.

[58] *D. Martin* and *W. Mucke*, Liebigs Ann.Chem.*682*, 90 (1965).

[59] *O. Dimroth*, Liebigs Ann. Chem. *364*, 183 (1909); *ibid. 373*, 336 (1910). For other examples of the Dimroth rearrangement of 1,2,3-thiadiazoles, see *J. Goerdeler* and *G. Gnad*, Chem. Ber. *99*, 1618 (1966).

[60] *H. J. Geelhaar*, Diploma Thesis, Universität Saarbrücken, 1966.

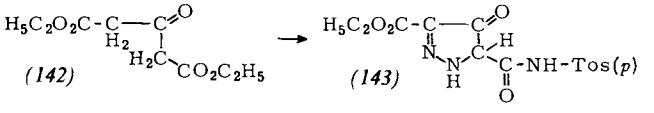


coupling (see also Sections II.A.5 and B) to give the pyrazolin-4-one *(141)* (tautomeric relationships uncertain) before a second diazo group is introduced (*(139)* → *(140)*). (For examples see Table 9.)

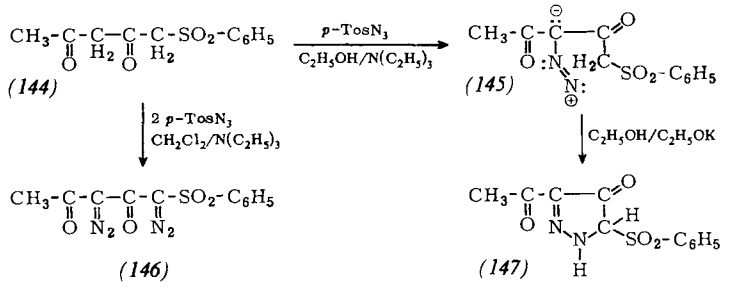
Table 9. 3,5-Diacylpyrazolin-4-ones synthesized.

	R′	Yield (%)	M.p. (°C)
Benzoyl	Benzoyl	88	263
4-Methoxybenzoyl	Benzoyl	79	236
Acetyl	Benzoyl	61	265
2-Pyridylcarbonyl	Benzoyl	77	228
3-Pyridylcarbonyl	Benzoyl	63	271
4-Pyridylcarbonyl	Benzoyl	91	267
4-Chlorobenzoyl	4-Chlorobenzoyl	81	293

Diethyl acetonedicarboxylate *(142)* reacts in accordance with the same scheme, but with simultaneous replacement of an ethoxy group by a *p*-toluenesulfonamide residue to give *(143)* (see also [18]). In the case



of 1-benzenesulfonylacetylacetone *(144)*, the monodiazo compound *(145)* can be isolated and then converted into the pyrazolin-4-one *(147)* by ring closure.



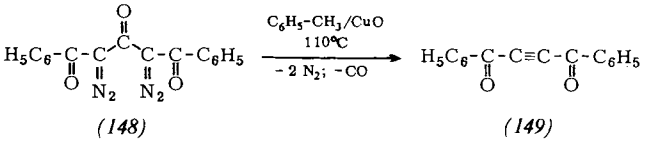
Double transfer to form the bisdiazo compound *(146)* also takes place in this case [60]. Double transfer is also possible with the 1,3,5-triketones *(138)* if their

Table 10. 2,4-Bisdiazo-1,3,5-triketones *(140)* prepared.

R	R′	*(140)* Yield (%)	M.p. (°C)	IR Diazo band (KBr) (cm^{-1})
Phenyl	Phenyl	57–67	107–109 (decomp.)	2146, 2114
4-Chlorophenyl	4-Chlorophenyl	52	137 (decomp.)	2160, 2137
4-Methoxyphenyl	4-Methoxyphenyl	21	111 (decomp.)	2146, 2110
4-Methoxyphenyl	Phenyl	14	107 (decomp.)	2155, 2119
4-Chlorophenyl	Phenyl	28	115 (decomp.)	2151, 2114
Methyl	Phenyl	37	84 (decomp.)	2151

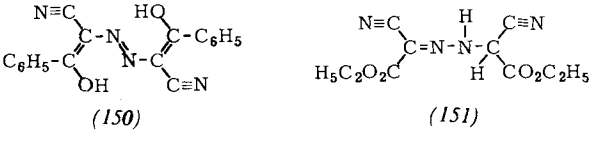
solutions in acetonitrile/triethylamine are added dropwise to *p*-toluenesulfonyl azide. (For examples see Table 10.)

However, the simultaneous pyrazolin-4-one ring closure cannot be entirely prevented. A surprising reaction is the thermal decomposition of 2,4-bisdiazo-1,3,5-trioxo-1,5-diphenylpentane *(148)* in toluene, which yields 65 % of dibenzoylacetylene *(149)* as the principal product [61].



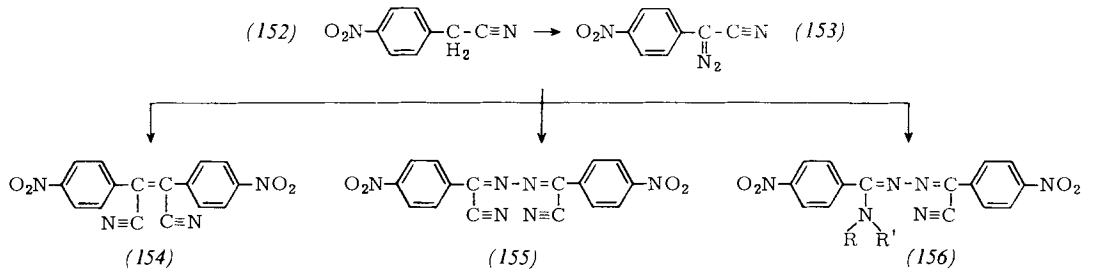
D. Reactions of Methylene Groups Activated by Cyanide

The diazo transfer reactions of α-cyanoacetophenone and ethyl cyanoacetate in ethanol/potassium ethoxide are immediately followed by azo coupling to give the azo enol *(150)* and the hydrazone *(151)* respectively [13,19,48] (see Section II.B).



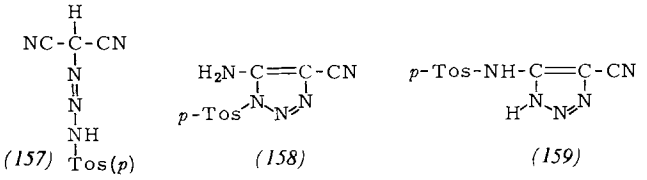
On the other hand, the behavior of 4-nitrobenzyl cyanide *(152)* is very complex. The primary product is evidently always cyano-4-nitrophenyldiazomethane *(153)*, which is very unstable to bases. Thus when triethylamine or bulky secondary amines such as diisopropylamine are used, the main product is the "carbene dimer", *i.e.* α,α′-dicyano-4,4′-dinitrostilbene *(154)*. Potassium ethoxide in ethanol or potassium hydroxide in methanol give partial retention of nitrogen and formation of α,α′-dicyano-4,4′-dinitrobenzaldehyde azine *(155)*. Ammonia, primary amines (methyl-, ethyl-, i-propyl-, or ethanolamine), and sterically unhindered secondary amines (dimethylamine, piperidine, or morpholine) are incorporated directly into the reaction product; a cyanide group is displaced with formation of α-amino-α′-cyano-4,4′-dinitrobenzaldehyde azines *(156)* [48].

[61] *H.J.Geelhaar*, Dissertation, Universität Saarbrücken, 1967.



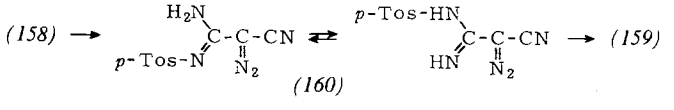
(152) (153) (154) (155) (156)

Malonodinitrile exhibits a reaction that had not been previously observed in reactions with *p*-toluenesulfonyl azide. In aqueous sodium hydroxide [62] or ethanol/potassium ethoxide [48], a very stable 1:1 *p*-toluenesulfonyl azide adduct is formed. Formulae under discussion at present are the triazene structure *(157)* [62] and the triazole formulae *(158)* [48] and *(159)* [63].



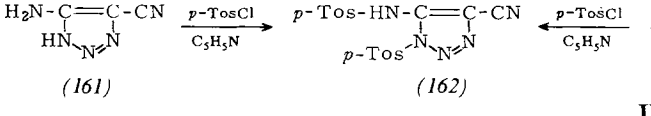
(157) (158) (159)

Formula *(158)* may be ruled out since it is incompatible with the dissociation constants of the adduct (water/acetone (9:1), 20 °C, $pK_1 = 3.2$, $pK_2 = 7.8$ [64]). Moreover, *N*-acylated nitrogen heterocycles are very readily hydrolysed [65,66], whereas the above adduct is stable. However, *(158)* may be an intermediate in the formation of *(159)*, since azide additions to malonodinitrile in accordance with *(158)* have been known for some time [67,68]. Compound *(158)* should then readily be converted into *(159)* by Dimroth rearrangement (see Section II.C.2), particularly since the strongly electron-attracting *p*-toluenesulfonyl group favors ring cleavage to form the diazo



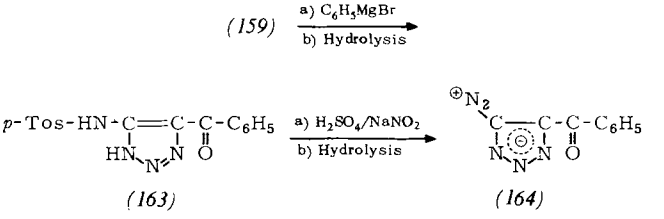
(158) (160) (159)

isomer *(160)*. The subsequent ring closure *(160)* → *(159)* of the electron-deficient terminal diazo nitrogen atom now takes place with the more strongly nucleophilic amidine nitrogen atom, *i.e.* with the nitrogen that is not *p*-toluenesulfonylated.



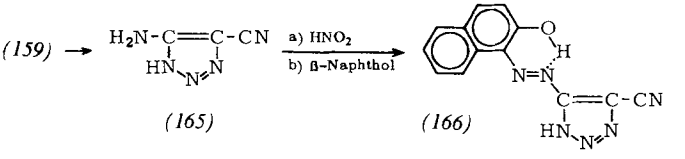
(161) (162)

The dissociation constants of the adduct agree with the formula *(159)* [63]; the cyclic structure is confirmed by the *p*-toluenesulfonylations *(161)* → *(162)* and *(159)* → *(162)*. Compound *(162)* also has the expected high acidity ($pK_a = 3.3$ in acetone/water (1:1) at 40 °C), and loses the ring *p*-toluenesulfonyl group on alkaline hydrolysis [63].



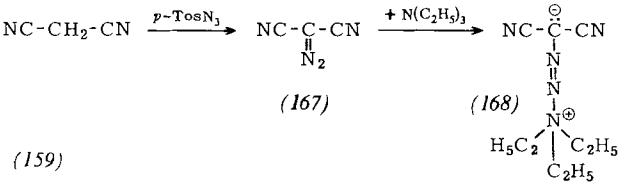
(159) (163) (164)

(159) reacts with phenylmagnesium bromide to give *(163)*, which yields the diazonium betaine *(164)* on removal of the *p*-toluenesulfonyl group and diazotization [48]. Cleavage of *(159)* with naphthalenesodium in tetrahydrofuran yielded the corresponding aminotriazole *(165)*, which was diazotized directly with nitrous acid and coupled with β-naphthol to form the azo compound *(166)* [63].



(159) (165) (166)

When the reaction of malonodinitrile is carried out in the presence of a weaker base such as triethylamine, diazomalonodinitrile *(167)* is clearly formed first but then adds on the base to form the betaine *(168)* [64].



(167) (168) (159)

III. Diazo Group Transfer with Azidinium Salts

The preparative scope is considerably widened by diazo transfers with azidinium salts. These are salts (mainly tetrafluoroborates) of mesomeric cations having the general formula *(169)*, and may be derived *e.g.* from benzothiazole, benzimidazole, pyridine, or quinoline [69]. In view of the relatively short-wave

[62] *J.P.Fleury, D.van Assche*, and *A.Bader*, Tetrahedron Letters *1965*, 1399.

[63] *W.Anschütz*, Diploma Thesis, Universität Saarbrücken, 1966.

[64] *D.van Assche*, Dissertation, Strasbourg University, 1966.

[65] *H. A. Staab*, Chem. Ber. *89*, 1927 (1956); Angew. Chem. *74*, 407 (1962); Angew. Chem. internat. Edit. *1*, 351 (1962).

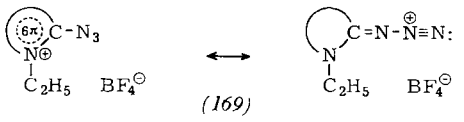
[66] *H. A. Staab* and *K. Wendel*, Liebigs Ann. Chem. *694*, 91 (1966); Chem. Ber. *93*, 2902 (1960).

[67] *J. R. E. Hoover* and *A. R. Day*, J. Amer. chem. Soc. *78*, 5832 (1956).

[68] *A. Dornow* and *J. Helberg*, Chem. Ber. *93*, 2001 (1960).

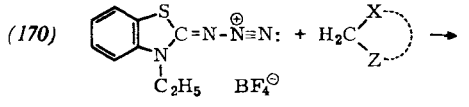
[69] *H. Balli* and *F. Kersting*, Liebigs Ann. Chem. *647*, 1 (1961).

asymmetric stretching bands of the N_2 groups (2175 cm^{-1}), the azidinium salts may be regarded as *N*-diazonium salts (or diazonium amidines) [70]; this

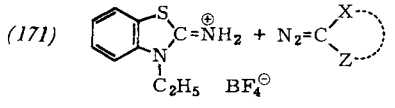


(169)

explains their ability to act as N_2-transfer agents. The overall transfer reaction for 3-ethyl-2-azidobenzothiazolium fluoroborate *(170)* is as follows:



(170)



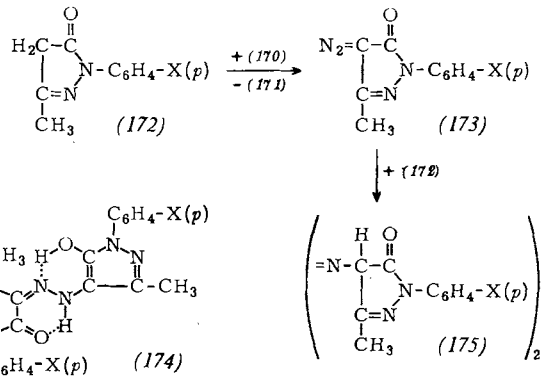
(171)

Thus the azidinium salt *(170)* gives a resonance-stabilized amidinium salt *(171)* [71], which is probably partly responsible for the smoothness of the reaction. The reaction takes place in aqueous-alcoholic solution or suspension at 0 to 80°C and at pH values of 0 to 8. Since the reaction proceeds only in the neutral and acid ranges, in which sulfonyl azides are unreactive, it is particularly suitable for diazo compounds that undergo coupling. Thus it has given good results in the synthesis of 2-diazo-2,3-dihydrothionaphthen-3-one 1,1-dioxide *(55)* (68 %) [72], α-cyano-α-diazoacetophenone (88 %) [71], and 4-diazo-3-methyl-1-phenylpyrazol-5-one (96 %) [71], whereas the transfer from *p*-toluenesulfonyl azide in basic media yields only coupling products (see Sections II.A.5, B, and D). Finally, the method has also proved suitable for the synthesis of α-diazo-α-nitro carbonyl compounds [73]. In addition to diazonitromethyl phenyl ketone (yield 23 %), methyldiazonitroacetate (yield 18 %) was synthesized for the first time. Some preparative examples are shown in Table 11.

Table 11. Results of diazo transfers with 3-ethyl-2-azidobenzothiazolium tetrafluoroborate.

Diazo compound	M.p. (°C)	Yield (%)
5-Diazobarbituric acid	278	84
2-Diazoindan-1,3-dione	149	84
2-Diazo-5,5-dimethylcyclohexane-1,3-dione	108	77
2,4-Bisdiazocyclohexane-1,3-dione	83	31
1,3,5-Trisdiazocyclohexane-2,4,6-trione	220	95
4-Diazo-3-phenyl-isoxazolone	74	77
1-Diazo-2-oxo-1,2-dihydronaphthalene	94	21

The requirement of an acidic to neutral reaction medium appears to form the limit of the preparative scope of the N_2 transfer with azidinium salts. This limit is probably reached when the proton activity of a methylene compound is so low that anion formation no longer occurs.

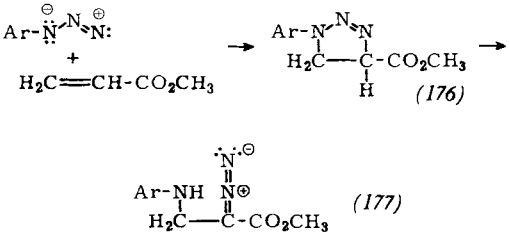


(a): X = H (97%) *(b)*: X = Cl (85%) *(c)*: X = COOH (80%)
(d): X = $CO_2C_2H_5$ (85%) *(e)*: X = NO_2 (77%) *(f)*: X = SO_3Na (58%)

2 - Azido - 3 - ethylbenzothiazolium tetrafluoroborate *(170)* reacts directly with 1-aryl-3-methylpyrazol-5-ones *(172)* (molar ratio 1:2) to give azopyrazolones *(175)* [74] (see also Section II.B), for which the chelated hydrazono-enol form *(174)* is deduced spectroscopically. The reaction proceeds in dimethyl-formamide/water (1:1) and at pH = 8. The diazopyrazolone *(173)* occurs as an intermediate, and then couples with *(172)* to give the dye. (The multi-stage mechanism is confirmed by kinetic measurements.) In the more strongly acidic region (pH = 3 to 4), on the other hand, the transfer reaction stops at the diazo stage *(173)*.

IV. Ring Cleavage of Adducts of Azides to Carbon-Carbon Multiple Bonds

Methyl acrylate adds on azides at room temperature to form the colorless 1,2,3-triazolines *(176)*, which are converted by basic catalysis (triethylamine) into the previously unknown esters *(177)* of β-arylamino-α-diazocarboxylic acids [75]. Esters of fumaric and crotonic acids and some α,β-unsaturated ketones react similarly,



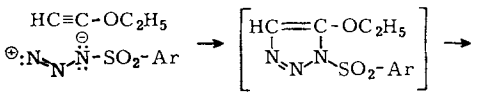
(176)

(177)

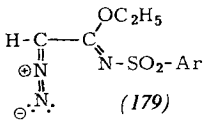
except that the ring cleavage takes place even under the conditions for cycloaddition, *i.e.* without the addition of a base.

A cyclic stage *(178)* could also be involved in the formation of ethyl α-diazo-*N*-arenesulfonylacetimid-

[70] *H. Balli*, Liebigs Ann. Chem. *647*, 11 (1961).
[71] *H. Balli* and *V. Müller*, Angew.Chem. *76*, 573 (1964); Angew. Chem. internat. Edit. *3*, 644 (1964).
[72] *H. Balli*, Marburg, personal communication (June 9, 1964).
[73] *H. Balli* and *R. Löw*, Tetrahedron Letters *1966*, 5821.
[74] *H. Balli* and *R. Gipp*, Liebigs Ann. Chem. *699*, 133 (1966).
[75] *R. Huisgen*, *G. Szeimies*, and *L. Möbius*, Chem. Ber. *99*, 475 (1966).



(178)



(179)

ates *(179)* from ethoxyacetylene and benzenesulfonyl azides[76]. Neither of these reactions involves a CH-acidic starting material, but they are mentioned here because the diazo groups in *(177)* and *(179)* are derived from azides.

The author and his co-workers are grateful to Professor Dr. B. Eistert for his interest in and support of this work. Thanks are also due to the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie for their generous financial support.

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German version: Angew. Chem. 79, 786 (1967)
Translated by Express Translation Service, London

[76] *P. Grünanger, P.V. Finzi,* and *C. Scotti,* Chem. Ber. *98*, 623 (1965).

Higher Coordination Numbers of the Typical Elements[**]

BY R. F. HUDSON[*]

The bonding in electron-deficient molecules, e.g. the boron hydrides and certain metal alkyls, and in molecules which appear to violate the rare gas rule, e.g. hydrogen bonded complexes, interhalogen compounds and compounds of the typical elements with high coordination numbers such as PCl_5 and SF_6 can be described by a simple molecular orbital treatment involving delocalized σ-bonds. The contribution of d-orbitals to the bonding in the interhalogen compounds and rare gas fluorides is very small. The stereochemistry and physical properties of the PX_5 system are explained readily by the delocalization treatment and it is likely that here also the importance of spd hybridization has been overemphasized in the past.

1. The Basis of the Octet Rule

The electronic structure of an atom is determined by two main principles.

a) According to the Pauli principle, no two electrons may have the same set of quantum numbers, and hence only a limited set of orbitals is available.

b) In the ground state, the electrons occupy the lowest levels, and Hund's rule states that electrons (which have the same spin) will occupy separate degenerate levels until such levels are filled.

Spectroscopic examination leads to values of orbital energies, which enables two fairly distinct kinds of atom to be recognised:

i. Typical elements

	core	valency electrons	excited levels
Silicon	$1s^2\ 2s^2\ 2p^6$	$3s^2\ 3p^2$	$3d^0\ 4s^0$
Phosphorus	$1s^2\ 2s^2\ 2p^6$	$3s^2\ 3p^3$	$3d^0\ 4s^0$
Sulfur	$1s^2\ 2s^2\ 2p^6$	$3s^2\ 3p^4$	$3d^0\ 4s^0$

Here the difference in energy between 3s, 3p, and 3d, 4s levels is very high[1] (*ca.* 8–10 eV) so that the characteristic compounds of these elements use 3s and 3p orbitals only[***] in most of their compounds. Thus the typical valency of sulfur is 2, of phosphorus 3, and of silicon 4 (through 3s → 3p promotion). It is the size of the 3s → 3d energy difference, such that the 3d orbitals are close to the continuum, which is responsible for the octet rule.

ii. Transition elements

For example:

	core	valency electrons
Scandium	$1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6$	$3d^1\ 4s^2\ 4p^0$
Manganese	$1s^2\ 2s^2\ 2p^6\ 3s^2\ 3p^6$	$3d^5\ 4s^2\ 4p^0$

Here the 4s and 3d levels have similar energies and the 3d levels are partially occupied, leading to spd hybridisation of the orbitals. The use of 3d orbitals and their importance in determining the stereochemistry and

[*] Dr. R. F. Hudson
University Chemical Laboratory, University of Kent
Canterbury, Kent (England)

[**] Based on a lecture given at the Review Symposium on "Modern Views of Valency and Bonding" at Southampton on April 21st and 22nd, 1966.

[1] *E. Moore,* Atomic Energy Levels, Vol. 1, Circular 467 Nat. Bur. Standards, 1949.

[***] Excited levels contribute to all bonding orbitals, but this is a secondary effect and will be neglected at this point. The influence of these orbitals will be considered in some cases at a later stage.

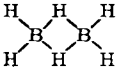
physical properties of transition metal compounds is beyond doubt.

This review deals solely with typical elements (*i.e.* non-transition elements) and particularly the electronic structures of compounds which appear to violate the octet rule. We shall not consider donor-acceptor complexes of the kind $H_2\overset{\oplus}{O} \rightarrow H$, $H_3\overset{\oplus}{N} \rightarrow H$ and $Cl\overset{\oplus}{I} \rightarrow Cl$, since in these cases the electron octet is maintained around the central atom. It is noted that the interhalogen cations *e.g.* $ICl_2^{\oplus}$, but not the corresponding anions $ICl_2^{\ominus}$, conform to the octet rule.

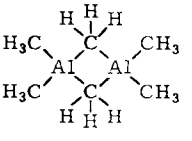
Abnormally high coordination numbers are found for molecules where too few electrons are available for electron-pair bonding (so-called electron-deficient compounds) and also in molecules where more than 4 electron pairs appear to be localized around a central atom. These two types of compound are considered further in the following sections.

1.1. Electron-Deficient Compounds

The structure of the boron hydrides [2] posed a classical problem of the nature of bonding in compounds in which the number of bonding electron pairs is less than the number of bonds. No progress in understanding their structures was made while the boron hydrides were regarded as abnormal relatives of hydrocarbons, and while the 2-electron bond was assumed to be necessary for σ-bonds, although many kinds of resonance structures were proposed [3]. The first structural determination (of B_4H_{10}) by *Kasper et al.* [4] established hydrogen bridges of the kind now known to be present in diborane *(1)*.



(1)



(2)

The same type of bonding by alkyl groups in certain metal alkyls was recognized about the same time [5], *e.g.* the structures of $Al_2(CH_3)_6$ *(2)*, $[(CH_3)_2Be]_n$, show carbon to be 5-coordinated.

Recent work [6] has shown that the carbon atoms in lithium alkyls are 6-coordinated in the solid state (cf. the CH_3Li tetramer in Fig. 1). Here the CH_3 groups in the bridges play the same role as the hydrogen atoms in boron hydrides, *i.e.* forming one electron bonds, *e.g.* as in *(3)*.

[2] *W. N. Lipscomb*, "Boron Hydrides", Benjamin, New York 1963.

[3] *H. C. Longuet-Higgins*, Quart. Rev. *11*, 121 (1957).

[4] *J. S. Kasper*, *C. M. Lucht*, and *D. Harker*, Acta crystallogr. *3*, 436 (1950).

[5] *R. E. Rundle*, J. phys. Chem. *61*, 45 (1957); J. chem. Physics *17*, 671 (1949).

[6] *E. Weiss* and *E. A. C. Lucken*, J. organometallic Chem. *2*, 197 (1964).

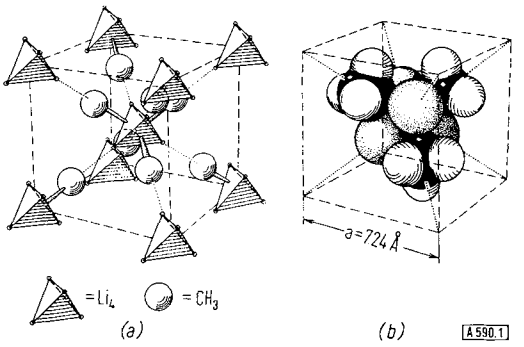
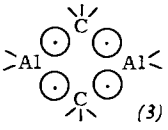
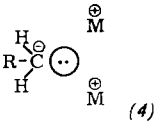


Fig. 1. (a) Unit cell of methyl-lithium. (b) Stuart-Briegleb atomic model of a tetrameric structural unit $(CH_3Li)_4$.

Electrostatic bonding of a carbanion to two cations could explain some of these structures, as for example in electrophilic substitution at a saturated carbon atom [7] *(4)* (shown



(3)



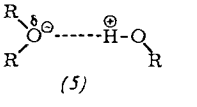
(4)

by the observed retention of configuration). Such an explanation can hardly hold for the boron hydrides in view of the similar electronegativities of boron and hydrogen. It will be shown that a simple MO description leads to a satisfactory treatment of the bonding in electron-deficient compounds, as well as "electron-excess" compounds which will now be considered.

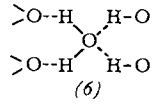
1.2. "Electron-Excess" Compounds

1.2.1. The Hydrogen Bond [8]

The hydrogen atoms in the boron hydrides have the unusual coordination number 2, although the electrons around the hydrogen atom can be accommodated in the 1s level. This is not the case for hydrogen bonded species, as it is quite clear from the Pauli exclusion principle that two localized electron-pair bonds cannot be formed by hydrogen. *Pauling* [9] recognised the electrostatic nature of the bonding, *e.g.* as in



(5)



(6)

structure *(5)*, and *Lennard-Jones* and *Pople* [10] calculated the hydrogen bond energy of water (~ 6 kcal/mole) using a localized point charge model, which took into consideration the lone pairs, as in *(6)*. In ice and in the ordered form of water, oxygen is 4-coordinated. In the solid state, ammonia also assumes a symmetrical structure [11] with nitrogen

[7] *D. J. Cram*: "Fundamentals of Carbanion Chemistry". Academic Press, New York 1965.

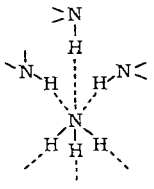
[8] *G. C. Pimental* and *A. L. McClellan*: "The Hydrogen Bond". Freeman, San Francisco 1960; *D. Hadzi*: "Hydrogen Bonding". Pergamon, London 1959.

[9] *L. Pauling*, Proc. nat. Acad. Sci. U.S.A. *14*, 359 (1928).

[10] *J. Lennard-Jones* and *J. A. Pople*, Proc. Roy. Soc. *205 A*, 155 (1951).

[11] *I. Olovsson* and *D. H. Templeton*, Acta crystallogr. *12*, 832 (1959).

6-coordinated, as in *(7)*; in view of the long NH–N bond length of 3.4 Å compared with the N–H covalent bond distance of 1.13 Å, the bonding is predominantly electrostatic.



(7)

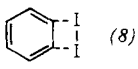
Several difficulties are however encountered, *e.g.* the infrared –OH vibration frequency of water is too high to be explained by electrostatic factors alone; more recent studies estimate at least 7–8 % covalent character[12].

The electrostatic model has been applied[13] to $HF_2^{\ominus}$, but here the molecule is symmetrical and the additional bond energy is 26 kcal/mole (*i.e.* 80 kcal/mole for each bond compared with 135 kcal/mole for HF). Considerable covalent bonding must be present in this molecule, but again we have the question – what kind?

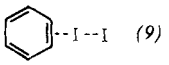
1.2.2. Polyhalogen Compounds[14]

There are three kinds of polyhalogen compounds, a) anionic, *e.g.* $Br_3^{\ominus}$, b) cationic, *e.g.* $ICl_2^{\oplus}$, and c) those made up of neutral molecules. All the complexes have an even number of electrons and with one exception (IF_7)[*] all the bond angles are 90° or 180°. The $X_3^{\ominus}$ molecules are linear (which may be compared with the linear reaction coordinate of a Walden inversion on carbon[15]), whereas $IX_2^{\ominus}$ is triangular. The bond lengths of the triiodide ion[16] in $As^{\oplus}(C_6H_5)_4I_3^{\ominus}$ are equal, whereas in NH_4I_3 and CsI_3 one bond is longer than the others[17], probably due to crystal field effects.

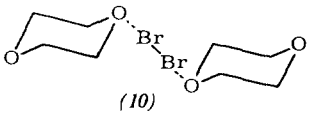
These compounds may be compared with the so-called charge-transfer compounds formed by the halogens, interhalogens, and halogen compounds (*e.g.* CCl_4, CHI_3) with electron donors (n or π). The original structure *(8)* proposed by *Reid* and *Mulliken*[18] was shown to be incorrect[19], as the influence of the ionic form, $D^{\oplus}\,I^{\ominus}$, is over-exaggerated[**], and in all the structures so far examined, the linear form *(9)* is observed.



(8)



(9)



(10)

The amount of charge transfer varies greatly with the type of donor as shown for example by the X–X distances[19] (Table 1).

Table 1. Iodine-iodine distances in charge-transfer complexes.

	r_{I-I} (Å)		r_{I-I} (Å)
I_2	2.67	$(CH_3)_3N{-}I_2$	2.83
1,4-Dithione-I_2	2.79	γ-Picoline-I_2	2.83
1,4-Diselenone-I_2	2.87	$(C_6H_5)_4As^{\oplus}I_3^{\ominus}$	2.90

The Br–Br distance in $C_6H_6{-}Br_2$ is equal to the bond distance of Br_2 within experimental error[19].

It is obvious therefore that the bonding in these compounds varies regularly from weak interactions, which may be described in terms of polarization forces, to strong interactions, described as covalent half-bonds. From this point of view the situation is similar to that encountered in hydrogen bonding. In connection with this gradual change, it is interesting to note that the charge on the terminal halogen atom is small in the case of weakly bonded complexes which may therefore form bridged structures[21] such as *(10)*. In these compounds the Br–Br length is 2.31 Å compared with 2.28 Å in Br_2. Tertiary amines, being better electron donors than ethers, do not form bridged structures and the Br–Br distance is considerably increased (2.43 Å).

In most of these anions the central halogen adopts a coordination number 2, but in some cases, as for most neutral interhalogen compounds, higher coordination numbers are observed (see below). In all these cases, the more electropositive atom is at the center of the structure. This will be discussed later when the nature of the bonding in these compounds is considered from a simple MO point of view.

As pointed out by *Rundle*[22], the rare gas fluorides (see Section 2.1.) are isoelectronic with the corresponding interhalogen anions. Thus XeF_2, like $ICl_2^{\ominus}$, is linear and XeF_4, like $ICl_4^{\ominus}$, is planar. This indicates a similar type of bonding, which will be discussed in a later section.

1.3. Second Row Typical Elements

In the introduction it was mentioned that the electronic structures of silicon, phosphorus, and sulfur (and their homologues) predict their typical valencies of 4, 3, and 2, respectively, if the octet rule is maintained. However, these elements form a considerable number of compounds with high coordination numbers, in particular octahedral compounds *e.g.* SF_6,

[12] *C. A. Coulson*, Research *10*, 159 (1957).

[13] *W. G. Schneider*, J. chem. Phys. *23*, 26 (1955); *W. S. Fyfe*, *ibid. 21*, 2 (1953).

[14] *E. E. Havinga* and *E. H. Wiebenga*, Recueil Trav. chim. Pays-Bas *78*, 724 (1959).

[*] This has usually been represented as a pentagonal bipyramid, but recent investigations have shown that the actual structure is very complex.

[15] *C. K. Ingold*: "Structure and Mechanism in Organic Chemistry". Bell, London 1953, p. 372.

[16] *R. C. L. M. Slater*, Acta crystallogr. *12*, 187 (1959).

[17] *R. C. L. Mooney*, Z. Kristallogr. Kristallgeometrie, Kristallphysik, Kristallchem. *90*, 143; *H. A. Tasman* and *K. H. Boswijk*, Acta Crystallogr. *8*, 59 (1955).

[18] *R. S. Mulliken* and *C. Reid*, J. Amer. chem. Soc. *76*, 3869 (1954).

[19] *O. Hassel* and *C. Rømming*, Quart. Rev. *16*, 1 (1962).

[**] The Mulliken theory gives a good interpretation of CT spectra, but does not give a satisfactory explanation of CT forces. The wave function $\Phi = a\,\psi_{D,A} + b\,\psi_{D^+A^-}$ should be replaced [20] by $\Phi = a\,\psi_{D,A} + \Sigma\, b\psi^{*}_{D,A}$.

[20] *M. J. S. Dewar*, J. Amer. Chem. Soc., in press.

[21] *O. Hassel* and *J. Hvoslef*, Acta chem. scand. *8*, 873 (1954).

[22] *R. E. Rundle*, J. Amer. chem. Soc. *85*, 112 (1963).

SeF_6, TeF_6, $PF_6^{\ominus}$ $SnCl_6^{2\ominus}$, $SiF_6^{\ominus}$, and also $F_5S\text{-}SF_5$, and pentacoordinated molecules of phosphorus, arsenic, and antimony, silicon, germanium, and tin.

The structures of oxyanions *e.g.* $SO_4^{2\ominus}$, $PO_4^{3\ominus}$, $ClO_3^{\ominus}$, $ClO_4^{\ominus}$, and higher oxides, such as SO_3 and IO_4, will not be considered here as these involve a detailed discussion of $p_\pi-d_\pi$ bonding [*] (this has been discussed in detail elsewhere). It should be pointed out, however, that these higher oxides and oxyacids are in general the most stable ones, and any interpretation of their bonding should bear this in mind.

In view of the unusual symmetry features of the MX_5 system, recent structural investigations of these molecules will be briefly reviewed.

1.4. The Pentacoordinated System

The MX_5 system cannot adopt the configuration of a regular polyhedron, but two geometrical forms, the trigonal bipyramid and the square pyramid represent systems of maximum symmetry. Until recently, only a few 5-coordinated molecules (*e.g.* PF_5, PF_3Cl_2, PCl_5, PBr_5SbCl_5) were known, and their structures were found to be bipyramidal [23] with the axial bonds significantly longer than the equatorial ones (Table 2).

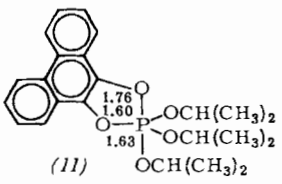
Table 2. Axial and equatorial bond lengths in PX_5 molecules.

	PF_5	PCl_5	Ph_5P	$(Cl_3P{=}NCH_3)_2$	
				P–Cl	P–N
P–X (axial) (Å)	1.55	2.19	1.99	2.152	1.776
P–X (equatorial) (Å)	1.50	2.04	1.85	2.02	1.629

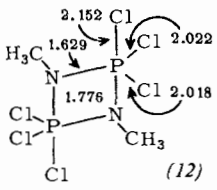
A range of 1:1 adducts of the tetrahalides of Si, Ge, and Sn have been reported in recent years [23] and some certainly exist in the ionized state, *i.e.* $R_3\overset{\oplus}{N}SiCl_3Cl^{\ominus}$, the tendency towards ionization increasing in the order Sn < Ge < Si. The structure of $(CH_3)_3Sn\,Cl{\cdot}C_5H_5N$ has been found to be bipyramidal with the most electronegative ligands, Cl and pyridine in the axial positions.

The compounds $(C_6H_5)_5P$ and $(C_6H_5)_5As$ also have the same structure (trigonal bipyramid) [**], whereas $(C_6H_5)_5Sb$ adopts a square pyramidal form [**] [24]. $SbCl_5$ is however bipyramidal [23] with $r_{ax.} = 2.34$ Å, $r_{eq.} = 2.29$ Å. As anticipated, therefore, the energy differences between the two forms is quite small.

A wide range of cyclic oxyphosphoranes has been prepared by *Ramirez et al.* [25], the ^{31}P–NMR shifts supporting the cyclized form [***]. The X-ray analysis of the phenanthrene derivative *(11)* shows this to be also pyramidal with one of the axial bonds longer than the other P–O bonds [27].



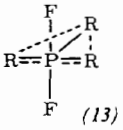
(11)



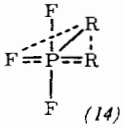
(12)

Recently the structure of the phosphinimine in the dimeric form *(12)* has been determined [28]. Here also the axial P–Cl and P–N bonds are longer than the corresponding equatorial bonds.

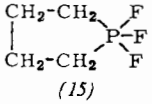
An extensive study has been made of a wide range of fluoro-phosphoranes [29], R_nPF_{5-n}. As in the case of F_3PCl_2 the more electronegative atoms occupy the axial positions. In R_3PF_2 compounds, the R groups and F groups are shown to be equivalent, and interatomic exchange was shown to be absent by F–H coupling of the NMR frequencies. These observations are in agreement with structure *(13)*.



(13)



(14)



(15)

^{19}F–NMR measurements on R_2PF_3 compounds indicate the presence of two kinds of fluorine atom, which is in agreement with structure *(14)*; however, the fluorine atoms are equivalent in *(15)*, except at low temperatures. All the fluorine atoms are equivalent in RPF_4, indicating either a square pyramidal structure or rapid interchange of the fluorine atoms. The latter explanation is supported by the observation that $(C_2H_5)_2NPF_4$ shows nonequivalence at low temperatures, and by the temperature effect on *(15)*. This positional exchange has been termed [30] "pseudorotation" since it involves the internal rotation of valency bonds as follows (Fig. 2).

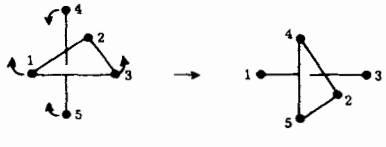


Fig. 2. Schematic representation of pseudorotation in the trigonal bipyramid.

[*] Their structures can be represented by coordinate bounds, thus conforming to the octet rule, *e.g.*



The participation of $d_\pi-p_\pi$ bonding involves the partial delocalization of the electrons on the oxygen atoms into the d orbitals of the central atom.

[23] *I. R. Beattie*, Quart. Rev. *17*, 382 (1963).

[**] These refer to X-ray investigations of the solid forms.

[24] *P. J. Wheatley* and *G. Wittig*, Proc. chem. Soc. (London) *1962*, 251; *P. J. Wheatley*, J. chem. Soc. (London) *1964*, 2206.

[25] *F. Ramirez*: Organo-Phosphorus Compounds. Butterworths, London 1964, p. 337.

[***] The products obtained from $[(CH_3)_2N]_3P$ and diethyl oxomalonate, diphenylpropanetrione, and phenanthrenequinone are reported to adopt an open zwitterionic form [26].

[26] *F. Ramirez, A. V. Patwardhan*, and *C. R. Smith*, J. Amer. chem. Soc. *87*, 4973 (1965).

[27] *I. Hamilton, S. Laplaca*, and *F. Ramirez*, J. Amer. chem. Soc. *87*, 127 (1965).

[28] *H. Hess* and *D. Forst*, Z. anorg. allg. Chem. *342*, 240 (1966).

[29] *R. Schmutzler*, Angew. Chem. *77*, 530 (1965); Angew. Chem. internat. Edit. *4*, 496 (1965).

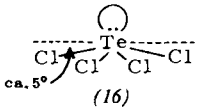
[30] *R. S. Berry*, J. chem. Physics *32*, 933 (1960).

Muetterties and *Schmutzler* [29] have calculated a value of 13 kcal·mole^{-1} for the activation energy of this process for $(C_2H_5)_2NPF_4$. Quite recently [31], the structures of CH_3PF_4 and $(CH_3)_2PF_3$ have been found by X-ray analysis to be distorted trigonal bipyramids with the fluorine atoms in the axial positions and the axial P–F bonds longer than the equatorial ones. For CH_3PF_4, $r_{P-F(ax)} = 1.612$ Å, $r_{P-F(eq.)} = 1.543$ Å. For $(CH_3)_2PF_3$, $r_{P-F(ax)} = 1.643$ Å, $r_{P-F(eq.)} = 1.553$ Å.

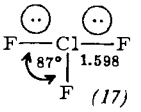
1.5. Analogous Systems with Lone Pairs

The PX_5 structure may be regarded from an electronic point of view [32] as involving the distribution of electron pairs in five bonds in the trigonal bipyramidal structure (as for an sp^3d hybridized system, although an alternative view will be presented in the following section). The same distribution in space readily explains the somewhat irregular structures of MX_4 molecules with a lone pair on M (*e.g.* $TeCl_4$), and MX_3 molecules with two lone pairs on M (*e.g.* ClF_3).

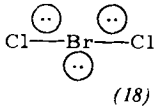
As already mentioned, the most electronegative groups tend to occupy the axial positions, so that the lone pair in MX_4 and the two lone pairs in MX_3 should occupy the equatorial positions as shown in *(16)* and *(17)*.



(16)



(17)



(18)

The relatively large X–M–X angles between the axial bonds may be attributed to repulsion between the electrons in the M–X bonds and the more diffuse lone pair. Finally, the trihalide ions (*e.g. (18)*) are ten-electron systems with the three lone pairs occupying the equatorial positions, the most electronegative atoms the axial ones.

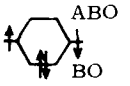
The following question is now posed. How can the bonds in all the structures so far considered be explained in a consistent manner? There are two general ways, (a) to assume the specific participation of high energy orbitals to accommodate electron pairs (*e.g.* 2s in the case of $HF_2^{\ominus}$ and 3d for $Br_3^{\ominus}$) or (b) to retain the octet rule as the main guide, as in the following section.

2. Theoretical Treatment

Let us take the simple view that the octet rule holds for typical elements [33] and that the small contributions of high-energy orbitals do not alter the general argument.

Consider the formation of a homopolar diatomic molecule. The combination of two atomic orbitals, each containing one electron gives two molecular orbitals, as shown by the following secular equation [*].

$$\begin{vmatrix} E-\alpha & \beta \\ \beta & E-\alpha \end{vmatrix} = 0 \qquad \alpha+\beta \quad \alpha-\beta$$



The two electrons in the bonding orbital produce a quantum-mechanical stabilization energy of 2β.

This simple treatment provides a theoretical basis for the stability of two-electron bonds, and of the Lewis-Langmuir extension [34] that a stable atom (other than hydrogen and transition elements) in a molecule, has four electron pairs distributed around the core. It does not however imply that one-electron bonds (or $1^1/_2$-electron bonds for that matter) necessarily lead to unstable structures. On the contrary, π-conjugated systems in which the bonds may be described by fractional orders are among the most stable organic compounds. The principle of electron delocalization leads to the important conclusion that $2n$ electrons are not necessary for the formation of n bonds of a stable molecule, whether the bonding is of the σ- or π-type [36].

This principle can be examined more closely by referring to the linear combination of three orbitals centered on three atoms [**]. In this case the corresponding secular equation leads to three solutions corresponding to bonding, non-bonding, and anti-bonding molecular orbitals as follows.

$$\begin{vmatrix} E-\alpha & \beta & 0 \\ \beta & E-\alpha & \beta \\ 0 & \beta & E-\alpha \end{vmatrix} = 0 \qquad \begin{matrix} \alpha+\sqrt{2}\beta \\ \alpha \\ \alpha-\sqrt{2}\beta \end{matrix} \qquad \begin{matrix} \text{ABO} \\ \text{NBO} \\ \text{BO} \end{matrix}$$

Now, so far, it has not been mentioned that bonding is only possible by the combination of two orbitals characterized by wave functions of the correct symmetry. The possible combinations of s and p orbitals to give resulting 3-center molecular orbitals can be represented as in Fig. 3.

It is a general principle that the configuration leading to maximum (bonding) overlap will be preferred, other things being equal. This can be readily understood in a general way since if two atomic orbitals do not overlap a bond cannot be formed.

---

[*] Of course in a complete treatment of σ-bonds, repulsion and Coulombic terms, changes in electronic kinetic energy, spin-spin interaction, and the overlap integral must be considered. At the present time, semiempirical treatments of the Pariser-Parr-Pople type [35] are being developed, but are beyond the scope of this review.

[31] *L. S. Bartell* and *W. Hansen*, Inorg. Chem. *4*, 1777 (1965).

[32] *R. J. Gillespie*, J. chem. Soc. (London) *1963*, 4672.

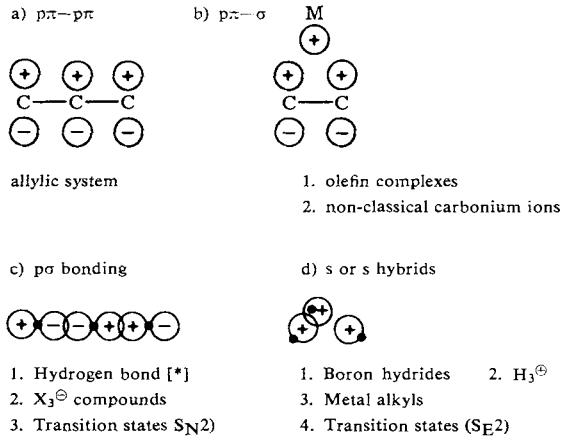
[33] *R. E. Rundle*, Survey Progr. Chem. *1*, 81 (1963).

[34] *G. N. Lewis*, J. Amer. chem. Soc. *38*, 762 (1916); *I. Langmuir*, *ibid. 41*, 868, 1543 (1919).

[35] *R. G. Parr* and *B. M. Gimarc*, Advances physic. Chem. *16*, 451 (1965); *G. Klopman*, J. Amer. chem. Soc. *86*, 4550 (1964).

[36] *R. P. Bell* and *H. C. Longuet-Higgins*, Proc. Roy. Soc. *183A*, 357 (1945); J. chem. Soc. (London) *1943*, 250.

[**] A linear combination of atomic orbitals does not of course imply that the molecule is linear.



[*] Here the central atom is an s orbital.

Fig. 3. Combination of s and p orbitals to give 3-center molecular orbitals (schematic).

One can see therefore why systems (b), (c), and (d) adopt these particular configurations in which overlap is a maximum[*]. In system (a) the configuration is fixed by the σ-bond skeleton.

The orbital energies for these systems show that when two electrons occupy the bonding orbital (as in the 3-center bonds of electron-deficient compounds[36]) the bond energy of the system is $2\sqrt{2}\beta$.

This treatment may be extended to more complex structures *e.g.* the alkyl-lithium tetramer (see Fig. 1). The simplest view[37] is a 4-center bond formed by orbital interaction as shown in Fig. 4. Thus each C–Li bond is formally a $^1/_3$ bond with significantly greater bond distances than estimated for a single C–Li bond.

More general treatments cover the whole structure and introduce Li–Li interactions (of s and p orbitals) in view of the small Li–C–Li angles (68 ° in CH_3Li).

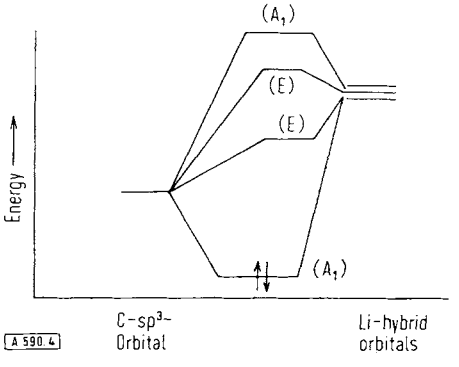
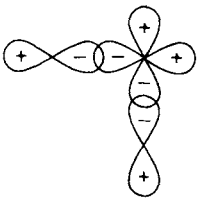


Fig. 4. Simplified energy-level diagram of molecular orbitals in tetrameric methyl-lithium.

A 4-electron system may adopt structure (c) (of Fig.3), or the alternative structure, *(19)*, in which two separate orbitals (p_x and p_y) of the central atom participate in the bonding.

[*] Hydrogen bonded structures adopt configuration (c) in preference to (d) owing to the strong repulsion between the negative charges on the terminal atoms (which are highly electronegative).

[37] *E. A. C. Lucken* and *E. Weiss*, J. organometallic Chem. *2*, 197 (1964).



(19)

In this structure, two single electron bonds are formed with a total energy of 2β. This is equal to the exchange energy of the $X^- + X_2$ system, hence structure *(19)* has no stabilization energy. The linear form, with 0.83 β units of stabilization energy is therefore preferred[*].

It must be noted, however, that these estimated stabilization energies are not absolute values – for the reasons already mentioned. Thus, this procedure predicts that the H_3 molecule and $H_3^{\ominus}$ ion are stable; but this is not the case[38]. The instability may be due to interelectronic repulsions, which will be large for small interatomic distances. On the other hand, hydrogen bonded molecules (*e.g.* $HF_2^{\ominus}$) are stabilized by the high Coulomb energies, and electronegativity differences can be included in the α values in the above treatment, which then enter into the final bond energy expressions.

Havinga and *Wiebenga*[14] have applied this simple treatment to all the known interhalogen compounds, and by using the approximation that $\alpha' = \alpha + n\beta$ where n increases in the order I < Br < Cl < F have

Table 3. Prediction of structures of $I_5^{\ominus}$ and BrICl [14].

Structure of $I_5^{\ominus}$	Zero approx.	1st order approx.
I–I–I I I	1.66 β	1.76 β
I–I–I I	1.66 β	1.67 β
I I		
I–I–I I	1.66 β	1.49 β
I–I–I–I–I	1.46 β	–
I–I–I–I I	1.23 β	–
Experimental values for $(CH_3)_4NI_5$	I–I–I 2.82, 3.17, 175°, 95° 3.17 I 2.82 I	
Structure of BrICl Br–I–Cl 16 α + 5.04 β	I–Br–Cl 16 α + 4.06 β	I–Cl–Br 16 α + 4.87 β

[*] Although the linear form of $X_3^{\ominus}$ is stable, a simple consideration of the orbitals in $X_3^{\ominus}$ shows the triangular form to have an exchange energy of 4β if two p orbitals can be used (as in the interhalogen compounds for example), and this should be more stable than the linear form. X-Ray measurements [39] on $ICl_2 \cdot SbCl_6$ and $ICl_2 \cdot AlCl_4$ support this prediction.

[38] *J. N. Bradley*, Trans. Faraday Soc. *60*, 1553 (1964); *H. C. Bowen* and *J. W. Linnett*, *ibid.* *60*, 1185 (1965); *H. Preuss*, Theoret. chim. Acta *2*, 344, 362 (1964).

[39] *C. G. Vonk*, Dissertation, Groningen, 1957, quoted in [13].

correctly predicted all the structures (with the exception of IF_7). Examples of their calculations for the $I_5^{\oplus}$ ion and BrICl are given in Table 3.

This treatment shows that the charge is located in the non-bonding orbital, *i.e.* on the terminal atoms, so that in unsymmetrical molecules, the more electronegative atoms (with high n values) occupy these positions. This conclusion is fully supported by the available experimental evidence. In particular, ^{35}Cl NQR frequencies[40] (which are sensitive to ionic character) of 19.2 and 22.3 MHz are found for $ICl_2^{\oplus}$ and $ICl_4^{\ominus}$. These are approximately one half of the value for I–Cl, indicating considerable localization of charge on the terminal chlorine atoms. The extent of participation of 5d orbitals in these bonds is thought to be low.

2.1. Rare Gas Fluorides[41]

The preparation of stable compounds of xenon stimulated intense interest in the nature of the bonding in such compounds[*]. Before the structures had in fact been determined, *Rundle*[22] explained the bonding as involving 5p orbitals by analogy with the interhalogen compounds of iodine, and subsequent more detailed calculations, and the measurement of the spectroscopic properties, have fully supported this interpretation[42,43]. As pointed out by *Pitzer*[44] the energy of formation, ΔE, is determined mainly by the ionization potential of the central atom (see Table 4).

Table 4. Ionization potentials (I_X) of the rare gases and halogens; tabulation of fluorides formed.

Atom	I_X (eV)	Fluorides formed
I	10.44	IF, IF_7, IF_5
Br	11.84	BrF, BrF_3, BrF_5
Xe	12.13	XeF_2, XeF_4, XeF_6
Cl	13.01	ClF, ClF_3
Kr	14.00	—

Thus assuming an electrostatic model, ΔE is given by,

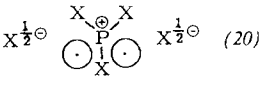
$$\Delta E = I_X - E_F + D_{F_2} - B\,(F{-}X{-}F)$$

where E_F is the electron affinity of fluorine, D_{F_2} its bond energy and B(F–X–F) the bonding term. As the last term will be determined mainly by the radius of X, and the X–F distances for I, Br, Xe, and Cl will be similar, the stability is determined mainly by the value of I_X.

A more complete MO treatment by *Boudreaux*[42] shows that the 5d, 6s, and 6p orbitals produce only small modifications of the orbital energies, and similarly *Coulson*[43] has concluded that the VB and MO methods which give equivalent descriptions of the systems are more correct than the alternative treatments invoking spd hybridization. The MO method is to be preferred for the interpretation of the spectroscopic properties[41].

2.2. Extension to MX_5 and MX_6 Systems

The same explanation given for the polyhalide ions may be applied[33] to the molecules PX_5, SX_6, and their analogues. Thus if we consider three of the P–Cl bonds in PCl_5 to be in the sp^2 state, then the interaction of the remaining p orbital with two chlorine atoms, *(20)*, gives molecular orbitals of the kind discussed for $X_3^{\ominus}$.



(20)

This is an MO description of the resonance structure, $\overset{\oplus}{P}X_4\overset{\ominus}{X}$, proposed originally[*] by *Pauling*[9].

The lower coordination numbers of first row elements[**] may be explained by increased non-bonded repulsions (and also perhaps by increased repulsion between bonding electrons) owing to the considerably smaller radius of first row atoms. Such repulsions are indicated by the large decreases in stability along the series $CF_4 \rightarrow CI_4$ and $BF_4^{\ominus} \rightarrow BI_4^{\ominus}$ *e.g.* CH_3I is quite stable whereas CI_4 readily dissociates. Various estimates of non-bonded repulsions have been made, where usually the ligands are regarded as hard spheres with a given van der Waals radius, *e.g. Rundle*[33] has calculated coordination numbers in this way (see Table 5).

These steric factors may also be important in coordination compounds of transition metals.

Table 5. Computed coordination numbers of MX_n from steric considerations.

M = Carbon				M = Phosphorus			
X	r_v [a]	d_c [b]	n [c]	X	r_v [a]	d_c [b]	n [c]
H	1.2	1.09	3.6	H	1.2	1.42	5.5
C	1.6	1.54	3.9	F	1.35	1.74	6.5
O	1.40	1.43	4.2	Cl	1.80	2.09	5.4
F	1.35	1.41	4.3	Br	1.95	2.24	5.3
Cl	1.80	1.76	4.0	I	2.15	2.43	5.1
Br	1.95	1.91	4.0				
I	2.15	2.10	4.0				

[a] r_v is the van der Waals radius of X.

[b] d_c is the M–X distance (sum of covalent radii).

[c] $n = 4\,d_c^2/2\sqrt{3}\,r_v^2$

[*] Electrostatic treatments [45], which take into account non-bonded repulsions (see below), show that the bipyramidal form is slightly more favored energetically than a square pyramidal form. Kinetic studies with optically active 4-coordinated phosphorus compounds also lead to the same conclusion [46]. Thus it is not necessary to postulate sp^3d hybridization to explain the stereochemistry.

[**] Except for electron-deficient compounds where a maximum of eight electrons around each atom is possible. Symmetry arguments show that d orbitals cannot be used here [47], and the energy requirements would also limit d-orbital participation considerably.

[40] *C. D. Cornwell* and *R. S. Yamasaki*, J. chem. Physics *27*, 1060 (1957).

[41] *J. G. Malm*, *H. Selig*, *J. Jortner*, and *S. A. Rice*, Chem. Reviews *65*, 199 (1965).

[*] For a complete review see [41].

[42] *E. A. Boudreaux*, J. chem. Physics *40*, 246 (1964).

[43] *C. A. Coulson*, J. chem. Soc. (London) *1964*, 1442.

[44] *K. S. Pitzer*, Science (Washington) *139*, 414 (1963).

[45] *J. Zemann*, Z. anorg. allg. Chem. *324*, 241 (1963).

[46] *R. F. Hudson* and *M. Green*, Angew. Chem. *75*, 47 (1963); Angew. Chem. internat. Edit. *2*, 11 (1963).

[47] *M. J. S. Dewar*, J. chem. Soc. (London) *1953*, 2885.

It might be mentioned at this point that such a structure as *(20)* is energetically possible [*] as indicated by the following empirical calculation [49]:

$$PCl_3 + Cl_2 \longrightarrow \overset{\oplus}{PCl_4}\,\overset{\ominus}{Cl} \xrightarrow{E\pm} \overset{\ominus}{Cl}\cdots\cdots\overset{\oplus}{PCl_4}$$

$$E = I - E_{Cl} + D_{Cl_2} - [D_{P-Cl} + E\pm] \approx 2\ \text{eV}\ \text{(experimental value} \approx 3.3\ \text{eV)}$$

where I is the ionisation potential of PCl_3, E_{Cl} is the electron affinity of chlorine, and D_{P-Cl} is taken as the P–Cl dissociation energy of PCl_3.

Although such a calculation is very crude, the same conclusion was drawn by *Pitzer* [50], who was also concerned about the source of the promotion energy if 3d orbitals are used. The recent experimental data [31] on the compounds RPF_4 and R_2PF_3 discussed in Section 1.4. can be explained readily on the basis of this model. Thus the longer and more polar axial P–F bonds, and the tendency for the most electronegative atom to occupy the axial position, follow directly from the model, but these observations cannot be explained in an obvious way by treatments based on extensive sp^3d hybridization of phosphorus [48]. The d-orbital angular functions certainly have the correct symmetry for hybridization with s and p orbitals (*e.g.* the d_{z^2} in the case of structure *(16)* and $d_{z^2-y^2}$ in the case of SF_6). From this point of view therefore, the formation of 5- and 6-coordinated compounds of second row elements involving ten to twelve valency electrons, and the inability of first row elements to form such compounds follows naturally from 3s3p3d hybridization, which would be more effective than 2s2p3d hybridization.

The radial functions however present a bigger problem. If one uses Slater orbitals (which are known to give rather poor descriptions of orbitals), the 3d orbitals are found to be too diffuse for bonding with p_σ or p_π orbitals unless the central atom carries a positive charge [48]. This is equivalent to assuming a partial ionization of the electrons from the spd hybrid orbital onto the electronegative terminal atoms [48]. On the other hand, recent Hartree-Fock calculations [51] using SCF orbitals suggest that the overlap is appreciable even for an uncharged central atom. (The recently reported stability of the $H_2S^{\ominus}$ radical anion [52] seems to lend some support to this view.)

There still remains the problem of the high 3s → 3d promotion energy, and although the 3d level must modify the energy of the NBO to some extent, the contribution may well be too small to determine the physical properties, in particular bond lengths and stereochemistry. The octahedral SF_6 system is simpler to deal with theoretically than the PCl_5 system and has been the subject of recent detailed treatments. In an electrostatic model, *Craig* and *Magnusson* [53] regard the sulfur atom as surrounded by six positive charges (representing electronegative ligands). The diffuse 3d Slater-type orbitals are contracted to become commensurate with the 3s and 3p orbitals, but the 3d promotional energy is greatly increased by the electrostatic field.

A later treatment by *Craig* and *Zauli* [54] replaced the electrostatic field model by a molecular model with six fluorine atoms surrounding the sulfur, and *Cruickshank* [55] has very recently introduced SCF orbitals into this treatment. The detailed calculations suggest that the ligand field (in contrast to the electrostatic field) stabilizes the system through 3d orbital participation to the extent of several electron volts.

It is reasonable, on general grounds, to suppose that $\equiv\overset{2\oplus}{S}\equiv$ uses d-orbitals (and other excited levels) more extensively than $\equiv\overset{\oplus}{P}=$; this is reflected in the different properties of the SO group in sulfones and sulfoxides (which can probably be represented satisfactorily by a coordinate bond). Moreover, the stability of molecules such as [56] $N\equiv SF_3$ seems to require the participation of strong p_π–d_π bonds, and the sp^3d^2 hybridization of sulfur.

In conclusion, however, the importance must be stressed of detailed spectroscopic investigation (particularly NMR, ESR, and NQR studies) in estimating the extent of participation of excited levels in the bonding of the types of molecules described here. Care should be taken in drawing conclusions as to the nature of bonding from bond length, bond energy, and stereochemical considerations. Similarly, the influence of conjugation on the energy of organic π-bonded systems [57] is difficult to determine from these properties, as changes in hybridization influence σ bonds to carbon to a considerable extent.

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[*] The ionization potential of PH_3 ($\sim$ 10 eV) and PCl_3 ($\sim$ 12.3 eV) lie within the range given in Table 4. Thus if the contribution of 5d orbitals in XeF_2 is small, the contribution in the less available 3d orbital in the axial X–P–X bond, by analogy, should also be small.

[48] *D. P. Craig, A. Maccoll, R. S. Nyholm, L. E. Orgel,* and *L. E. Sutton,* J. chem. Soc. (London) *1954*, 332; *H. H. Jaffé,* J. Chem. Phys. *21*, 258 (1953).

[49] *R. F. Hudson*: "Structure and Mechanism in Organo-Phosphorus Chemistry". Academic Press, New York 1965, p. 50.

[50] *K. S. Pitzer,* J. Amer. chem. Soc. *70*, 2140 (1948).

[51] *D. W. J. Cruickshank, B. C. Webster,* and *D. F. Mayers,* J. chem. Physics *40*, 3733 (1964).

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[53] *D. P. Craig* and *E. A. Magnusson,* J. chem. Soc. (London) *1956*, 4895.

[54] *D. P. Craig* and *C. Zauli,* J. chem. Physics *37*, 601, 609 (1962).

[55] *D. W. J. Cruickshank,* paper presented at the Symposium on "Modern Views of Valency and Bonding", Southampton 1966.

[56] *W. H. Kirchoff* and *E. Bright Wilson,* J. Amer. chem. Soc. *84*, 335 (1962).

[57] *M. J. S. Dewar* and *H. N. Schmeising,* Tetrahedron *5*, 166 (1959).

Electrochemical Processes for the Enrichment of Isotopes

BY H. D. FREYER AND K. WAGENER [*]

The principles of electrochemical methods of isotope separation and the results obtained are described. The migration of ions in salt melts and solutions, complex formation in the homogeneous phase, electrolysis, ion-exchange equilibria, and exchange electrolysis are discussed in detail.

1. Introduction

With very few exceptions, any desired isotope separation can in principle be carried out nowadays without appreciable development work. Electromagnetic separators [1a] give almost complete separation of mixtures (even those containing more than two isotopes) in a single step. However, the equipment is very costly and many problems are encountered in its operation. This type of separator cannot be considered for use in industrial-scale separation.

Apart from the various forms of electromagnetic separation, the main processes are based on distillation, diffusion, chemical exchange, thermal diffusion, and ionic migration [1b]; these processes are described as statistical processes. All the methods described below also belong to this group.

A common feature of these "physico-chemical" processes is that a very small separation effect ("elementary effect") must be repeated many times in order to achieve a greater separation (which can then be continued to any desired degree). Elementary separating effects can occur in equilibrium states (*e.g.* equilibrium between two phases, chemical exchange) as well as in irreversible transport processes (*e.g.* diffusion, ionic migration). The magnitude of the elementary effect is characterized in the former case by the ratio of the distribution coefficients of the two components and in the second case by the ratio of their kinetic coefficients. If separation takes place, these ratios differ from 1, and their values are generally expressed in the form $1 + \varepsilon$.

The only processes suitable for most practical separations are countercurrent processes, in which the elementary effect is repeated many times in a continuous manner. In processes such as distillation and thermal diffusion, this can be very readily achieved by "self-cascading" *e.g.* in rectifying columns and in the Clusius-Dickel thermal diffusion separating tube. Self-cascading can also be achieved in other processes, but the establishment of a satisfactory countercurrent flow (particularly in two-phase processes) is sometimes difficult, or at least involves considerable expense.

A characteristic of electrochemical separations is that they are generally adaptable without modification of the apparatus or of the method. They are therefore particularly well suited to conditions in the laboratory.

The elementary effect $(1 + \varepsilon)$ is related to the separation achieved by this process as follows:

$$\text{Separation factor } Q = \frac{([\text{component 1}]/[\text{component 2}])_{\text{end of column}}}{([\text{component 1}]/[\text{component 2}])_{\text{beginning of column}}} = (1 + \varepsilon)^{n_B}$$

where n_B is the number of repetitions of the elementary effect, *i.e.* the number of theoretical plates in the column.

2. Processes Based on Ionic Migration

2.1. General

The isotope effect in ionic migration is described by the ratio of the mobilities of the ions u ($cm^2V^{-1}sec^{-1}$) of the isotopes in question:

$$\frac{u_1}{u_2} = 1 + \varepsilon.$$

Since ε is generally much smaller than 1,

$$\varepsilon = \frac{u_1 - u_2}{u_2} \approx \frac{u\Delta}{\bar{u}},$$

where $\bar{u} = \gamma_1 u_1 + \gamma_2 u_2$ (with $\gamma_1 + \gamma_2 = 1$) is the mean mobility of the isotope mixture.

The migration of isotopic ions has been studied in aqueous solution, in ionic crystals, in salt melts, in liquid metals, and in molten iodine. The observed

[*] Dipl.-Ing. H. D. Freyer and Priv.-Doz. Dr. K. Wagener [**]
Hahn-Meitner-Institut für Kernforschung,
Sektor Kernchemie
Glienickerstr. 100
1 Berlin 39 (Germany)

[**] Present address: Scripps Oceanographic Institute, La Jolla, Calif. (U.S.A.).

[1a] Cf., e.g. *J. Koch*: Electromagnetic Isotope Separators and Applications of Electromagnetically Enriched Isotopes. North Holland Publ. Co., Amsterdam 1958,

[1b] These processes are described in detail in *H. London*: Separation of Isotopes. George Newnes Ltd., London 1961. The earlier publications are cited by *G. M. Begun*: Isotope Separation and Isotope Exchange. Oak Ridge National Lab., Tenn., Rept. ORNL-2852 (1959). Publications on isotope separations based on ionic migration are listed in the form of tables by *M. Gazith* and *A. Roy*: Separation of Isotopes by Electromigration. Israel Atomic Energy Commission, Rept. IA-832 (1963); Electrochem. Technol. *2*, 85 (1964).

isotope effects can be compared by means of *Klemm*'s "mass effect".

$$\mu = \frac{\Delta u/\bar{u}}{\Delta \bar{m}/m}$$

where $\Delta m = m_1 - m_2$ is the difference in mass and $\bar{m} = \gamma_1 m_1 + \gamma_2 m_2$ is the mean mass of the isotopes.

Since this equation relates the relative difference in the mobilities of isotopic ions to the relative difference in mass, the mass effect defined by the equation should have a value of -0.5 according to the simplest kinetic model (ionic mass low in relation to the molecular weight of the medium; isotropic scattering) [*]. μ values very close to this figure have occasionally been observed in ionic migration in crystals; however, the values are generally much lower (some examples are given in Table 1).

Table 1. Isotope and Mass Effects in Ionic Migration.

Isotope pair	Medium	$\Delta u/\bar{u}$	μ
$^{22}Na/^{24}Na$	NaCl single crystal	0.040	−0.46
$^{22}Na/^{24}Na$	$NaNO_3$ — melt (300 °C)	0.00957	−0.11
$^{22}Na/^{24}Na$	10 % aq. $NaNO_3$ soln.	0.00296	−0.034
$^{39}K/^{41}K$	Molten potassium (100 °C)	0.00000067	+0.0000134

The only experiments of any practical importance at present are those carried out in salt melts and in aqueous solution. Though ionic crystals give large isotope effects, the yields are too low because of the generally low ionic conductivity [2,5]. In metals, on the other hand, the isotope effects are extremely small, and the efficiency is very low owing to the large amount of electronic transport [3]. The experiments in molten iodine also failed to show any advantage, since the isotope effect, for rubidium in the case in question, is smaller than in aqueous solution [4].

[*] The expected value $\mu = -0.5$ is obtained when the drift velocity (or ionic mobility) of a particle in an external force field is inversely proportional to the root of the particle mass. The ratio of the ionic mobilities of two isotopic particles 1 and 2 would thus be

$$u_1/u_2 = (m_2/m_1)^{1/2}$$

which, for $\Delta m/\bar{m} \ll 1$ (as is nearly always the case for isotopes), gives

$$\frac{\Delta u/\bar{u}}{\Delta \bar{m}/\bar{m}} \approx -1/2.$$

Deviations from this expected value can be explained by failure of the system to satisfy the conditions of this model (*e.g.* because of solvation of ions in solution or because of coupling effects between ions in salt melts: cf. [7b,22b].

[2] *M. Chemla* and *P. Sue*, C. R. hebd. Séances Acad. Sci. *236*, 2397 (1953); *M. Chemla* in: Proc. Intern. Symp. Isotope Separation, Amsterdam 1957. North Holland Publ. Co., Amsterdam 1958, p. 288.

[3] In cation migration in liquid metals, in contrast to other media, the light isotope accumulates at the anode. This phenomenon was first observed by *E. Haeffner* [Nature (London) *172*, 775 (1953)], and was named after this author; *A. R. E. Lodding* [J. Chim. physique *60*, 254 (1963)] played a particularly prominent part in further investigations.

[4] *K. Clusius*, Private Communication.

Isotope separation by ionic migration in salt melts was studied by *Klemm*, following his observation in 1944 that the passage of a current through solid α-AgI resulted in separation of the silver isotopes [5]. The first successful separation by ionic migration in salt melts was achieved with lithium and potassium in 1947 [6]. Since then the process has been applied to other isotope mixtures, usually as the readily fusible halides or nitrates.

The melt electrolysis is generally carried out in countercurrent flow. A typical experimental set-up, which was used for the separation of the lithium isotopes, is shown in Figure 1 [7a,7b]. The U-shaped electrolysis tube contains molten LiCl. To reduce convection, the tube is packed with a fine-grain zirconium dioxide powder. To keep the overall concentration of the lithium ions constant at each part of the apparatus during the electrolysis, cathodic deposition of lithium is prevented by the continuous introduction of chlorine. The separation of the lithium isotopes within the stationary salt distribution is due to their difference in mobility. The current is transported by the chloride ions migrating in one direction. To permit the removal of the ^{7}Li-enriched LiCl from the anode compartment without interruption of the process, $PbCl_2$ is used before the anode as an auxiliary electrolyte. The boundary between the LiCl and the $PbCl_2$ remains sharp because of the higher mobility of the lithium ions in the melt.

Other isotopic cations can be separated in a similar manner. Results have been reported for Li [7a,7b,9,23], K [10], Rb [11], Mg [12], Ca [12–14], Sr [12], Ba [12], Cu [15], Zn [16], Ag [17], Cd [14], Tl [18], and Pb [14,19].

An example of the separation of isotopic anions is the enrichment of the chlorine isotopes in fused TlCl [8]. In this case the anode consists of a reservoir of molten thallium, which reacts at the contact surface with electrically transported chlorine. The separation of bromine isotopes has also been recorded [20].

[5] *A. Klemm*, Naturwissenschaften *32*, 69 (1944); Z. Naturforsch. *2a*, 9 (1947).

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[7b] *A. Klemm*, Physikertagung Wiesbaden 1955. Physik-Verlag, Mosbach/Baden 1956, p. 73.

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[10] *A. Lunden, C. Reutersward*, and *N. G. Sjoberg*, Z. Naturforsch. *10a*, 279 (1955).

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[12] *A. Neubert* and *A. Klemm*, Z. Naturforsch. *16a*, 685 (1961).

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[16] *A. Klemm, E. Lindholm*, and *A. Lunden*, Z. Naturforsch. *7a*, 560 (1952).

[17] *S. Floberg, A. Klemm*, and *C. Lang*, Z. Naturforsch. *8a*, 562 (1953).

[18] *A. Klemm, H. Hintenberger*, and *W. Seelmann-Eggebert*, Z. Naturforsch. *3a*, 622 (1948).

[19] *A.Lunden* and *G.Blomquist*, Z. Naturforsch.*15a*, 950 (1960).

[20] *A. Lunden* and *A. Lodding*, Z. Naturforsch. *15a*, 320 (1960).

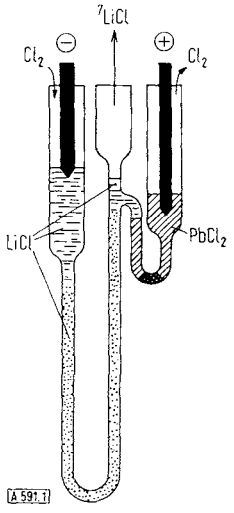


Fig. 1. Apparatus used by Klemm [7b] for the enrichment of ^{7}Li at the boundary between fused LiCl and fused $PbCl_2$.

Melt electrolysis on the industrial scale is associated with certain difficulties[21]. Since salt melts are highly corrosive, the electrolytic cells must be made of corrosion-resistant materials (Supremax glass, Pyrex glass). Special care must be taken to avoid the cathodic deposition of alkali metals. To avoid air bubbles in the tube packing, the salt melts are introduced into the cells under vacuum.

The mass effect in the migration of isotopic ions in salt melts is generally much smaller than $|0.5|$. This is evidently due to coupling effects, so that the mobility of the "jumping" ion is not determined solely by the mass of the isotope. The mass effect μ_+ found for isotopic cations in salt melts can be represented by the empirical formula

$$\mu_+ = \mu' \cdot \frac{2.1\ m_-}{2.1\ m_- + m_+}$$

(m_- = mass of the anion; m_+ = mass of the cation; $\mu' \approx \mu_+$ for $m_- \gg m_+$)

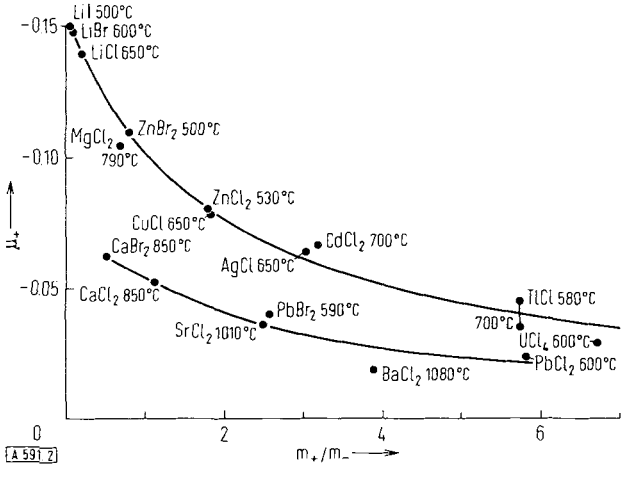


Fig. 2. Mass effect μ_+ of the cations in fused halides at various temperatures [22b].

Upper curve: $\mu_+ = -0.15\ [2.1\ m_-/(2.1\ m_- + m_+)]$;
Lower curve: $\mu_+ = -0.079\ [2.1\ m_-/(2.1\ m_- + m_+)]$.

In this way one obtains variously correlated μ_+ values for the halides, depending on the valence relationship and lattice type of the salt in question[22a,22b]. Such a relationship for pure salts is shown in Figure 2. It is interesting to note that mass effects in binary salt mixtures also depend on the composition of the mixture.

Isotope separation by ionic migration in fused salts is of industrial interest in view of the large isotope effects and the basically simple procedure. Thus a continuous process based on this method has been developed for the isolation of ^{7}Li in a purity of 99.97 %[23].

2.3. Controlled Countercurrent Processes in Aqueous Solution

Ionic migration in aqueous solution was the method used in the earliest attempts to separate isotopes. Following the suggestion by *Lindemann* (1921)[24] that it should be possible to enrich isotopes in this way, *Kendall* and others[25] carried out a number of experiments based on the zone-electrophoresis principle. These experiments were unsuccessful, but probably only because isotope analysis by chemical atomic weight determination was too inaccurate to permit the detection of the effect, since very similar experiments carried out by *Chemla et al.*[2,26] in 1956 did in fact show the expected separation. Though electrophoretic experiments of this nature very quickly show the magnitude of the isotope effect in ionic migration, they cannot be used for the preparation of isotopes in reasonable quantities.

However, a process suitable for the continuous separation of substances had been developed by *Brewer et al.*[27] as early as 1941 (but was kept secret until 1946). This process is countercurrent ionic migration. In this process, which was novel at that time, the isotopic ions migrating in the electric field move countercurrent to the solvent. With a suitable countercurrent flow, the position of the center of gravity remains constant, the faster (lighter) isotopes migrating upstream while the slower (heavier) isotopes are gradually washed back. *Brewer*'s countercurrent principle has two decisive advantages: (i) a much larger quantity of salt can be electrolysed than in electrophoresis and (ii) the mixture of ions can be allowed to

[21] The technological problems are summarized in the dissertation by *A. Lunden*, Doktorsavhandl. Chalmers Tekn. Högskola, No. 12 (1956).

[22a] *A. Klemm*, Z. Naturforsch. *6a*, 487 (1951).

[22b] Cf. Summary: *A. Klemm*, J. Chim. physique *60*, 237 (1963).

[23] *A. Klemm* in: Proc. Intern. Symp. Isotope Separation, Amsterdam 1957. North-Holland Publ. Co., Amsterdam 1958, p. 275.

[24] *F. A. Lindemann*, Proc.Roy.Soc. (London) *99* A, 102 (1921).

[25] *J. Kendall* and *E. D. Crittenden*, Proc. nat. Acad. Sci. USA *9*, 75 (1923), *J. Kendall*, Physic. Rev.*21*, 389 (1923); *J. E. G. Pilley*, Philos.Mag. (6) *49*, 889 (1925); *E.R.Jette*, *ibid.* (7) *3*, 258 (1927).

[26] *H. J. Arnikar* and *M. Chemla* in: Radioisotopes in Scientific Research, Proc. Intern. Conf. UNESCO, Paris, 1957. Pergamon Press, London-New York 1958, Vol. II, p. 421; *M. Chemla*, J. Chromatography *1*, 2 (1958).

[27] *A. K. Brewer*, *S. L. Madorsky*, and *J.W. Westhaver*, Science (Washington) *104*, 156 (1946); *A. K. Brewer*, *S. L. Madorsky*, J. *K.Taylor*, *V. H. Dibeler*, *P. Bradt*, *O. L. Parham*, *R.J. Britten*, and *F. G. Reid*, J. Res. nat. Bur. Standards *38*, 137 (1947); *S. L. Madorsky* and *S. Straus*, *ibid. 38*, 185 (1947); *41*, 41 (1948); *S. L. Madorsky* and *A. K. Brewer*, US.-Pat. 2645610 (1953).

migrate for very large distances (*e.g.* several hundred meters) in relation to the solvent, so that pronounced separations are possible. Owing to the countercurrent operation, the whole process takes place over only a short distance. *Brewer*'s work led to the first separation of an isotope mixture by ionic migration, the isotopes in question being those of potassium, chlorine, and copper.

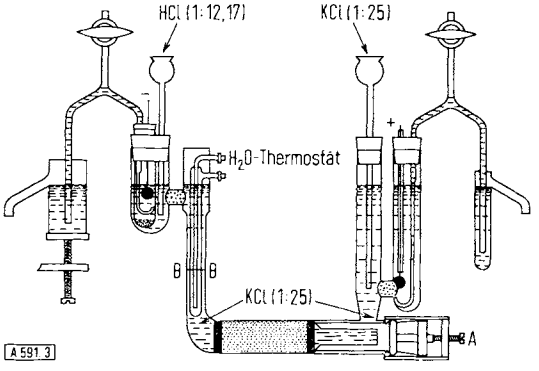


Fig. 3. Cell for the enrichment of potassium isotopes, after *Brewer* and *Madorsky* [27]. The anode compartment is continuously flushed with natural KCl solution. The feed of HCl solution into the cathode compartment is controlled in such a way that the boundary B—B remains constant.

Figure 3 shows a typical cell as used for the enrichment of potassium isotopes. It is made of glass, and the central part is packed with sand between a fixed and a movable diaphragm, which can be compressed by the device A to minimize channel formation. The electrodes are made of platinum gauze. The lower and right-hand part of the cell is filled with KCl solution, and the cathode compartment is filled to the boundary B—B with HCl solution. The boundary between the HCl and KCl solutions remains stable while the current is flowing, provided that the condition

$$\frac{[HCl]}{[KCl]} = \frac{t_{H^+}}{t_{K^+}}$$

is satisfied (t = transport number). If the solution were stationary, the passage of 1 F would move the boundary in such a way that it passes over a volume of

$$\frac{t_{K^+}}{[KCl]}$$

in the tube. To keep the boundary stationary, the same volume of solution must be introduced into the cathode compartment for every 1 F. The solution must also contain one equivalent of HCl. The condition that no overall transport of potassium should take place

$$E \cdot \bar{u}_+ + v_L = 0$$

with $\bar{u}_+ = \gamma_{39_K} u_{39_K} + (1-\gamma_{39_K}) u_{41_K}$,

[E(V cm^{-1}) = electric field strength, $\bar{u}_+$ (cm^2·V^{-1}·sec^{-1}) = mean mobility of the potassium ions, v_L (cm·sec^{-1}) = flow rate of the liquid in the separating column].

would then be satisfied, and the flow rate (averaged over the cross section) would lie between the migration velocities of the two isotopes:

$$v_{39_K} > |v_L| > v_{41_K}.$$

An attempt was made to control the process in this sense with the aid of remote sensing elements and an automatic control system.

However, the columns used by *Brewer* proved unreliable in continuous use owing to channel formation in the sand packing and to the ultimate formation of gas bubbles which, because they could not escape, caused a decrease in cross section and thus led to local overheating. Trouble regularly started after an operating time of a few hundred hours. The plate heights, which were, in favorable cases, of the same order of magnitude as the particle diameter, were smallest at the end of the sand packing nearer the cathode, *i.e.* the end at which the solution entered. However the height of the theoretical plate increased rapidly with increasing penetration depth in the packing, until any further increase in the length of the column (beyond about five times the diameter of the tube) had no effect.

An important advance was made by *Clusius*, *Ramirez*, and *Huber* [28], who did not use a column packing and deliberately did not suppress convection, but used a large number of diaphragms to confine convection to directions perpendicular to the field direction. This leads to faster equalization of concentration within the electrolyte and good heat dissipation. At the same time channel formation and trouble due to gas bubbles (which can escape through openings on the top of the horizontal separating tube) are avoided. This arrangement was used for the separation of the rare earths and of the isotopes of lithium and rubidium. The liquid countercurrent flow was controlled by oxygen-hydrogen electrolytic cells; the gas evolved displaced a corresponding quantity of liquid from a storage vessel, and the liquid was then led in countercurrent to the separating column. The current strength in the oxygen-hydrogen cells was controlled by a conductivity measuring cell in series, this cell being situated in the separating column.

Martin et al. [29], who developed a countercurrent process independently of the American workers, carried out the electrolysis in packed columns between the anode and cathode compartments, which were in the form of containers at the ends of the column. They enriched deuterium and ^{26}Mg, and also achieved a separation of rare earths. However, the control of this process is more elaborate than that used by *Brewer* and *Clusius*.

Konstantinov et al. [30] have recently reported experiments similar to those carried out by *Brewer*. Solutions of lithium, potassium, and rubidium salts were electrolysed and the isotope effect in ionic migration was determined.

These four groups of workers all used ionic migration countercurrent to the solvent, the "equilibrium"

[28] *K. Clusius* and *E. R. Ramirez*, Helv. chim. Acta *36*, 1160 (1953); *E. R. Ramirez*, J. Amer. chem. Soc. *76*, 6237 (1954); J. physic. Chem. *62*, 760 (1958); *K. Clusius* and *M. Huber*, Swiss Pat. 362681 (1958) and 374367 (1959).

[29] *H. Martin*, Z. Naturforsch. *4a*, 28 (1949); *H. Martin* and *E. Ruhtz*, Z. Elektrochem., Ber. Bunsenges. physik. Chem. *54*, 560 (1950); *H. Martin* and *E. Harmsen*, *ibid. 62*, 152 (1958); *H. Martin* and *H. J. Lübke*, Z. Naturforsch. *19a*, 115 (1964).

[30] *B. P. Konstantinov* and *V. B. Fiks*, Ž. fiz. Chim. *38*, 1647 (1964); *38*, 1904 (1964); *38*, 2255 (1964); *V. B. Fiks*, *ibid. 38*, 2257 (1964); *V. B. Fiks* and *E. V. Stepin*, *ibid. 38*, 2260 (1964); *B. P. Konstantinov* and *E. A. Bakulin*, *ibid. 39*, 3 (1965).

between the electrical transport of the ions and their convective backward motion being controlled by remote sensing elements and control units. The countercurrent equilibrium necessary for the separation of the components requires that the flow rate of the liquid should lie between the migration velocities of the faster and of the slower ionic species. However, if the difference in mobility is very small, as is naturally the case in mixtures of isotopes, the sensitivity required for this control is so great that any attempt to regulate the electrolysis is extremely expensive. On the other hand, any disturbance of the countercurrent equilibrium endangers the efficiency of the separation. According to *Wagener* [31a, 31b], this difficulty can be avoided by the method described in Section 2.4.

2.4. Self-stabilizing Countercurrent Electrolysis in Solution

Self-stabilizing countercurrent electrolysis can be most readily understood if the process is thought of as being divided into two steps. The first step comprises the mechanism that leads to a stationary distribution of the mixture as a whole in the separating column (all the ions in the mixture being assumed for the time being to migrate at the same velocity). The second step comprises the actual separation of the components within the stationary overall distribution. The essential novel idea of this method is contained in the first step. This idea is that the required "equilibrium" between the electric transport of ions and entrainment by the solvent is no longer achieved by control of the liquid flow, but follows automatically under the given (but more or less arbitrary) operating conditions.

The principle is based on the fact that at a given current intensity the local field strength in the column, which determines the equilibrium ($E.u + v_L = 0$), depends on the local salt concentration. At the start of electrolysis this involves displacement of the salt concentration in the column, whereas it is necessary in the controlled countercurrent process to prevent any concentration displacements.

A scheme of a plant for use in this process is shown in Figure 4. The main part of the apparatus, *i.e.* the separating column 6, is shown here as a trough divided into compartments by diaphragms. The shape and dimensions of the trough may be adapted to suit widely varying requirements, and various forms, ranging from capillary tubes [32] to troughs having a capacity of about 10 l (which may also be connected to an end container) have proved suitable [31a, 31b]. The operating conditions that have to be chosen in advance are the flow rate of the electrolyte solution, the electric field strength (or the electric current), and the temperature of the solution. Items 1 to 5 (storage vessel, constant-level intermediate tank, filter, and thermostatted capillary) ensure that the electrolyte solution is supplied at a constant feed rate. This solution passes through the separating column in the longitudinal direction and then runs through an overflow 7 into a collector vessel 8, from which it can be returned to the storage vessel.

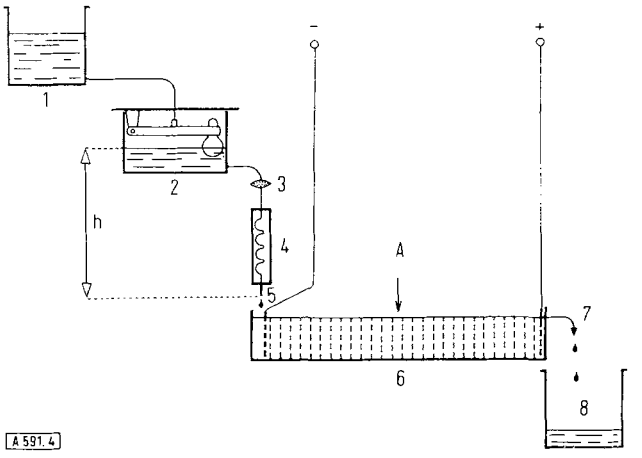


Fig. 4. Construction of an electrolytic separation plant for the self-stabilizing countercurrent process (schematic).

Explanations are given in the text.

The stationary salt distribution extends over the greater part of the separating column, but ends shortly before the overflow end. The separated components are withdrawn in solution at the ends of the salt distribution; fresh solution is added in the middle of the salt distribution. Both operations can be carried out discontinuously (*e.g.* every 24 hours).

The electrodes produce an electric field whose direction and strength are so chosen that all the ions of the mixture in question (which are introduced into the column as a salt solution at an arbitrarily chosen point A) migrate countercurrent to the liquid toward the "upstream" end of the column, where they accumulate. (An eventual deposition of the ions on the electrode can be avoided by the use of a protective electrolyte [31b].) During this migration of the mixture of ions, the condition

$$| E \cdot \bar{u} | > | v_L |$$

is satisfied. If the introduction of the salt solution into the trough is continued, ions continue to accumulate at the "upstream" electrode, and the conductivity of the solution increases in this part of the column [*]. The driving force for the migration of further ions into the neighborhood of those already present is the electric field. According to Ohm's law, the strength of this field, at a given current density j depends only on the conductivity $\varkappa$ of the solution. If we assume for simplicity that the conductivity of the electrolyte (acid, base, or a buffer mixture) dissolved in the countercurrent liquid is negligible in the salt sphere, an approximately reciprocal relationship exists between the field strength related to the salt concentration c_s (Λ_s = equivalent conductivity of the salt):

$$E = \frac{j}{\varkappa} \approx \frac{j}{\Lambda_s c_s}$$

Thus as further salt ions migrate, the field strength decreases until the salt concentration reaches its maximum value under the experimental conditions:

$$c_s = \frac{I.t}{F.\dot{M}} \text{ (mol·cm}^{-3}\text{)}.$$

[I (A) = current, t = transport number of the mixture of ions in question, F = Faraday constant, $\dot{M}$ (cm³·sec⁻¹) = feed rate of countercurrent solution].

[31a] *K. Wagener*, Z. Elektrochem., Ber. Bunsenges. physik. Chem. *64*, 922 (1960); Chemie-Ing. Techn., in press.

[31b] *K. Wagener*, Habilitation thesis, Technische Universität Berlin, 1964; Hahn-Meitner-Institut für Kernforschung Berlin, Rept. HMI-B 44 (1965).

[32] *K. Wagener* and *B. A. Bilal*, Z. Naturforsch. *21a*, 1352 (1966).

[*] In the separation of isotopic cations, the upstream electrode is the cathode. The mixture of cations is then at rest in relation to the separating column, while the anions migrate through the column with a velocity $| v_- | = | E \cdot u_- | + | v_L |$. The principle of electric neutrality is always satisfied. To separate isotopic anions, one need only reverse the direction of the field; generally a different countercurrent electrolyte is used.

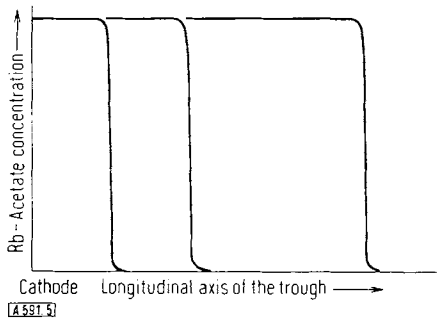


Fig. 5. Concentration distribution of rubidium acetate in the trough of the apparatus shown in Figure 4 with stepwise addition of salt and at a given current intensity I.

(Data: I = 1 A at an electrolysis voltage of about 1000V; transport number of Rb^+ in rubidium acetate solution = 0.66; feed rate of countercurrent liquid: $\dot{M}$ = 0.1 cm³ sec⁻¹, from which the stationary salt concentration (see Section 2.4) is calculated to be c_S = 0.07 N, as is in fact observed).

Further added ions do not increase the concentration, but accumulate in compartments situated farther away from the electrode (a right-angled distribution is obtained for the salt concentration, see Fig. 5). As can be seen from the last equation, arbitrary values of c_S can be obtained by an appropriate choice of the ratio $I/\dot{M}$. It can also be seen that the concentration distribution of the salt is stable, provided

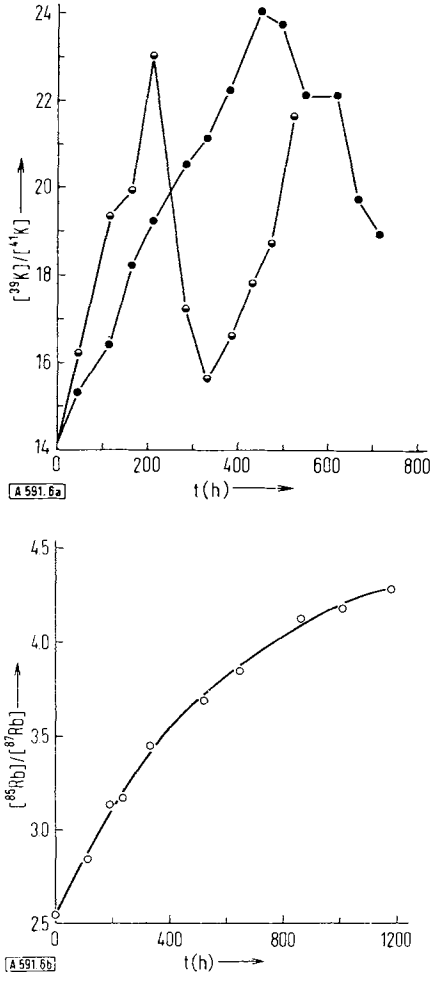


Fig. 6. Isotope ratio at the end of the column (cathode compartment) as a function of time.

Upper diagram: Example of the separation of potassium by the *Brewer* method with the cell shown in Figure 3. The discontinuity is due to disturbances of the countercurrent equilibrium.

Lower diagram: Example of the separation of rubidium in the apparatus shown in Figure 4.

that the operating conditions are kept constant. Thus if a small local disturbance (increase or decrease) of the salt concentration occurred, the field strength at this point would immediately change, and ions would migrate away from or toward this point to compensate for the disturbance.

The effectiveness of this self-stabilization mechanism can be very clearly seen from Figure 6, which shows a comparison of the course of enrichment at the column end with time in the Brewer and in the Wagener methods.

The apparatus required for self-stabilizing countercurrent electrolysis is very simple, since no control equipment is required, and the plant consequently no longer contains any moving parts. Numerous continuous tests extending over periods of weeks and months have shown that this process is very reliable. An interesting result is the sharpness of the separation obtained with separating columns consisting of troughs divided into compartments. The number of theoretical plates per meter is generally of the order of 1000.

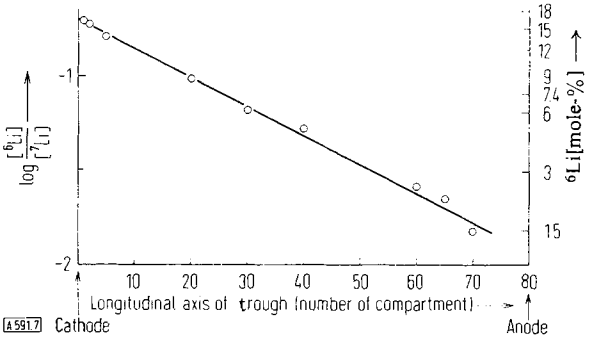


Fig. 7. Distribution of lithium isotopes (natural mixture: 7.4 mole-% of ^6Li) along a separating column in the final separation state in the apparatus shown in Figure 4. The separation effect acts over the whole of the column.

(The column consisted of 80 compartments and was constructed by the filter-press principle with an alternation of U-shaped rubber seals and square separating plates (total length of the column about 65 cm, volume of column about 1.2 l). The openings in the separating plates were covered with fine-pore nylon gauze (pore width 53 microns).

The process has been successfully used for the separation of isotopes of lithium[33,34] (see also Fig. 7), potassium[35,36], rubidium[37], calcium[38], strontium[35], and carbon (formate)[39], as well as for the separation of rare earths[35] and the extreme purification of various alkali metal salts[40]. Figure 8 shows arrangements (with one end container) suitable for the enrichment of the fastest or slowest components of a mixture of ions.

[33] *W.Thiemann* and *K.Wagener*, Z.Naturforsch. *18a*, 228 (1963).

[34] *D. Behne* and *K. Wagener*, Ber. Bunsenges. physik. Chem. *69*, 378 (1965).

[35] *K. Wagener*, unpublished.

[36] *K. Wagener* and *D. Behne*, unpublished.

[37] *K. Clusius* and *K.Wagener*, Z.Elektrochem., Ber. Bunsenges. physik. Chem. *65*, 701 (1961); Angew. Chem. *73*, 476 (1961); *K.Clusius*, *M.Huber*, and *K.Wagener*, J.Chim. physique *60*, 263 (1963); *K. Wagener*, Ber. Bunsenges. physik. Chem., *71*, 627 (1967).

[38] *K. Wagener* and *H. D. Freyer*, unpublished.

[39] *W.Thiemann*, Dissertation, Technische Universität Berlin, 1966.

[40] *P. Schmeling*, unpublished.

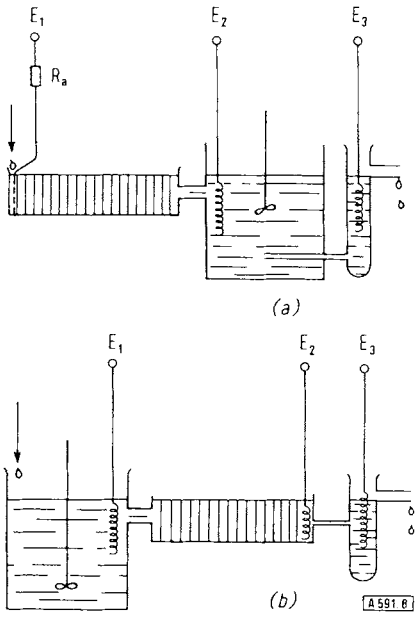


Fig. 8. (a) Apparatus for the enrichment of the faster-migrating component. Reservoir vessel containing the natural isotope mixture at the overflow end of the column.

(b) Apparatus for the enrichment of the slowest component. Reservoir vessel at the feed end of the column.

The separation takes place between the electrodes E_1 and E_2. An additional potential difference is applied between E_2 and the auxiliary electrode E_3; this potential difference must be so great that no salt can escape from the reservoir container and the trough, despite the flow. The ohmic resistance R_a can be used for stabilization (cf. [31b]).

3. Utilization of Dissociation and Complex Formation Equilibria in the Homogeneous Phase

The isotope effects observed in ionic migration in aqueous solutions are of the order of $\Delta u/\bar{u} \approx 10^{-3}$ in the cases known at present (except in the case of hydrogen isotopes). In chemical exchange equilibria, on the other hand, the isotope effects are generally about ten times as great, *i.e.* (for nuclides that are not too heavy) $\Delta K/\bar{K} \approx 10^{-2}$ (= relative difference in the equilibrium constants) [41], so that these equilibria would seem much more useful for the enrichment of isotopes.

To combine the advantages of the countercurrent electrolytic separation process (self-cascading, large number of theoretical plates) with the generally large isotope effect of an exchange equilibrium, one must seek for suitable ion-exchange equilibria (complex formation) in the homogeneous phase [42]. The simplest model case would be the dissociation of a 1,1 salt, where *e.g.* the metal M consists of two isotopes. Only the ions migrate in the electric field, while the flowing liquid transports charged and uncharged particles to the same extent. The result of an isotope effect in the dissociation equilibrium $MX \rightleftharpoons M^+ + X^-$ is that the time-average charge numbers $\bar{z}_1$ and $\bar{z}_2$ of the two isotopes are different, since the isotope having the greater dissociation constant will exist preferentially in the ionic form [*].

The isotope effect in the dissociation equilibrium is translated in this way into the isotope effect in the migration velocity of the isotopic components. Since the equilibrium isotope effect is much greater than that shown in the migration of the free isotopic ions, the separation can be optimized by determination of the conditions under which $\Delta\bar{z} = \bar{z}_1 - \bar{z}_2$ has its maximum value, since the difference in the rates of migration of the two isotopes is then greatest. In the simple dissociation equilibrium mentioned, $|\Delta\bar{z}|$ reaches a maximum when the degree of dissociation is 0.5 (based on the element M, and not on one of its isotopes) [**]. The concentrations in the electrolyte (salt, complex former) must therefore be such that $[MX] \approx [M^+]$. Under these conditions $\Delta\bar{z}/\bar{z} = (\Delta K/\bar{K})/2$, *i.e.* the isotope effect that is used in the ionic migration and which can be multiplied by cascading is half as great as the isotope effect in the dissociation equilibrium [43].

In order to be suitable in this respect for isotope separation by ionic migration, a complex must exhibit a sufficiently large isotope effect $\Delta K/\bar{K}$ in its formation equilibrium. Moreover, the value of the complex formation constant must not be too extreme, but should lie between 1 and 10^2, *i.e.* weak complexes are necessary.

Figure 9 shows the concentration-dependence of the isotope effect observed in the migration of lithium ions in the acetate system [34]. The effect is independent of concentration in very dilute solutions, undoubtedly because of the difference in the mobilities of the free isotopic ions. The isotope effect increases rapidly with increasing lithium acetate concentration; from the above arguments, a maximum should be expected in approximately 1 N solution.

The disadvantage that only part of the elementary effect is utilized in the multiplication of the equilibrium isotope effect by ionic migration is probably compensated for in most cases

[41] Cf. *e.g. S. S. Roginski*, Theoretische Grundlagen der Isotopenchemie. Deutscher Verlag der Wissenschaften, Berlin 1962. In the case of the lithium isotopes, isotope effects of up to 7.6% have been found by *D. A. Knyazev* and *E. V. Sklenskaya* [Ž. fiz. Chim. *37*, 2094 (1963)] by exchange between the aquo complex and the complex with uramil-7,7-diacetic acid.

[42] *H. Martin* (cf. [29]) had already suggested in 1949 that any isotope effect existing in the equilibrium of an incomplete dissociation should be utilized for the separation of the components by ionic migration. However, the isotope effect obtained in 1958 by this author for magnesium was so small that he expressed the view, in 1964, that the effects are predominantly of a kinetic nature, *i.e.* that they are due to differences in rate between the free ions.

[*] In the above example we have for the isotope 1:

$$\bar{z}_1 = \frac{[M_1^+]}{[M_1X]\,[M^+]} \quad \text{and} \quad K_1 = \frac{[M_1^+]\,[X^-]}{[M_1X]}.$$

The charge number and the dissociation constant are related by:

$$\frac{1}{\bar{z}_1} = \frac{[X^-]}{K_1} + 1.$$

[**] $\Delta\bar{z} = \bar{z}_1 - \bar{z}_2 = 1/([X^-]/K_1 + 1) - 1/([X^-]/K_2 + 1)$

$$\approx \frac{[X^-]/K}{([X^-]/\bar{K} + 1)^2} \cdot \frac{\Delta K}{\bar{K}}$$

The value of this fraction is greatest for $[X^-]/\bar{K} = 1$, *i.e.* when the degree of dissociation is 0.5.

[43] *D. Behne, H. D. Freyer*, and *K. Wagener*, Ber. Bunsenges. physik. Chem. *69*, 893 (1965); *K. Wagener, ibid. 64*, 1163 (1960).

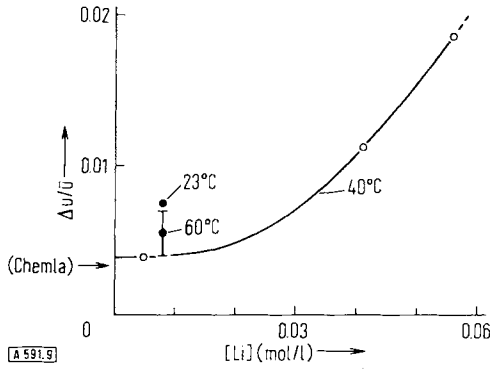


Fig. 9. Relative difference in the mobilities of ^6Li and ^7Li ions in 0.5 N acetic acid, as a function of the temperature and concentration of the lithium salt solution.

by the advantages and the convenience of a continuous process such as ionic migration in solution as compared with an exchange between two phases (cf. *e.g.* Section 5).

4. Direct Electrolysis

Isotopic ions are deposited at different rates during electrolysis. This effect is particularly pronounced for the hydrogen isotopes in the electrolysis of water. Light hydrogen is liberated more rapidly, so that as electrolysis proceeds, the deuterium concentration in the aqueous residue increases. Using this method, *Lewis* and *MacDonald* (1933) prepared pure D_2O for the first time from an aqueous alkali solution [44].

The elementary separation factor α (= ratio of the H/D values in the gas liberated and in the aqueous electrolyte) is about 3 to 12, depending on the experimental conditions. A value of about 5 is reached in industrial electrolytic cells. The exchange reaction

$$HD_{gas} + H_2O_{liq.} \rightleftharpoons H_{2gas} + HDO_{liq.}$$

which is catalysed by the electrode metal, reaches equilibrium when no current is passing; at 25 °C the equilibrium constant $K = \frac{[H_2]\,[HDO]}{[HD]\,[H_2O]} = 3.8$. An external current imposes a kinetic separation effect, which reaches a maximum at a current density of about ten times the exchange current density. An earlier belief that the kinetic separation effect is related to the hydrogen overvoltage on metals appears from recent investigations to be incorrect [45]. However, α is strongly dependent on the electrode metal and on the state of its surface (α is always decreased by impurities or by aging of the cathode surface). On the other hand, the nature and concentration of the electrolyte solution and the deuterium content appear to have little influence on α. An increase in temperature generally leads to a decrease in α [46]. The discharge reaction is assumed to be responsible for the kinetic isotope effect in the liberation of hydrogen [47].

Industrially, the electrolysis is carried out in cells containing NaOH or KOH solutions and equipped with nickel or iron cathodes, the cells being arranged in cascades. At each stage the electrolysis is continued until only about 1/10 of the quantity of water used is left. The water (after neutralization with CO_2) is then distilled out of the electrolyte and passed on to the next stage. The hydrogen liberated, which also contains considerable quantities of deuterium in the final stages, is burnt to form water and returned to the preceding stage. Since the ratio of heavy hydrogen to light hydrogen in natural water is only about 1:7000, very large quantities of water must be processed [48].

The power consumption in the electrolytic process is particularly high in comparison with other processes for the production of heavy water. Other methods are therefore used nowadays for preconcentration (isotope exchange between H_2S and H_2O or NH_3 and H_2, distillation of water, low-temperature rectification of liquid hydrogen) [49]. However, electrolysis plants are still used for final concentration, since in addition to the high separation factor, the valuable enriched material can be processed safely.

The elementary separation factors for other elements are much lower. A value of $\alpha = 1.069$ has been reached in the separation of the lithium isotopes on mercury cathodes [50]. *Selecki* proposed a continuous process in which the cathodic mercury phase and the aqueous electrolyte solution are fed past each other in countercurrent flow [51]. A value of $\alpha = 1.0054$ [52] was obtained for the separation of potassium isotopes on mercury cathodes.

Fractionation of the oxygen isotopes also takes place during the electrolysis of heavy water; however, the elementary separation factor of 1.03 [53] is much too low to be of any practical use. An α value of 1.006 was obtained for the nitrogen isotopes in the electrolysis of ammonium chloride on mercury cathodes [54].

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[48] According to the Rayleigh formula

$$\left(\frac{N}{N_0}\right) \cdot \left(\frac{1-N_0}{1-N}\right)^{1/\alpha} = \left(\frac{V_0}{V}\right)^{\frac{\alpha-1}{\alpha}}$$

approximately 2×10^5 l (= V_0) of natural water are required for the production of 1 l ($V = 1$) of heavy water with an enrichment of 99 atoms-% ($N = 0.99$) ($N_0 = 1/7000$) when the separation factor is $\alpha = 5$.

[49] Cf. e.g. *G. M. Murphy*: Production of Heavy Water. National Nuclear Energy Ser., Div. III-4F. McGraw-Hill Inc., New York 1955; *E. W. Becker*, Angew. Chem. *68*, 6 (1956); *A. P. Murrenhoff*, Kerntechn., Isotopentechn. u. -chem. *6*, 558 (1964); *U. Schindewolf*, Atomwirtschaft *9*, 571 (1964).

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[51] *A. Selecki* in: Dritte Arbeitstagung über stabile Isotope, Tagungsbericht, Leipzig 1963. Akademie-Verlag Berlin, 1965, p. 265; Nature (London) *201*, 61 (1964).

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5. Processes Involving Heterogeneous Isotope Exchange

5.1. Ion-Exchange Equilibria

Ion-exchange chromatography has not acquired much importance for the separation of isotopes. The advantages of this method are that with very little outlay on apparatus, it is adaptable and affords a large number of theoretical plates. However, these advantages are opposed by a number of serious disadvantages[55]. Thus it has been found that the isotope effect in the exchange equilibrium between the exchanging phase and the aqueous electrolyte solution is only of the order of 10^{-3} or even less in most cases. The difference in free energy between the bound state and the dissolved state is practically the same for isotopic ions[56]. Moreover, the exchange equilibrium between the solid ion-exchanging phase and the electrolyte solution is reached only very slowly in most cases, so that the throughput through an ion-exchange column must be kept very small if the number of the theoretical plates is to be kept high. Another disadvantage is that the process must be carried out discontinuously because of the immobile solid phase.

The first successful isotope separation, *i.e.* the separation of lithium isotopes, was achieved in 1938 by *Taylor* and *Urey* on a zeolite ion exchanger[57]. The elementary separation factor for this process was calculated to be 1.022; however, this value seems doubtful, and later measurements on zeolites gave much smaller values[58] (1.004 to 1.005). Experiments on ion-exchange resins (Dowex-50 type) gave values of between 1.002 and 1.0027 for the elementary separation factor of the Li isotopes[59].

The dependence of the isotope effect on the degree of cross-linking and on the eluent were also studied[60]. *Dickel* and *Richter*[61] determined the elementary effect directly in equilibrium experiments, and were able to study the dependence of this effect on concentration. They found a pronounced maximum in approximately 0.1 N solutions, in which the separation factor reaches a value of 1.012. The light isotope ^{6}Li is preferentially bound by the exchanger.

The ^{10}B content of boric acid solutions could be reduced from 19.7 % to 14.8 % on an anion exchanger (Amberlite CG-400)[62]; the elementary separation factor was found to be 1.016. The separation of the radioisotopes ^{22}Na and ^{24}Na on Dowex 50 was studied[63]; the elementary separation factor varied in this case between 1.00007 and 1.00018, depending on the temperature[64]. In the case of uranium isotopes the ^{234}U-abundance could be changed by about 4–5 % on a Dowex-50 column[65].

The best results with exchange resins were obtained by *Spedding*, *Powell*, and *Svec*[66] in the separation of the nitrogen isotopes *via* $NH_4^{\oplus}$ ions. The elementary separation factor in this case is particularly high, the value obtained being 1.025. This is because two equilibria are superimposed on each other, *i.e.* that of the exchange between bound and free $NH_4^{\oplus}$ ions and that of the exchange between free ammonium ions and dissolved ammonia, the latter of these equilibria evidently makes the greater contribution to the total separation factor. The authors connected several columns in a cycle, through which the exchanger zone containing $NH_4^{\oplus}$ ions could be passed over very large distances by successive elution with NaOH; moreover, the front of the migrating zone, in which the ^{15}N concentration had been reduced, was regenerated at intervals with fresh solution having the natural isotopic composition. The ^{15}N content could be increased from 0.36 to 44.8 %, corresponding to a separation factor of 225, by this chromatographic process.

Panchenkov[67] described a continuous countercurrent ion-exchange process which is similar to the method described by *Spedding* and *Powell*, and which should allow an even more efficient separation because of the use of a mobile exchanger phase.

Blasius and *Neumann*[68] tried to combine heterogeneous isotope exchange on ion exchangers with electrolytic ionic migration. Their experiments with ^{134}Cs and ^{137}Cs on a Dowex-50 column gave an elementary isotope effect of 1.0011, which is practically the same as that obtained in ionic migration in fused sodium nitrate[2]. It is therefore concluded that the isotope effect in the heterogeneous ion exchange must be very small. Similar experiments carried out with lithium isotopes in a two-dimensional arrangement by a group of Japanese workers[69] gave elementary isotope effects of 1.0049 to 1.0069 (depending on the anion and the experimental conditions), which are made up from equilibrium effects and kinetic contributions.

[55] Cf. The contribution by *E. Glueckauf* in *H. London*: [1b], p. 209.

[56] *E. Glueckauf*, Trans. Faraday Soc. *51*, 1235 (1955).

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[62] *Y. Yoneda*, *T. Uchijima*, and *S. Makishima*, J. physic. Chem. *63*, 12 (1959); *ibid. 63*, 2057 (1959).

[63] *R. H. Betts*, *W. E. Harris*, and *M. D. Stevenson*, Canad. J. Chem. *34*, 65 (1956).

[64] *E. Glueckauf*, Trans. Faraday Soc. *54*, 1203 (1958).

[65] *F. H. Spedding* and *J. E. Powell*, Ames Lab., Iowa, Rept. ISC-475 (1954, declassified 1958).

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[67] *V. I. Gorshkov*, *I. A. Kuznetsov*, and *G. M. Panchenkov*, Doklady Akad. Nauk SSSR *143*, 643 (1962); Ž fiz. Chim. *36*, 611 (1962); *G. M. Panchenkov*, J. Chim. physique *60*, 107 (1963).

[68] *E. Blasius* and *W. Neumann*, Z. Elektrochem., Ber. Bunsenges. physik. Chem. *65*, 475 (1961).

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5.2. Exchange Electrolysis

The separation effect on which this process is based occurs in the exchange equilibrium between an amalgam phase and an electrolyte solution, *i.e.* an electronically and an ionically conducting phase. Ion exchange between these two phases is described as exchange electrolysis. The elementary separation effect of such an exchange electrolysis can be multiplied if the two phases are passed through a column in countercurrent flow.

This process was first used in 1936 by *Lewis* and *MacDonald*[70] for the separation of the lithium isotopes. Droplets of amalgam were allowed to fall through an alcoholic lithium chloride solution moving upward in a vertical tube. The lithium was washed out of the amalgam phase at the base of the column with alcoholic hydrochloric acid, and the resulting LiCl solution was reprocessed in the same manner. In this way the authors enriched ^{6}Li from 8 % to 16.3 % within 24 hours; the elementary separation factor was given as 1.02. Two patents concerning improvement of this separation were published recently, but no details of the experimental conditions are given[71]. The essential improvement appears to be the use of dimethylformamide as the solvent. The elementary separation effect between the amalgam phase and dimethylformamide is about 1.05[72].

Arkenbout et al.[73] recently described an exchange electrolysis using the same principle; the authors are of the opinion that this process is suitable for use in the enrichment of lithium isotopes on the industrial scale. In a sand-packed column 2 m long and 2.5 cm in diameter, approximately 10 theoretical plates were obtained when the flow rate of the two phases was 0.2 ml min^{-1} cm^{-2}. Technical difficulties involving phase inversion at the top of the column (cathodic reflux), where the lithium must be transferred from the electrolyte phase into the amalgam phase, could be avoided by the use of n-propylamine (instead of dimethylformamide) as the solvent for the electrolyte phase.

Similar processes based on exchange electrolysis have also been used for chemical separations (separation of rare earths and U/Th mixtures, and removal of fission products from nuclear fuels)[74]. In these cases the exchange takes place in the melt between a metallic phase (liquid Bi or Zn) and a salt phase (LiCl/KCl melt).

6. Concluding Remarks

The most important factor in the selection of a process for a given separation is the quantity of product desired.

If small quantities (*e.g.* 1 mole or less) are required once only, economic factors are generally of no importance. It is much more important to obtain a high concentration in a single column if possible. Another important point for laboratory work is that the apparatus should, if possible, be suitable for use in various isotope separations.

On the other hand, the most important factor in the case of kilogram or ton quantities is the economic factor. The size of the plant required to obtain a product of the desired concentration and in the desired quantity per unit time, the time taken to reach the desired degree of concentration, and the power consumption are all proportional to $1/\varepsilon^2$. Consequently, in isotope separations on the industrial scale, it is generally more important to achieve a large elementary effect than to give a reversible separation process preference over an irreversible process (see Introduction). The choice of a process will also be determined by the possibility of multiplication of an elementary effect. The best solution to this problem must be established specially for each individual separation.

The feasibility of using electrochemical separation processes for the enrichment of isotopes on the industrial scale must be checked for each individual case. The possibility is likely to be good only for light to medium-heavy elements. Estimated production costs for a product of a given concentration are available for a number of processes on the laboratory scale (ionic migration in salt melts[12] or in solution[35] and exchange electrolysis[73]). However, these figures are not sufficient for a critical comparison of various processes, since each process will present its own technological differences.

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Translated by Express Translation Service, London

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[71] *E. Saito*, French.-Pat. 1195421 (1959); Brit.-Pat. 902755 (1962).

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[73] *G. J. Arkenbout*, Dissertation, Universität Utrecht, 1965; *G. J. Arkenbout*, *A. J. H. Boerboom*, and *W. M. Smit*, Ber. Bunsenges. physik. Chem. *70*, 658 (1966); *A. J. van Bennekom*, *G. J. Arkenbout*, and *W. M. Smit*, *ibid.* *71*, 215 (1967).

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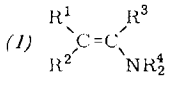
Synthesis and Reactions of the Alkynylamines[1]

BY H. G. VIEHE[*]

Alkynylamines $R-C\equiv C-NR_2^1$ have been known for only a few years. They are stable compounds, some of which have now become commercially available. Their high reactivity toward electrophiles as well as toward nucleophiles (particularly on acid catalysis) makes them very versatile starting materials. An interesting practical application is their use as condensing agents in peptide syntheses. They are superior to dicyclohexylcarbodiimide as dehydrating agents for organic acids. They condense with polar multiple bonds and dipolar systems to form cyclic structures.

1. Introduction

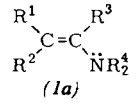
Whereas alkenylamines *(1)* (enamines) have been well known for many years[2, 3], the first alkynylamines *(2)* (ynamines[4][**]) were not prepared until 1958.



(1)

$R-C\equiv C-NR_2^1$ *(2)*

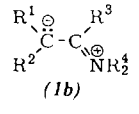
Both classes of compounds are characterized by conjugation of the multiple bond with the amino group. This means that both the nitrogen atom and the β-carbon atom can react as nucleophilic centers, as indicated by the resonance structures *(1a)* and *(1b)* as well as *(2a)* and *(2b)*.



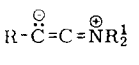
(1a)

$R-C\equiv C-\ddot{N}R_2^1$

(2a)



(1b)



(2b)

Experience so far indicates that the amino group in the ynamines must be tertiary. All attempts to synthesize ynamines with primary amino groups have led to the tautomeric nitriles[5–8].

$[R-C\equiv C-NH_2] \rightarrow R-CH_2-C\equiv N$

The reactions of the ynamines are also related to those of the acetylene ethers *(3)*[9]. The ynols, on which the latter are based, are known only in the form of the

$R-C\equiv C-OR^1$

(3)

tautomeric ketenes. If the basic reaction for the industrial preparation of ketene, *i.e.* dehydration of acetic acid, could be applied to *N,N*-disubstituted acetamides, it should give ynamines. However, only the reverse reaction is known at present, *i.e.* ynamines, like the acetylene ethers, are versatile dehydrating agents.

On the basis of these formal comparisons, the ynamines may be expected to undergo numerous reactions. Since the first ynamines were synthesized only a few years ago, the reactions described below probably represent only the beginning of this development.

2. Stability and Principles of Synthesis

V. Wolf and *F. Kowitz* thought that they had synthesized the first ynamine in 1960 when they obtained *N,N*-diethylphenylethynylamine *(4)* in a yield of 1.7 %[10].

$$C_6H_5-C\equiv C-Li + ClN(C_2H_5) \rightarrow C_6H_5-C\equiv C-N(C_2H_5)$$

(4)

The synthesis of compound *(4a)*[11], which was first achieved in 1958 but was regarded as doubtful[10], was not confirmed[12] until 1965.

[*] Doz. Dr. H. G. Viehe
Union Carbide European Research Associates S.A.
95, rue Gatti de Gamond
Bruxelles 18 (Belgium)

[1] A more detailed treatment of this class of compounds is given in *H. G. Viehe*: Chapters on the Chemistry of Acetylenic Compounds. Marcel-Dekker, New York, publication planned for 1968.

[2] *J. Smuszkovicz*, Advances org. Chemistry *4*, 96 (1963).

[3] The name enamine was introduced by *G. Wittig* and *H. Blumenthal*, Ber. dtsch. chem. Ges. *60*, 1085 (1927).

[4] *H. G. Viehe*, Angew. Chem. *75*, 638 (1963); Angew. Chem. internat. Edit. *2*, 477 (1963).

[**] The simple designation "ynamine" [4] has also been adopted by Chemical Abstracts.

[5] *J. J. Rinke*, Recueil Trav. Chim. Pays-Bas *39*, 704 (1920); *46*, 268 (1927); *48*, 960 (1928).

[6] *R. A. Raphael*'s suggested [7] reaction of acetylenic Grignard compounds with methoxylamine leads as predicted, to substituted acetonitriles [20].

[7] *R. A. Raphael*: Acetylenic Compounds in Organic Synthesis. Butterworth, London 1955, p. 61.

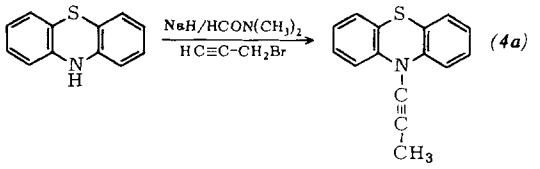
[8] *H. G. Viehe* and *E. Franchimont*, Chem. Ber. *95*, 319 (1962).

[9] Reviews: *J. F. Arens*. Advances Org. Chemistry *2*, 117 (1960); a detailed treatment is presented by *L. Brandsma, H. J. T. Bos*, and *J. F. Arens* in [1].

[10] *V. Wolf* and *F. Kowitz*, Liebigs Ann. Chem. *638*, 33 (1960).

[11] *H. E. Zaugg, L. R. Swett*, and *G. R. Stone*, J. org. Chemistry *23*, 1389 (1958).

[12] *J. L. Dumont*, C. R. Acad. Sci. Paris *261*, 1710 (1965).



(4a)

On the other hand, all other reports of syntheses published since 1892 [13–15] appear to be based on errors, as was demonstrated later mainly by spectroscopic analysis [16, 17]. Nevertheless, the original belief that the ynamines are too unstable to be isolated in practical quantities had been proved incorrect. After the ynamine *(4)* had become available in yields of more than 80 % [4] as a result of our attempted nucleophilic substitution of halogen on an acetylenic carbon atom [8, 18], this and other ynamines were found to have a surprising thermal stability, in addition to the expected reactivity.

Most ynamines are water-clear, stable liquids with a more or less pronounced amine odor. They have now become commercially obtainable [19], and they can normally be handled in air without deterioration. Alkylethynyldiethylamines showed no appreciable decomposition even on vacuum distillation through porcelain tubes at 400 °C [20].

Thus the thermal stability of acetylenes substituted with elements of the first period increases with decreasing electronegativity of the substituent, from the extremely unstable 1-fluoroalkynes [8, 21–23], which oligomerize, *via* the more stable, but often readily fragmentable, acetylene ethers [9], to the ynamines and the dialkylacetylenes:

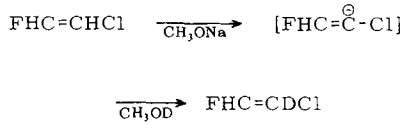
$$F-C\equiv C-R < R^1O-C\equiv C-R < R_2^1N-C\equiv C-R < R_3C-C\equiv C-R$$

The stability varies in the same order, though the variation is less pronounced, in the heterosubstituted olefins, particularly fluoroethylenes [24]. Thus the stability of a molecule in which an electronegative carbon atom (*i.e.* an sp or to a smaller extent an sp^2 carbon atom) carries an electronegative substituent decreases with increasing electronegativity of the substituent [25]. For substituents of the second and higher periods, stabilizing d-orbital resonance is superimposed on the above effect. Thus 1-chloroalkynes, for example, are thermally more stable than 1-fluoroalkynes.

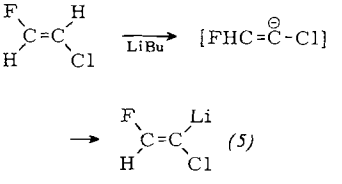
It therefore follows that for hetero-substituted acetylenes and olefins:

a) The ease of addition of anions or free radicals to the multiple bond increases with increasing electronegativity of the substituent.

b) A negative charge (or a free-radical electron) on the carbon atom α to the hetero substituent is best stabilized by the hetero atom if the latter belongs to the second or a higher period of the periodic system. Consequently, in *cis*- and *trans*-chlorofluoroethylene, for example, the hydrogen α to the chlorine atom is replaced by deuterium much more readily than the hydrogen α to the fluorine atom [25].



Similarly, the reaction of *trans*-chlorofluoroethylene with butyl-lithium yields only the lithium compound *(5)*, in which the chlorine and the metal are attached to the same carbon atom.



(5)

Where attack takes place in only one of two possible directions, as in this example, the reaction is described as "directiospecific". If one direction of attack predominates, the reaction is "directioselective". These two phenomena are observed, not only in substitutions but also in additions and eliminations [26].

Like all substituted acetylenes, the ynamines can be prepared *a priori* by three possible routes: (i) The triple bond may be formed by elimination from a molecule in which the substituent is already present; (ii) an acetylene group may be joined to the substituent, the acetylene group being supplied as an acetylide or, less commonly, as a halogenoacetylene (or acetylene ether); and (iii) the isomerization of propargyl derivatives.

All these routes were originally subject to difficulties. The eliminations were readily suppressed by substitution of the halogen, *e.g.* in the reactive amide chlorides [27]. Only a few chloroenamines (which are often unstable) are available, and there is a lack of suitable catalysts for the isomerizations leading to *N*-dialkylynamines. The synthesis that seems simplest, *i.e.* the substitution of chloroalkynes, is hindered by the low reactivity of the halogen [4] when the acetylene

[13] *J. Bode*, Liebigs Ann. Chem. *267*, 268 (1892).

[14] *F. Moulin*, Helv. chim. Acta *34*, 2416 (1951).

[15] *E. Ott*, *G. Dittus*, and *H. Weissenburger*, Ber. dtsch. chem. Ges. *76*, 84 (1943).

[16] *F. Klages* and *F. Drerup*, Liebigs Ann. Chem. *547*, 65 (1946).

[17] *K. E. Schulte* and *M. Goes*, Arch. Pharmaz., Ber. dtsch. pharm. Ges. *290/62*, 157 (1957).

[18] *H. G. Viehe*, Chem. Ber. *92*, 3064 (1962).

[19] Fluka AG., Buchs, Switzerland.

[20] Unpublished results from our research group.

[21] *H. G. Viehe*, *R. Merényi*, *J. F. M. Oth*, and *P. Valange*, Angew. Chem. *76*, 888 (1964); Angew. Chem. internat. Edit. *3*, 747 (1964).

[22] *H. G. Viehe*, Angew. Chem. *77*, 768 (1965); Angew. Chem. internat. Edit. *4*, 764 (1965). See also [30].

[23] *W. J. Middleton* and *W. H. Sharkey*, J. Amer. chem. Soc. *81*, 803 (1959).

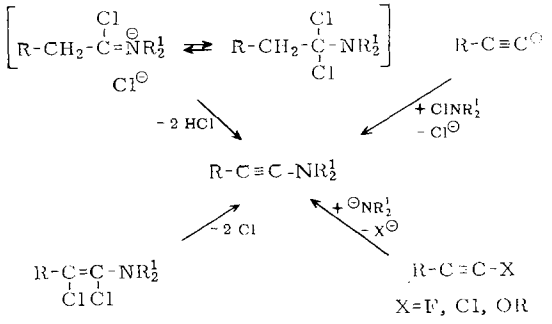
[24] Review: *R. Huisgen*, *R. Grashey*, and *J. Sauer* in *S. Patai*: The Chemistry of Alkenes. Interscience, London, New York, Sidney 1964.

[25] *S. Y. Delavarenne* and *H. G. Viehe*, IUPAC Fluorine Symposium in Estes Park, Colorado, USA, July 1967.

[26] *S. Y. Delavarenne* and *H. G. Viehe*, unpublished.

[27] *H. Eilingsfeld*, *M. Seefelder*, and *H. Weidinger*, Angew. Chem. *72*, 836 (1960).

Eliminations: *Substitutions:*

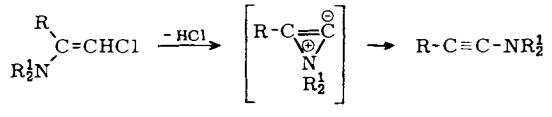


Isomerization of propargyl derivatives:

$$R{-}C{\equiv}C{-}CH_2{-}NR_2^1 \rightarrow [R{-}CH{=}C{=}CH{-}NR_2^1] \rightarrow R{-}CH_2{-}C{\equiv}C{-}NR_2^1$$

group does not carry an electronegative substituent [8]. The limitations of the reaction of acetylides with chloroamines, which are not very susceptible to nucleophilic substitution of the chlorine, are shown by the low yield of 1.7 %, which was obtained by *Wolf* and *Kowitz* [10].

However, all the routes outlined have now been successfully used. Moreover, in the study of nucleophilic substitution on chloroalkynes, a rearrangement reaction of general importance was discovered. This is the "onium rearrangement" [28], which is particularly useful for the synthesis of ynamines.



3. Ynamines by Substitution

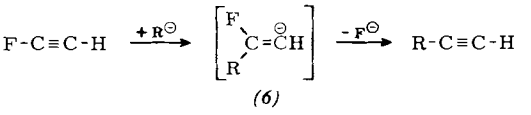
3.1. Ynamines from 1-Halogenoalkynes and Metal Amides. A New Mechanism of Nucleophilic Substitution of Halogen Attached to Multiply Bonded Carbon Atoms

The normal, low reactivity of chloroalkynes is illustrated by the following reaction, which gives an overall yield of 82.5 % when carried out as a single-vessel reaction in liquid ammonia [29].

$$Cl{-}CH{=}CH{-}Cl \xrightarrow{NaNH_2} [HC{\equiv}C{-}Cl] \xrightarrow{NaNH_2} Na{-}C{\equiv}C{-}Cl$$

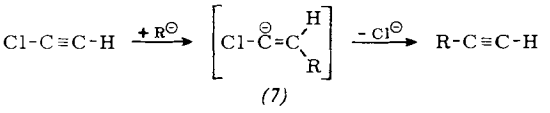
$$\xrightarrow{Br(CH_2)_2Br} Cl{-}C{\equiv}C{-}(CH_2)_4{-}C{\equiv}C{-}Cl$$

Nucleophilic substitution of the halogen [4] *is much easier in fluoroalkynes than in chloroalkynes.* This is plausibly explained on the basis of the discussion of the stability of hetero-substituted acetylenes and the directiospecificity of their reaction (Section 2). Fluoroacetylene adds on the nucleophilic reagent at the α carbon atom. The hypothetical intermediate *(6)* can



(6)

readily lose the fluoride ion by β-elimination. In chloroacetylene, on the other hand, the nucleophilic reagent adds to the β-carbon atom, since the chlorine atom can stabilize a negative charge on the α-carbon atom by d-orbital resonance. The chloride ion must then be lost from the hypothetical intermediate by α-elimination, which is energetically less favorable [28].



(7)

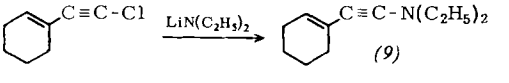
Accordingly, the ynamine *(7a)* can be prepared from lithium diisobutylamide only with fluoroacetylene, and not with chloroacetylene [20].

$$F{-}C{\equiv}C{-}H \xrightarrow{2\ LiN(-iC_4H_9)_2} Li{-}C{\equiv}C{-}N(i{-}C_4H_9)_2$$

$$\xrightarrow{CH_3OH} HC{\equiv}C{-}N(i{-}C_4H_9)_2 \quad (7a)$$

The chlorine in chloroalkynes can be readily substituted by means of *N,N*-disubstituted alkali metal amides if the acetylene carries an "electronegative" substituent [8, 30]. Thus chlorophenylacetylene reacts with lithium dimethylamide to give the ynamine *(8)* in 87 % yield [31], and even chlorocyclohexenylacetylene reacts with lithium diethylamide to give the ynamine *(9)* in 64 % yield [20]; however, these reactions probably proceed *via* α-additions.

$$C_6H_5{-}C{\equiv}C{-}Cl \xrightarrow{LiN(CH_3)_2} C_6H_5{-}C{\equiv}C{-}N(CH_3)_2 \quad (8)$$



(9)

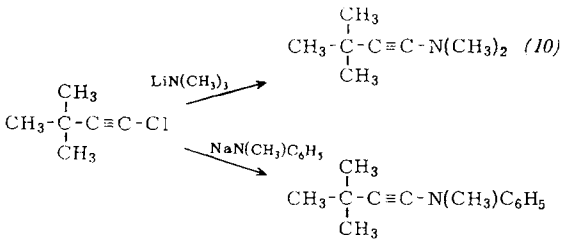
t-Butylchloroacetylene reacts with lithium dimethylamide only in the strongly polarizing solvent hexamethyl phosphorus triamide (HMPT) recommended by *H. Normant*, the reaction being exothermic and giving the ynamine *(10)* in a yield of about 70 %. The chlorine in t-butylchloroacetylene can also be substituted by means of sodium *N*-methylanilide if the mixture is heated at 100 °C for 6 hours in a sealed tube.

[28] *H. G. Viehe* and *S. Y. Delavarenne*, unpublished.

[29] *H. G. Viehe*, Chem. Ber. *92*, 1270 (1959).

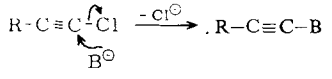
[30] Review on halogenoacetylenes: *S. Y. Delavarenne* and *H. G. Viehe* in [1].

[31] *H. G. Viehe* and *M. Reinstein*, Angew. Chem. *76*, 537 (1964); Angew. Chem. internat. Edit. *3*, 506 (1964).

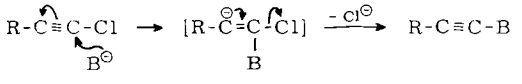


Various reagents have been used with t-butylchloroacetylene in efforts to obtain information about the substitution mechanism. As a result of this work, a new mechanism has been proposed for the substitution of halogen on multiply bonded carbon atoms [28]. Three mechanisms had formerly been discussed for the nucleophilic substitution of halogen (chlorine, bromine, iodine) on multiply bonded C atoms [18,28,32,33]; these mechanisms are illustrated below for an alkylchloroacetylene.

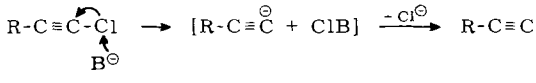
Direct substitution:



α-Addition and β-elimination:



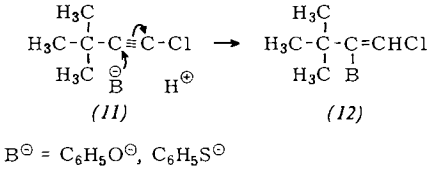
Attack on the hetero atom followed by direct substitution [34]:



Direct substitution is unlikely for several reasons [1,28]. The reactivity of chlorine attached to a triply bonded C atom is very low, evidently because the difference in electronegativity between the chlorine and the carbon is smaller than in chloroalkanes, and because conjugation makes the chlorine atom more positive and strengthens the C–Cl bond [18,30].

The attack on the hetero atom with subsequent direct substitution is also conceivable only in special cases. Thus alkoxide $RO^{\ominus}$ or amide $R_2N^{\ominus}$ as $B^{\ominus}$ would lead to the little-reactive hypochlorites ROCl or to the similarly weakly reactive chloroamines R_2NCl.

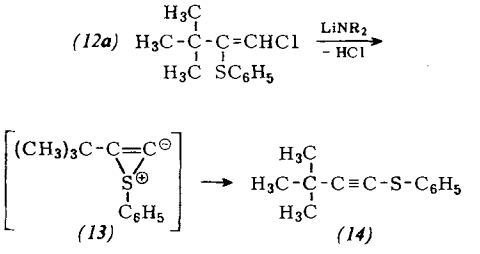
Consequently, the route generally regarded as most likely is the α-addition and β-elimination [28,32,33]. However, this mechanism is refuted by the directiospecificity of the β-addition of phenoxide and of thiophenolate to t-butylchloroacetylene *(11)*, despite steric hindrance by the t-butyl group.



(11) *(12)*

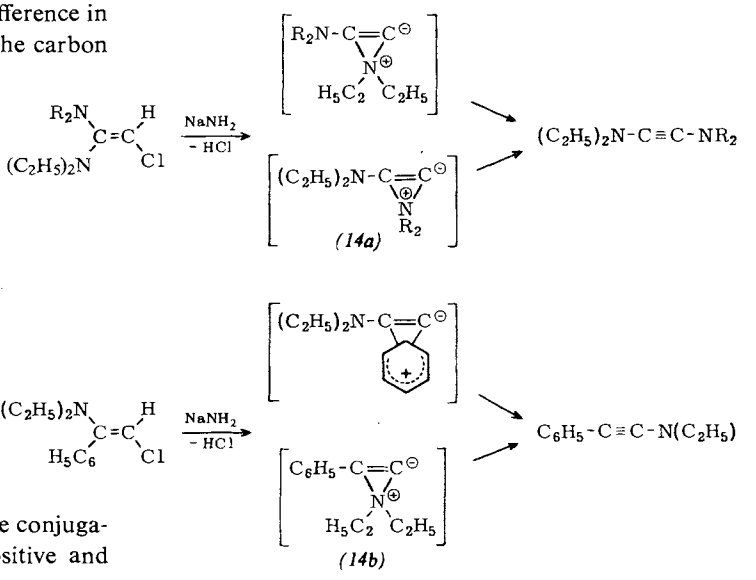
$B^{\ominus} = C_6H_5O^{\ominus}, C_6H_5S^{\ominus}$

The thiophenolate adduct *(12a)*, like many β-chloroenamines can rearrange with α-elimination of HCl to give the acetylene derivative *(14)* [26]. This rearrangement apparently proceeds *via* the onium compound *(13)*.



(13) *(14)*

Examples of this reaction, of which the Fritsch-Wiechell-Buttenberg reaction is a special case [33], have been described in detail elsewhere [26,28]. We shall therefore consider only two examples, which are interesting in that the onium intermediates *(14a)* and *(14b)* both contain two groups that can migrate. It is not yet known whether both groups do in fact migrate, and if so in what ratio. However, it is now conceivable



(14a)

(14b)

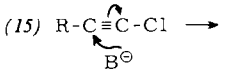
[32] *E. R. Ziegler, C. A. Welch, C. E. Orzech, S. Kikkaway,* and *S. I. Miller,* J. Amer. chem. Soc. *85*, 1648 (1963).

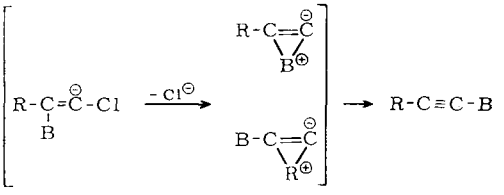
[33] *G. F. Köbrich* and *P. Buck* in [1].

[34] *J. F. Arens,* Recueil Trav. Chim. Pay-Bas *82*, 183 (1963).

that in the substitution of halogens on olefins and aromatic compounds, the nucleophile can not only attack the β-carbon atom, but can also remain there.

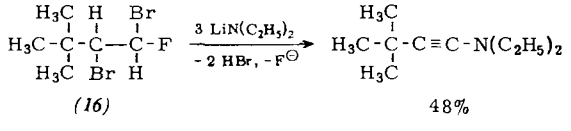
The new mechanism of nucleophilic substitution of halogen by α-elimination and onium rearrangement could also be involved in the synthesis of ynamines from t-butylchloroacetylene and similar halogenoalkynes *(15)* (but not for the fluoroacetylenes)[28].



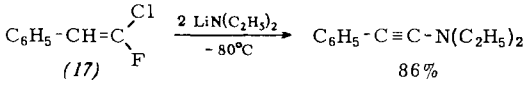


3.2. Ynamines from Dihalogenoalkenes and Trihalogenoalkanes with Alkali Metal Amides

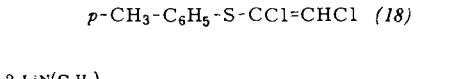
Though the fluoroalkynes had been found to be the most suitable halogenoalkynes for the preparation of ynamines by substitution of halogen[18], the limited availability of these starting materials prevented any practical utilization of this knowledge. However, instead of fluoroalkynes or reactive chloroalkynes, it is possible[4,31] to use compounds, *e.g. (16)* to *(18)*, that may be regarded as precursors of the halogenoalkynes under the conditions of the reaction with *N,N*-disubstituted lithium amides:



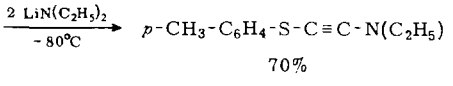
(16) 48%



(17) 86%



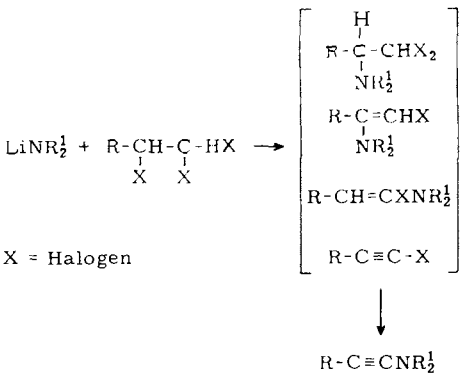
p-CH_3-C_6H_5-S-CCl=CHCl *(18)*



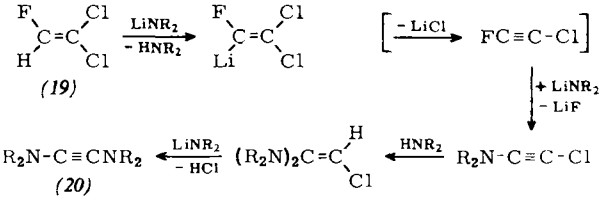
70%

It is not necessary to assume that the halogenoalkynes are formed first, since primary substitution of the halogen on the olefin or alkane can lead to ynamines on subsequent α- or β-elimination with or without onium rearrangement.

An example of a practically simple ynamine synthesis whose mechanism involves several steps, as could be shown by the isolation or interception of the formulated intermediates (except that in brackets)[26], is the



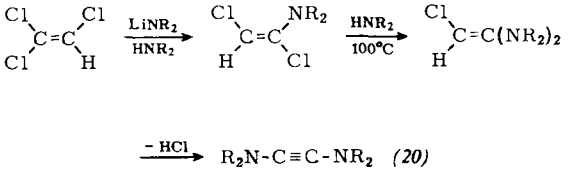
condensation of 2,2-dichloro-1-fluoroethylene *(19)* with 3 mol. equiv. of lithium diethylamide in ether at −80 °C. The yield of *(20)* (based on *(19)*) is about 60 % for R = C_2H_5[31].



(19)

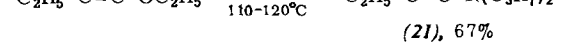
(20)

The isolation of the ynediamine *(20)* again shows the thermal stability of the ynamines, particularly when one remembers that difluoroacetylene FC≡CF has so far only been detected spectroscopically[35] and that no acetylene diethers RO–C≡C–OR have yet been isolated[9]. Ynediamines *(20)* are also obtained from trichloroethylene by dehydrochlorination and onium rearrangement[26].



3.3. Ynamines from Acetylene Ethers with Tertiary Alkali Metal Amides

In the laboratory of *F. Arens*, who is responsible for most of our knowledge on the chemistry of acetylene ethers (since their discovery by *T. L. Jacobs*[9]), *P. Montijn*, *E. Harryvan*, and *L. Brandsma*[36] found that the acetylene ethers also react readily with *N,N*-disubstituted alkali metal amides, with replacement of the alkoxy group and formation of ynamines. This method is particularly useful for the preparation of *C*-alkylynamines *(21)*.



(21), 67%

[35] *W. J. Middleton*, U.S.-Pat. 2831835 (1958).

[36] *P. P. Montijn*, *E. Harryvan*, and *L. Brandsma*, Recueil Trav. Chim. Pays-Bas *83*, 1211 (1964).

3.4. Ynamines from 1-Halogenoalkynes and Tertiary Aliphatic Amines

Ynamines should be weak N-bases. This is in agreement with the fact that halogenoalkynes and tertiary aliphatic amines react to form ynamines *(23)*, with elimination of halogenoalkane from the initially formed ammonium salt *(22)* [1, 20, 37].

$$C_6H_5-C\equiv C-X \xrightarrow[N(CH_3)_3]{40\ h/55^\circ C} C_6H_5-C\equiv C-\overset{\oplus}{N}(CH_3)_3\ \overset{\ominus}{X} \xrightarrow{-CH_3X}$$

(22)

$$\longrightarrow C_6H_5-C\equiv CN(CH_3)_2 \quad (23)$$

X = Cl, Br

This reaction, which is closely related to the von Braun degradation of tertiary amines with cyanogen bromide [38], readily gives ynamines on a 100 g scale. It has also been used to prepare the diynamines *(24)*, which, under special conditions, are able to regenerate the salts by *N*-alkylation [12].

$$C_6H_5-C\equiv C-C\equiv C-Br \xrightarrow{N(CH_3)_3} C_6H_5-C\equiv C-C\equiv C-\overset{\oplus}{N}(CH_3)_3Br$$

$$\overset{+\,CH_3Br}{\underset{-\,CH_3Br}{\rightleftharpoons}}$$

$$C_6H_5-C\equiv C-C\equiv C-N(CH_3)_2$$

(24)

In addition, the reaction has been employed for the preparation of ethyl chloroethynylphosphate *(25)* [39].

$$(C_2H_5O)_2\overset{O}{\overset{\|}{P}}-C\equiv C-Cl \xrightarrow[25^\circ C]{N(C_2H_5)_3} (C_2H_5O)_2\overset{O}{\overset{\|}{P}}-C\equiv C-\overset{\oplus}{N}(C_2H_5)_3\overset{\ominus}{Cl}$$

(25)

$$\xrightarrow[10\ min,\ 80^\circ C]{C_6H_6(-C_2H_5Cl)} (C_2H_5O)_2\overset{O}{\overset{\|}{P}}-C\equiv C-N(C_2H_5)_2$$

3.5. Ynamines by Alkylation of Lithium Aminoacetylides

J. Ficini and *C. Barbara* [40] prepared the now easily accessible lithium aminoacetylides *(26a)* and *(26b)* and converted them in good yields into ynamines by

$$C_6H_5(CH_3)N-C\equiv C-Li \xrightarrow{C_4H_9Br} C_6H_5(CH_3)N-C\equiv C-C_4H_9$$

(26a) 76%

$$(C_2H_5)_2N-C\equiv C-Li \xrightarrow{CH_3O-Tosyl} (C_2H_5)_2N-C\equiv C-CH_3$$

(26b) 50%

alkylation in hexamethyl phosphorus triamide (HMPT) or in HMPT/ether, thereby opening a general route to ynamine derivatives.

4. Ynamines by Elimination

4.1. Elimination of Halogen from α,β-Dichloroenamines

α,β-Dichloroenamines *(27a)* and *(27b)* are readily available. *J. Ficini* and *C. Barbara* [40] have shown that ynamines can be obtained in high yields from these compounds with n-butyl-lithium.

$$C_6H_5-\underset{Cl}{\overset{|}{C}}=\underset{Cl}{\overset{|}{C}}-N(C_2H_5)_2 \xrightarrow[-Cl_2]{Li-C_4H_9} C_6H_5-C\equiv C-N(C_2H_5)_2$$

(27a) 70%

$$Cl-\underset{Cl}{\overset{|}{C}}=\underset{Cl}{\overset{|}{C}}-N(CH_3)C_6H_5 \xrightarrow{2\ Li-C_4H_9} Li-C\equiv C-N(CH_3)C_6H_5\ [*]$$

(27b)

$$\xrightarrow{H^\oplus} HC\equiv C-N(CH_3)C_6H_5 \quad 72\%$$

4.2. Ynamines by Dehydrohalogenations from Dihalogenoalkylamines

It should be formally possible to synthesize ynamines from the following dihalogenoalkylamines:

(i) Amide chlorides $R-CH_2-CCl_2NR_2^1$.

(ii) Halogen adducts of enamines $R-CHX-CHXNR_2^1$ *(28)* or $R-C(NR_2^1)X-CH_2X$ *(29)* (elimination of HX with onium rearrangement).

(iii) β,β-Dihalogenoalkylamines $RCX_2-CH_2NR_2^1$ or $R-CH(NR_2^1)-CHX_2$ (elimination of HX with onium rearrangement).

Ynamines have so far been synthesized mainly from amide chlorides [41], but compounds of the type *(28)* have also been used [20]. β,β-Dichloroalkylamines *(30)* have recently been prepared by the addition of *N*-chloroamines to chloroolefins [42],

$$R-\underset{Cl}{\overset{|}{C}}=CH_2 + ClNR_2^1 \longrightarrow R-CCl_2-CH_2NR_2^1 \quad (30)$$

but they are surprisingly inert and are unaffected by attempts to eliminate HCl with bases as strong as sodamide in liquid ammonia [43]. Interesting reactions have been observed with *N,N*-disubstituted lithium amides, but the desired ynamines were not formed [43].

Thus, for the present at least, practically the only dihalogenoalkylamines that can be used for the synthesis of ynamines are the amide chlorides, which

[37] *H. G. Viehe, S. I. Miller,* and *J. I. Dickstein,* Angew. Chem. *76*, 537 (1964); Angew. Chem. internat. Edit. *3*, 582 (1964).

[38] *J. v. Braun,* Ber. dtsch. chem. Ges. *33*, 1438 (1900); Liebigs Ann. Chem. *445*, 201 (1925).

[39] *B. I. Jonin* and *A. A. Petrov,* Ž. obšč. Chim. *35*, 2258 (1965).

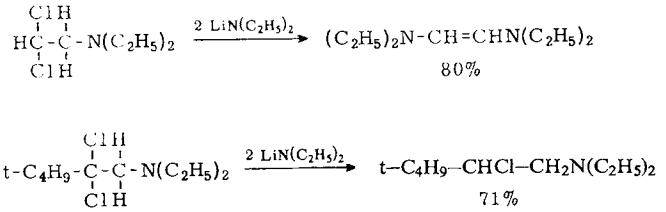
[40] *J. Ficini* and *C. Barbara,* Bull. Soc. chim. France *1964*, 871; *1965*, 2787.

[*] According to *J. Ficini, A. Dureault,* and *C. Barbara* (personal communication) these lithium acetylides undergo the expected reactions with carbonyl compounds.

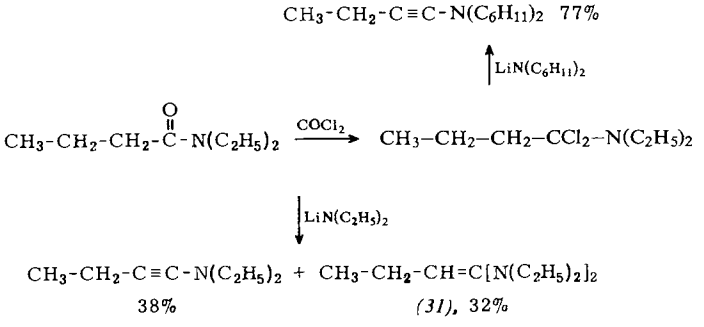
[41] *R. Buijle, A. Halleux,* and *H. G. Viehe,* Angew. Chem. *78*, 593 (1966); Angew. Chem. internat. Edit. *5*, 584 (1966).

[42] *R. S. Neale,* Tetrahedron Letters *1965*, 483.

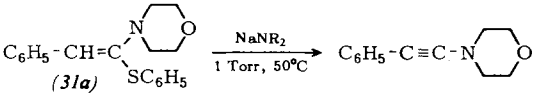
[43] *A. Halleux* and *H. G. Viehe,* unpublished.



are readily obtainable from tertiary amides and phosgene [27]. Several ynamines have been prepared from amide chlorides and *N,N*-disubstituted lithium amides [41]. The ynamine formation frequently proceeds smoothly, depending on the amide chloride and the base, but is often accompanied by the formation of alkenylidenediamines *(31)*.

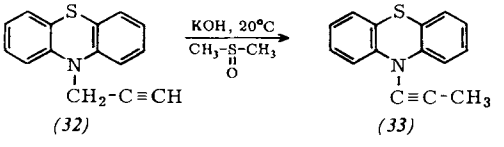


The elimination of thiolate from ketene *S,N*-acetals *(31a)* with alkali metal amides has been described as another method for the synthesis of ynamines [41] [*].

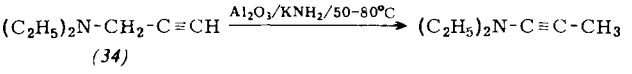


5. Ynamines by Isomerization of Propargylamines

The first (accidental) ynamine synthesis [11] was the reaction of phenothiazine with sodium hydride and propargyl bromide. This reaction could involve the intermediate formation of propargylamine *(32)*, which was later isolated under different conditions [12] and which isomerizes to the ynamine *(33)* in the presence of potassium hydroxide.



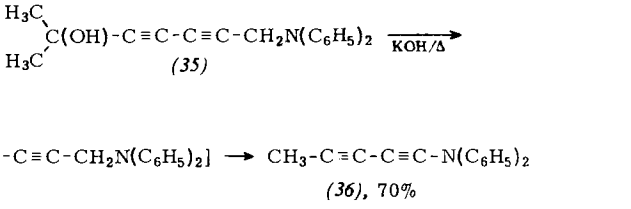
Only tertiary *N*-arylpropargylamines can isomerize to ynamines under such mild conditions [12]. *N,N*-Diphenylpropargylamine gives the ynamine in a yield of 51%. However, catalysts have recently been found



[*] The reaction of t-butylate with enamines and chloroform constitutes an interesting synthesis of enynamines – *T. C. Shields, W. E. Billups,* and *A. N. Kurtz* (Angew. Chem., in press).

that also permit the preparation of ynamines in high yields (60 to 90%) from the readily obtainable *N,N*-dialkylpropargylamines, *e.g. (34)* [44].

N-Arylmethyldiynamines *(36)* have been obtained from the dimethylcarbinols *(35)*, which can be cleaved under the isomerization conditions [12].



6. Properties of the Ynamines

More than fifty ynamines have now been prepared [1]. The substituents on the nitrogen may be alkyl, aryl, or heterocyclic groups, while the substituents on the acetylenic carbon may be alkyl or aryl groups, H, lithium, NR_2, SR, $PO(OC_2H_5)_2$, or halogen.

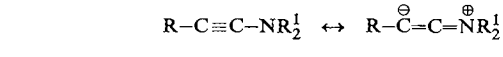
Despite their high reactivity, the ynamines are generally stable liquids or crystals. However, compounds with special substituents, such as the halogenoynamines, are very unstable and have not yet been obtained in the pure state [20,45]. Consequently, the (so far unreproducible) synthesis of a bromoynamine [46] by heating of *N,N*-diethylbromoacetamide with PCl_5 appears improbable.

Like the fluoroalkynes and the acetylene ethers, the ynamines generally give a stronger C≡C absorption in the IR spectrum than their group homologues (*e.g.* with Cl, S, P as substituents). For most substituted ynamines, this absorption band is situated at 4.5 μ (2220 cm^{-1}); it is displaced in particular by *C* substitution, SR causing a shift to about 4.6 μ (2173 cm^{-1}), H to about 4.7 μ (2127 cm^{-1}), and lithium to about 4.9 μ (2050 cm^{-1}).

7. Reactions of the Ynamines

7.1. General Reaction Behavior

Ynamines are characterized by the possibility of resonance interaction between the lone pair of electrons on the nitrogen and the triple bond.

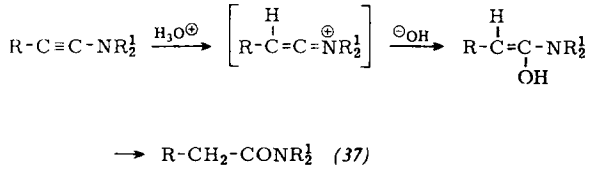


The ynamines are therefore effective nucleophilic reagents. However, they also react as if they were electrophiles, particularly on acid catalysis, though, in reality, reactions of this type probably proceed *via* ketene-iminium structures. An example of such a

[44] *A. Hubert* and *H. G. Viehe*, unpublished.

[45] *J. Ficini*, personal communication.

[46] *Yu. Yu. Tsmur* and *V. I. Ivanik*, Ž. obšč. Chim. *33*, 1653 (1963).



$\longrightarrow$ R-CH_2-$CONR_2^1$ *(37)*

reaction is the exothermic acid-catalysed addition of water [10,47] to form amides *(37)*.

The addition of alcohols also proceeds readily under acidic conditions or with BF_3-ether as a catalyst [48,49]; however, it is also possible to add on *e.g.* methanol under basic conditions [20]. In the acid-catalysed addition of various primary and secondary amines, strongly basic amines evidently hinder the formation of the ketene-iminium structure and thus react more slowly than their less basic counterparts [48].

The reaction behavior of the ynamines is strongly dependent on the substituents. Thus *N,N*-diarylynamines are weaker nucleophiles than the *N,N*-dialkyl compounds [40].

Ynamines whose substituents permit the formation of an allene structure frequently react less readily than ynamines with *C*-substituents such as phenyl, t-butyl, or SR. Consequently, compounds having these last-named substituents should always be used to test an unknown ynamine reaction.

7.2. Hydration of Ynamines

7.2.1. Formation of Acid Anhydrides by Ynamines

Ynamines are superior to dicyclohexylcarbodiimide and ethoxyacetylene as dehydrating agents for the formation of acid anhydrides (Table 1).

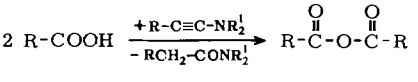


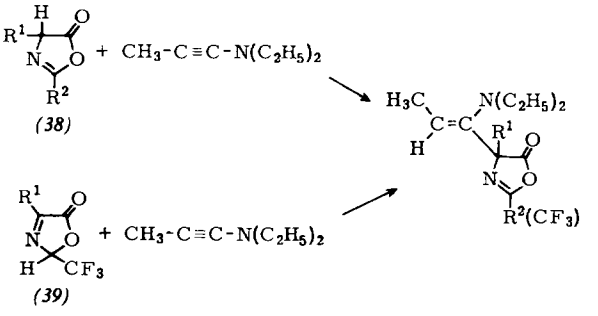
Table 1. Yields in the formation of acid anhydrides with ynamines, dicyclohexylcarbodiimide, and ethoxyacetylene (5 min at 10 °C in benzene).

R	Anhydride formation with			
	C_6H_5–C≡C–$N(CH_3)_2$	t-C_4H_9–C≡C$N(CH_3)_2$	$(C_6H_{11}$–N=$)_2$C	HC≡C–OC_2H_5
n-C_3H_7	96 %	93 %	70 %	0 %
C_6H_5	98 %	97 %	63 %	0 %

7.2.2. Peptide Synthesis and Formation of Amides with Ynamines [47,50,51]

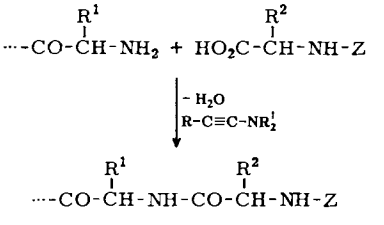
The use of ynamines for the synthesis of peptides has been described in several articles [47,50,51]. The yields reported are almost quantitative, but the reaction conditions must be rigidly controlled to avoid racemization [52]. Thus in the stepwise synthesis of polypeptides, the peptide chain carries the free amino group, while the amino acid to be attached carries the free acid group in order to avoid racemization by azlactone formation. According to *F. Weygand*, it has not so far been possible to avoid partial racemization in the linking of two peptides with ynamines.

Side reactions were observed in some cases [50,52]. Thus the ynamines can add onto intermediate oxazol-5-ones *(38)* or 2-trifluoromethylpseudooxazol-5-one *(39)*.



Another side reaction, *i.e.* the addition of *N*-acylamino acid anhydrides to ynamines, is described in Section 7.5.

One advantage claimed for the ynamines as compared with the widely used carbodiimides in the synthesis of



peptides, apart from their greater reactivity, is the greater ease of processing of the reaction mixture [51,52]. Ynamines give *N,N*-disubstituted amides, which can generally be easily extracted from the peptides with petroleum ether, whereas the disecondary urea derivatives formed from carbodiimides can often be removed only by recrystallization of the peptides.

7.2.3. Ester Formation with Ynamines

Since ynamines react with an excess of dry HCl to give amide chlorides, which convert alcohols into alkyl chlorides [27], it is not surprising that HCl, HBr, and HF react with alcohols in the presence of ynamines to

[47] *R. Buijle* and *H. G. Viehe*, Angew. Chem. *76*, 572 (1964); Angew. Chem. internat. Edit. *3*, 582 (1964).

[48] *H. G. Viehe, R. Fuks*, and *M. Reinstein*, Angew. Chem. *76*, 571 (1964); Angew. Chem. internat. Edit. *3*, 581 (1964).

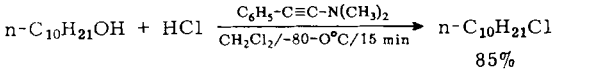
[49] *J. Ficini* and *C. Barbara*, Tetrahedron Letters *1966*, 6425.

[50] *F. Weygand, W. König, R. Buijle*, and *H. G. Viehe*, Chem. Ber. *98*, 3632 (1965).

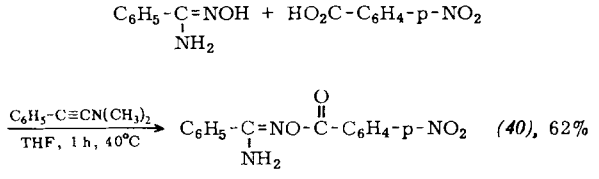
[51] *F. Weygand*, personal communication; *F. Weygand, W. Steglich, W. König*, and *G. Höfle*, Chem. Ber., in press.

[52] *A. S. Van Mourik, E. Harryvan*, and *J. F. Arens*, Recueil Trav. Chim. Pays-Bas *84*, 1 (1965).

form alkyl halides[48]. However, it is not yet certain whether the reaction proceeds *via* the amide chloride or the α-chloroenamine.

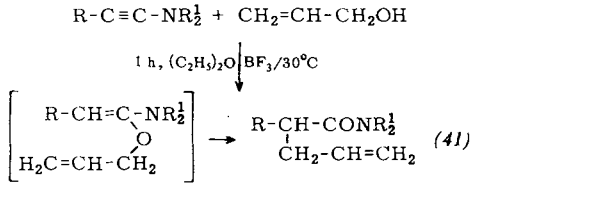


The synthesis of activated esters, *e.g.* *(40)*, which is easy to achieve with ynamines, and which is useful in peptide chemistry, could be of practical importance[1,20].

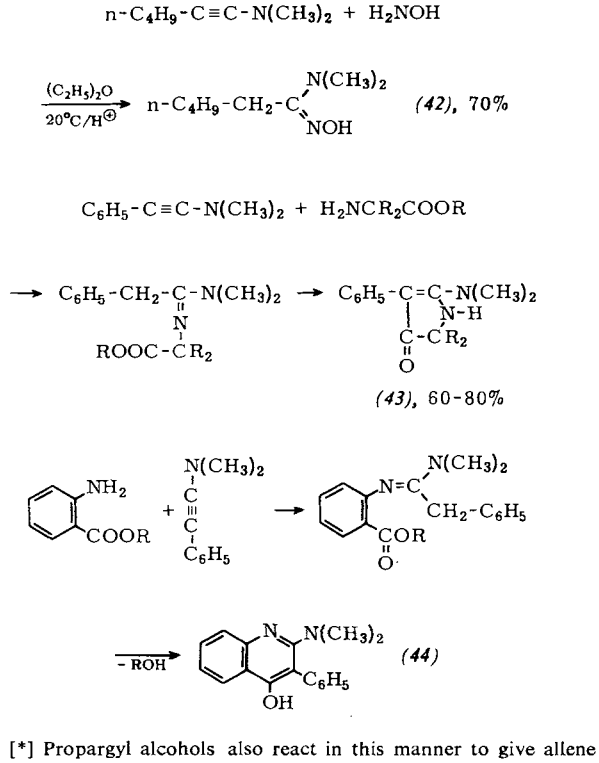


7.3. Addition of Alcohols and Amines to Ynamines

The easy addition of alcohols to ynamines is preparatively useful in the case of allyl alcohols, since subsequent Claisen rearrangement yields γ-acrylamides *(41)*[49][*].



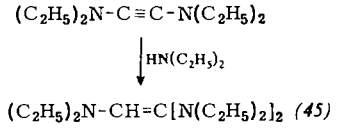
A similar reaction sequence is occasionally observed with allylamines[49], but the rearrangement occurs at about 250 °C[*].



[*] Propargyl alcohols also react in this manner to give allene amides — *J. Ficini* and *J. Pouliqueu*, personal communication.

More commonly used reactions are the addition of primary and secondary amines to amidines *(42)* and to alkenylidenediamines[48]. These reactions are particularly useful for the formation of derivatives of secondary amines and for the incorporation of amino acids into heterocycles *(43)*, *(44)*[53].

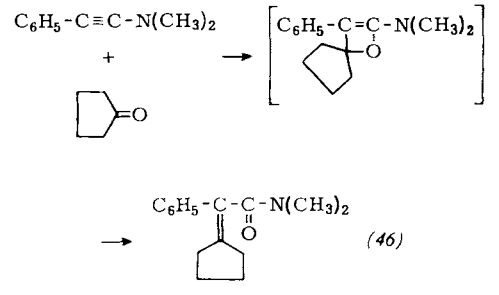
Ynediamines react with secondary amines to give high yields of enetriamines *(45)*[26], which had previously been unknown, and which are interesting for comparison with the enetetramines.



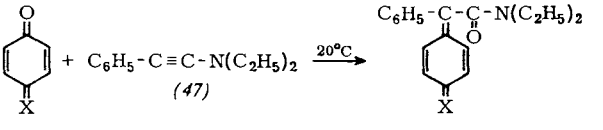
7.4. Addition Reactions of Ynamines

7.4.1. Addition Reactions with Carbonyl Compounds and their Imines

Ynamines react more readily than other acetylenes with aldehydes, ketones, and reactive carbonyl compounds[54], such as ethyl formate and dimethylformamide, to give derivatives of α-acrylamides *(46)*. With BF_3 or acid catalysts in ether, the reaction is generally exothermic.



Allylamines can be readily obtained from the α-acrylamides by reduction with lithium aluminum hydride. The condensation of ynamines with acid anhydrides[51] (see Section 7.5) and with *p*-quinone and *N*-phenyl-*p*-quinonimine is also of preparative interest. The condensations of these last two compounds with diethylphenylethynylamine *(47)* are exothermic in benzene, and require no catalyst[55][*].



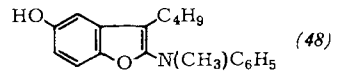
[53] *R. Fuks* and *H. G. Viehe*, unpublished. Review: *R. Fuks* and *H. G. Viehe* in [1].

[54] *R. Fuks*, *R. Buijle*, and *H. G. Viehe*, Angew. Chem. *78*, 594 (1966); Angew. Chem. internat. Edit. *5*, 585 (1966).

[55] *J. Ficini* and *A. Krief*, Tetrahedron Letters *1967*, 2497.

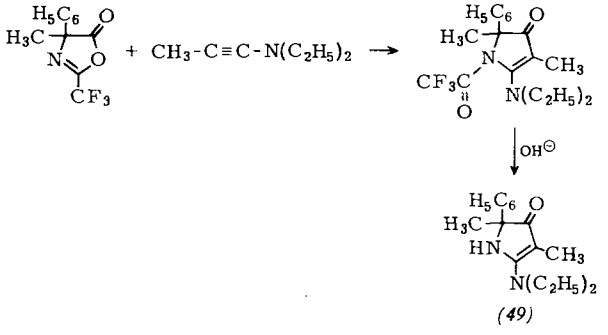
[*] *J. Ficini* and *A. Krief* (personal communication) have condensed ynamines with aryl isocyanates to give 6-membered ring systems.

p-Quinone and n-C_4H_9–C≡C–$N(CH_3)C_6H_5$ give the benzofuran derivative *(48)* in 13 % yield, together with polymers.



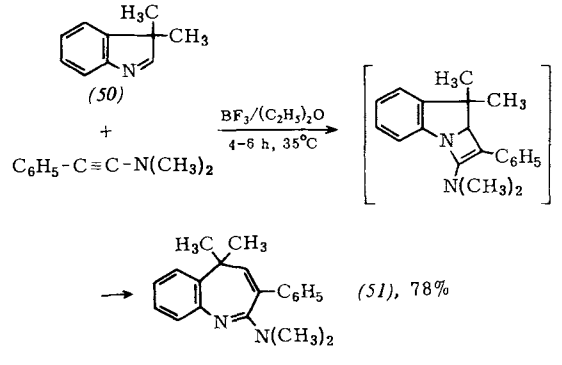
(48)

The reaction of 4,4-disubstituted oxazol-5-ones with ynamines yields 3-oxopyrroline derivatives [51], *e.g. (49)*.



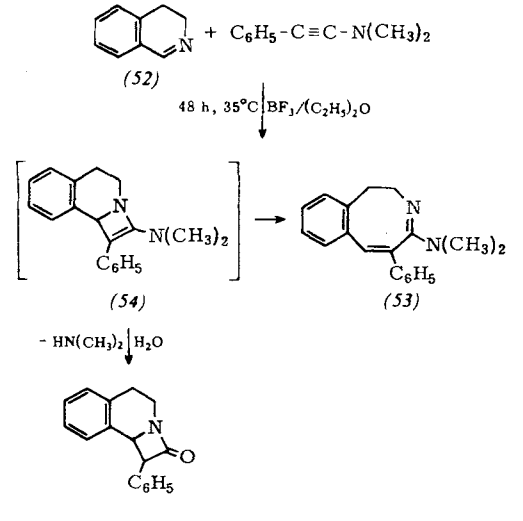
(49)

The imines of the carbonyl compounds mentioned here react in the same manner as the carbonyl compounds themselves, though generally less readily. The condensation of ynamines with cyclic imines leads to ring expansion [53,54].



(51), 78%

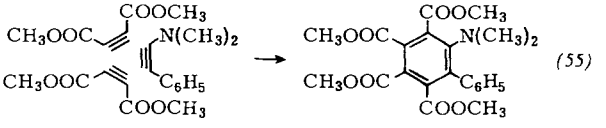
Dihydroisoquinoline *(52)* reacts with expansion of the six-membered hetero ring into the eight-membered ring of *(53)*. The intermediate azetidine *(54)* can be detected in this case by competitive hydrolysis [53].



(54) *(53)*

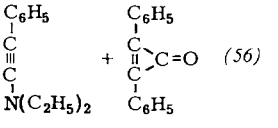
7.4.2. Addition Reactions with Polar C≡C and C=C Bonds

Whereas enamines react with esters of acetylenedicarboxylic acid, to give cyclobutene derivatives, most of which are unstable [56], the reaction with ynamines yields benzene derivatives, *e.g. (55)* [40,48].

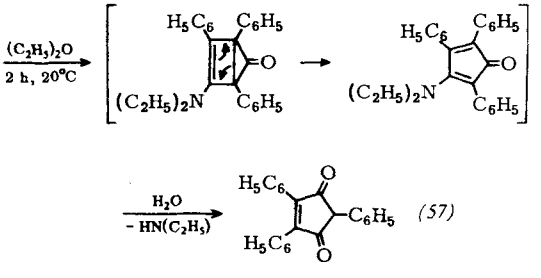


(55)

1,3,4-Triphenylcyclopentene-2,5-dione *(57)* can be synthesized from diphenylcyclopropenone *(56)* [57].



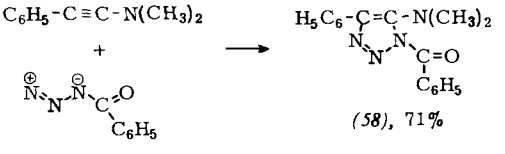
(56)



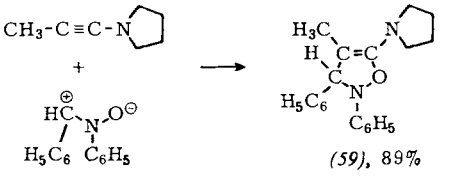
(57)

7.4.3. Addition of 1,3-Dipoles

As expected, the readily polarizable ynamines react with 1,3-dipoles to give compounds of the types *(58)* and *(59)* in good yields. For example, the reactions leading to *(58)* and *(59)* [54] proceed in accordance with thoroughly investigated models [58].



(58), 71%



(59), 89%

7.5. Acylation of the Ynamines

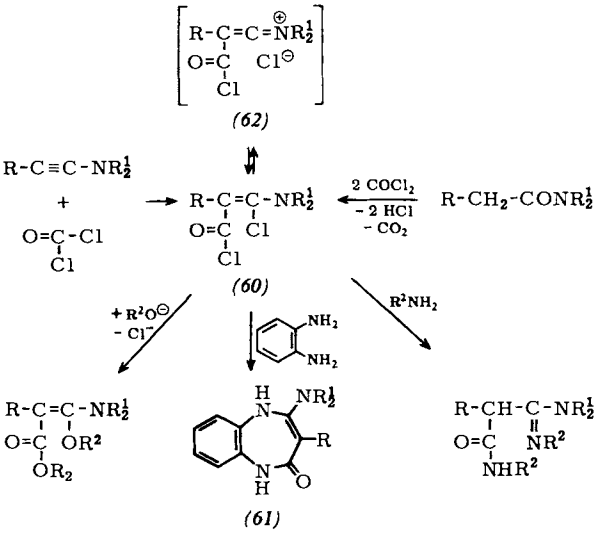
Ynamines react with chlorides of organic and inorganic acids, generally with almost quantitative addition. The phosgene adducts *(60)*, which can be obtained from

[56] *K. C. Brannock, R. D. Burpitt, V. W. Goodlett*, and *J. G. Thweatt*, J. org. Chemistry *38*, 1464 (1963); *29*, 818 (1964).

[57] *M. Franck-Neumann*, Tetrahedron Letters *1966*, 341.

[58] *R. Huisgen*, Angew. Chem. *75*, 604 (1963); Angew. Chem. internat. Edit. *2*, 565 (1963).

amides, are particularly useful. They act as bifunctional reagents toward amines and alkoxides, and so permit *e.g.* the synthesis of heterocycles such as *(61)* [59].

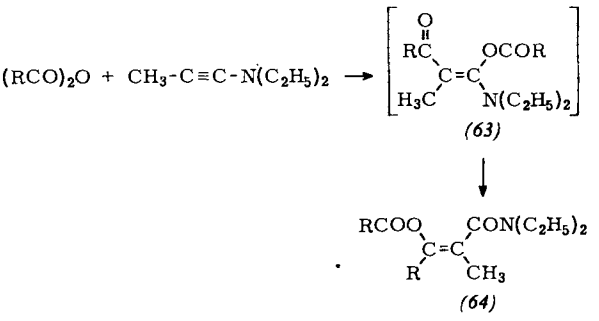


(62)

(60)

(61)

The new β-acyl-α-chloroenamines are very stable (they can often even be distilled) possibly because the β-acyl group opposes the formation of the polar ketene-iminium resonance structure *(62)* (see Section 7.6.).



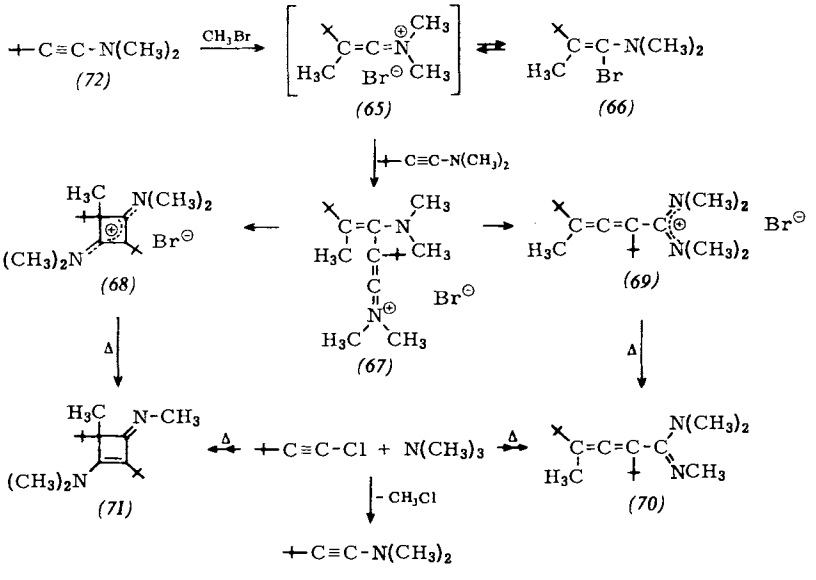
(63)

(64)

way from reaction with esters of amino acids. However, the side reaction can be avoided if the ynamine is added dropwise to the acid, and is not used in excess [50].

7.6. Dimerization of Ynamines with Nucleophiles [61]: Alkylation, Halogenation, and Protonation (with Strong Acids)

The alkylation of 3,3-dimethyl-1-butynyldimethylamine with methyl bromide provides an interesting comparison with the enamines. β-*C*-Alkylation probably leads to the inisolable ketene-iminium compound *(65)*, which probably exists in equilibrium with the



(72) *(65)* *(66)* *(68)* *(67)* *(69)* *(71)* *(70)*

Acid anhydrides add on smoothly to ynamines in the same manner as the acid chlorides [51]. However, the initially formed β-acyl-α-acyloxyenamines *(63)* are unstable, and immediately rearrange under the reaction conditions to give enol esters of the β-keto acid dialkylamides *(64)* [60].

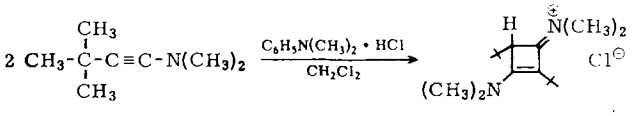
The enol esters *(64)* can also be prepared from the β-acyl-α-chloroenamines *(60)* and carboxylates [51]. The acylation of ynamines by anhydrides is particularly important in peptide syntheses, since the intermediate *N*-acylamino acid anhydrides can be withdrawn in this enamine structure *(66)*. With a further mole of ynamine, the enamine-ketene-iminium salt *(67)*, which is capable of intramolecular *C*- and *N*-alkylation, should be formed. The salt mixture, which is isolated in a yield of 73 %, contains 35 % of cyclobutenecyanine salt *(68)* and 65 % of the allene amidinium salt *(69)*. The two salts can be separated by crystallization. Pyrolysis of *(69)* leads to dealkylation and formation of the allene-amidine *(70)*, whereas the cyanine salt *(68)* decomposes to give aminocyclobutenimine *(71)*.

[59] *R. Buijle* and *H. G. Viehe*, unpublished.

[60] *R. B. Woodward* and *R. A. Olofson*, J. Amer. chem. Soc. *83*, 1007 (1961); Tetrahedron Suppl. No. 7, 415 (1966).

[61] *H. G. Viehe, R. Buijle, R. Fuks, R. Merényi*, and *J. M. F. Oth*, Angew. Chem. *79*, 53 (1967); Angew. Chem. internat. Edit. *6*, 77 (1967).

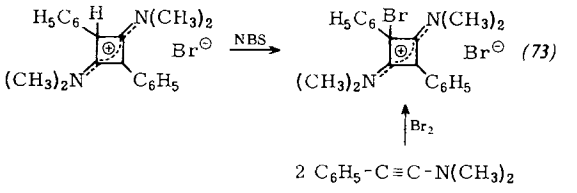
As can be seen from the above scheme, the compounds *(70)* and *(71)* are also obtained as by-products in the synthesis of ynamines from t-butylchloroacetylene and trimethylamine (which is described in Section 3.4.). On slow addition (to avoid amide chloride formation and side reactions) of strong acids to the ynamine *(72)*, the only product formed in the presence of tertiary amines, *e.g.* dimethylaniline, is the salt *(73)* (yield 95 %) corresponding to the cyclobutene cyanine *(68)* – the reaction probably takes this course for steric reasons [53].



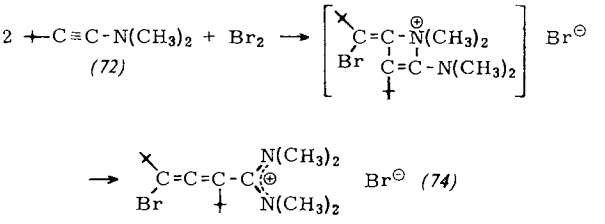
(72) *(73)*, 95%

The cyclobutene cyanine can be readily synthesized in the presence of HBF_4 even without special precautions [49,61], possibly because the weakly nucleophilic $BF_4^{\ominus}$ anion makes the conversion of the ketene-iminium structure *(65)* into the less polar enamine structure *(66)* impossible.

A number of phenylethynyldialkylamines react smoothly with strong acids to form the corresponding cyanines, which can be converted into bromine derivatives *(73)* by treatment with *N*-bromosuccinimide (NBS); *(73)* can also be obtained by direct bromination of the ynamine in dioxane [53]:



Bromination of the t-butylethynylamines instead of the phenyl compounds leads to only the allene amidinium salts *(74)* in yields of up to 87 %; this is apparently due to steric factors [53].



(74)

I am grateful to Prof. Weygand for stimulating discussions and for the exchange of information on peptide reactions and to Prof. Jacqueline Ficini for interesting discussions and for the communication of unpublished results. I should also like to express my thanks to my colleagues, particularly R. Buijle, S.Y. Delavarenne, E. Franchimont, R. Fuks, A. Gerondal, A. Halleux, A. Hubert, M. Reinstein, W. Rennerts, and P. Valange, for their valuable contributions.

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Spatial Arrangement and Preparative Organic Synthesis

BY L. VELLUZ, J. VALLS, AND J. MATHIEU [*]

This review deals with the stereoselective formation of organic compounds. A number of examples of such syntheses, especially those of alkaloids and steroids, are described. An asymmetric synthesis, which avoids the intricacies and wastefulness of optical resolution, has been successful in a few cases only. The procedures of configurational change and of optical resolution, as well as the planning of multi-step stereoselective syntheses, are discussed.

From a technical or economic point of view the total synthesis of sterically intricate carbon compounds has become so important that a new field of preparative stereochemistry has been established which embodies a number of specially developed techniques. This is especially the case in the syntheses of alkaloids and antibiotics, and above all in the plant-scale production of hormonal steroids [1].

Three possible approaches are open for the synthesis of an optically active isomer of a compound having several asymmetric centers:

a) As is the case for most of the syntheses described in the literature, the reactions can be performed stereoselectively in the racemic series, optical resolution then being undertaken only at the end of the reaction sequence.

b) Conversely, for preparative purposes it is desirable to exclude unwanted optical isomers at the earliest possible stage, thus avoiding the expense, in time and effort, of having to treat a reaction mixture laden with products of no interest.

[*] Prof. L. Velluz, Dr. J. Valls, and Dr. J. Mathieu
Centre de Recherches Roussel-Uclaf
35 Boulevard des Invalides
Paris 7è (France)

[1] *L. Velluz, J. Valls,* and *G. Nominé*, Angew. Chem. 77, 185 (1965); Angew. Chem. internat. Edit. 4, 181 (1965).

c) The resolution problem can be theoretically avoided by asymmetric synthesis, but this promising method has not yet been applied on a truly preparative scale.

Thus it is only after a thorough study of the stereochemical possibilities that the chemist finally adjusts the sequence of the reactions, usually after a consideration of convergence, and the economics involved.

The present paper is devoted to the study of this practical aspect of the relations between spatial arrangement and preparative organic synthesis.

In addition to examples taken from the literature we have referred in several instances to investigations concerning the total synthesis of steroids that have been carried out at our research center during the past ten years[1], and in which measurements of optical circular dichroism[2,3] contributed to the solution of a number of stereochemical problems.

I. Selective Creation of Chiral Carbon Atoms[*]

Asymmetric centers arise mostly as the result of a conversion of trigonal carbon atoms into tetragonal ones at the site of unsaturated functions such as carbonyls, enols, enamines, and at isolated or conjugated olefinic double bonds.

In order to predict the stereochemical course of these conversions, the following factors must be considered:

a) Initial conformation of the molecule.

b) Ease of approach of reagents.

c) Energy of the transition states.

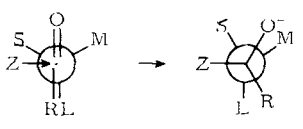
d) Stability of the reaction product.

It is necessary also to consider the stereochemical possibilities offered by

e) indirect methods.

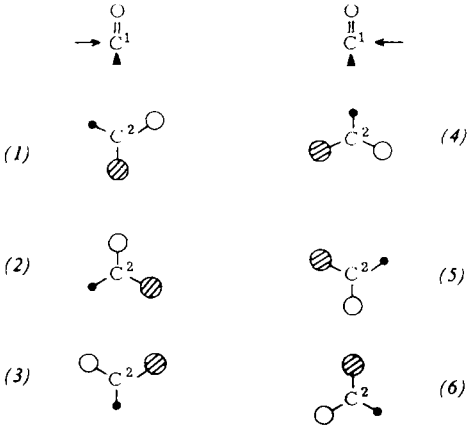
a) Initial Conformation

The importance of the initial conformation of the molecule is illustrated by the semi-empirical rule of *Cram*[4], according to which the preponderant isomer is the result of attack from the least hindered side, *i.e.* as in Scheme 1 when the carbonyl group is already situated between the two smallest substituents.



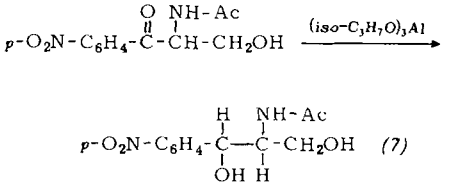
Scheme 1. Relation between direction of attack and size of substituents. S = smallest, M = medium sized, and L = largest substituent.

However, it must be noted, with respect to the six characteristic conformations of a carbonyl compound whose α-arbon atom bears three groups of different size, that the attack on the conformations *(2)* and *(3)* from the least hindered side would yield the same isomer as that resulting from attack on *(1)*, whereas the other epimer would result from an attack, under the same conditions, on a conformation such as *(4)*, *(5)*, or *(6)*.



In other respects, Cram's rule must be modified if a substituent complexes the reagent and thereby enforces a particular conformation at the time of attack[4–7].

This influence is especially encountered in the synthesis of chloramphenicol where it favors formation of the intermediate *(7)* in the *threo* form[8].



Johnson and *Malhotra* have also shown the importance of the initial conformation of the molecule in cyclic compounds and in the case of exo- or endocyclic enols[9,10]. In structures of type *(8)*, steric interaction between R and Z leads to a conformational inversion where R becomes axial. This phenomenon was utilized for a total synthesis of antibiotics of the cycloheximide series such as *(10)*, where the final configuration resulted from the acylation of an enamine in a half-chair conformation of the type *(8b)*[11,12]. The form

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[*] For the definition of the word "chiral" cf. *R. S. Cahn*, *C. Ingold*, and *V. Prelog*, Angew. Chem. *78*, 413 (1966), a note therein on p. 415; Angew. Chem. internat. Edit. *5*, 385 (1966), also p. 386.

[4] *D. J. Cram* and *F. A. Abd Elhafez*, J. Amer. chem. Soc. *74*, 5828 (1952).

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[6] *J. H. Stocker*, *P. Sidisunthorn*, *B. M. Benjamin*, and *C. J. Collins*, J. Amer. chem. Soc. *82*, 3913 (1960).

[7] *J. Sicher*, *M. Svoboda*, *M. Hrda*, *J. Rudinger*, and *F. Šorm*, Collect. czechoslov. Commun. *18*, 487 (1953).

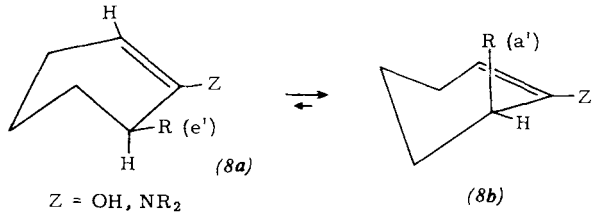
[8] *L. M. Long* and *H. D. Troutman*, J. Amer. chem. Soc. *71*, 2473 (1949).

[9] *F. Johnson* and *S. K. Malhotra*, J. Amer. chem. Soc. *87*, 5492 (1965); *S. K. Malhotra* and *F. Johnson*, *ibid. 87*, 5493 (1965).

[10] *S. K. Malhotra* and *F. Johnson*, J. Amer. chem. Soc. *87*, 5513 (1965).

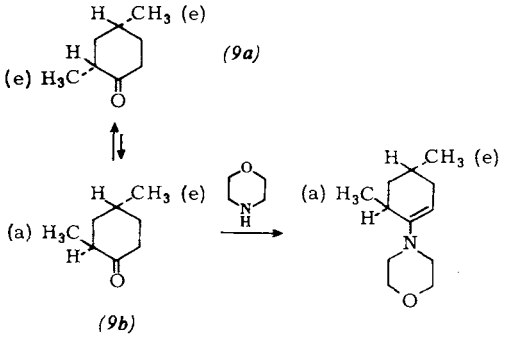
[11] *F. Johnson*, *N. A. Starkovsky*, *A. C. Paton*, and *A. A. Carlson*, J. Amer. chem. Soc. *86*, 118 (1964).

[12] *H. J. Schaeffer* and *V. K. Jain*, J. org. Chemistry *29*, 2595 (1964).

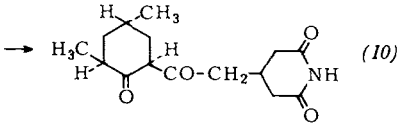


Z = OH, NR_2

(8a) *(8b)*



(9a) *(9b)*



(10)

(9b) corresponding to *(8b)* is formed by the prior epimerization of the 2-methyl group from the equatorial α-orientation to the β-axial orientation.

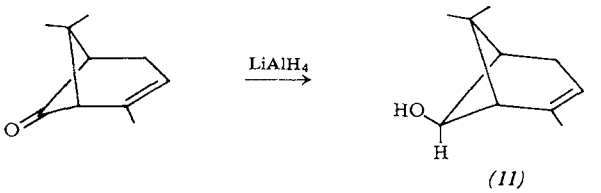
b) Ease of Approach of Reagents

The influence of steric factors on the approach of reagent has been studied, especially by *Barton* and *Dauben*. However, it remains a subtle and much-discussed problem, even in such simple cases as the cyclohexanones [1, 13–16].

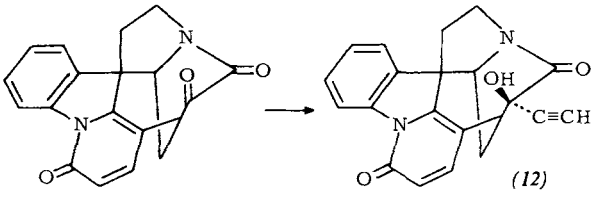
From the preparative point of view, however, the presence or absence of hindrance on one side of the molecule remains the safest means of governing the direction of attack.

In the case of the carbonyl compounds the difference of accessibility allows selective reactions, *e.g.* in a reduction step of the synthesis of chrysanthenol *(11)* [17] or an ethynylation step in the synthesis of an intermediate of strychnine *(12)* [18], to take place.

At the site of olefinic double-bonds this steric factor acts as well for *cis* reactions, such as the stereoselective hydroboration to give the intermediate *(13)* in the synthesis of valeranone [19] as it does for *trans* reac-

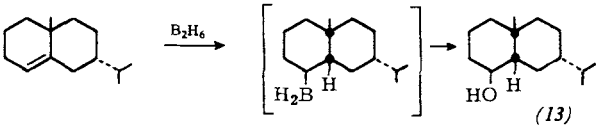


(11)

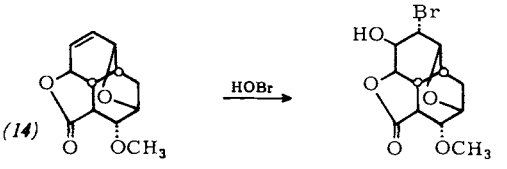


(12)

tions. Its importance in *trans* reactions is exemplified by the synthesis of reserpine [20] where the hindrance of the concave side of a folded molecule *(14)* leads to attack of the convex side.

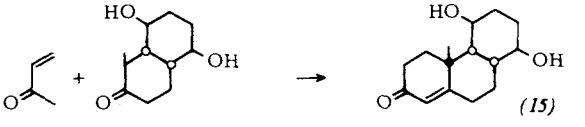


(13)



(14)

The folding of molecules can also determine the mode of attack in reactions of enols, as is shown by *Sarrett*'s synthesis of cortisone, where the tricyclic structure *(15)* is obtained *via* a stereoselective attack of this type [21].



(15)

In the presence of polar substituents unexpected stereoisomers may be formed if the polar assistance prevails over steric influences. This phenomenon has been studied by *Henbest* and others for the attack on olefins by peracids [22–24] or by carbenes [25–28]. It was

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[19] *J. A. Marshall, W. I. Fanta*, and *G. L. Bundy*, Tetrahedron Letters *1965*, 4807.

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[23] *H. B. Henbest, B. Nicholls, W. R. Jackson, R. A. L. Wilson, N. S. Crossley, M. B. Meyers*, and *R. S. MacElhinney*, Bull. Soc. chim. France *1960*, 1365.

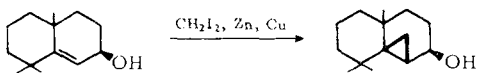
[24] *K. Takeda, K. Hamamoto, K. Sasaki, N. Maezono*, and *A. Murabayashi*, Steroids *2*, 27 (1963).

[25] *S. Winstein* and *J. Sonnenberg*, J. Amer. chem. Soc. *83*, 3235 (1961).

[26] *W. G. Dauben* and *G. H. Berezin*, J. Amer. chem. Soc. *85*, 468 (1963).

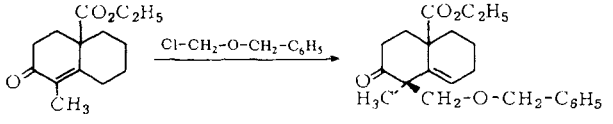
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[28] *R. Ginsig* and *A. D. Cross*, J. Amer. chem. Soc. *87*, 4629 (1965).



applied in an essential step of the synthesis of thujopsene [29].

A similar example of an hydroxyl-assisted reaction has been used by *Woodward* for the reduction of an intermediate product at the most hindered side of the molecule during the synthesis of strychnine [18]. Another example is provided bythe inversion of the direction of alkylation of a bicyclic derivative *(16)* under the directing effect of a carbethoxyl group [30].



(16)

c) Energy of the Transition States

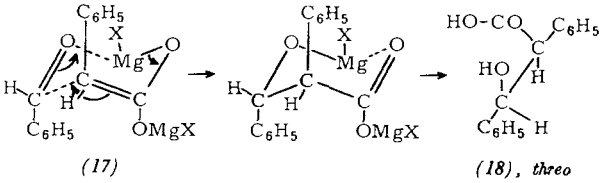
A number of transition states correspond to the different possible modes of approach of the reagent. The structure of the energetically favored state often plays a decisive role in the stereochemistry of the addition of reagent. Furthermore, according to the Curtin-Hammett principle this role is in general more important than the influence of the initial conformation of the molecule.

Accurate analysis of the transition states corresponding to the transformation of unsaturated functions is not possible because of the lack of knowledge of their true nature. Too little is known about the degree of hybridization of the atoms which can be either close to the initial trigonal state or close to the final tetragonal one.

Nevertheless, despite these difficulties an approximate analysis is often possible [1]. The energy level of these transition states depends on the stereoelectronic factors originating from the principle of maximum overlap of the reacting orbitals, and on steric or polar interactions which lead to internal and torsional stress.

Thus, steric interactions occur at the level of the transition state of hydroxy-alkylation reactions of acyclic compounds, according to a scheme whose general validity was emphasized by *Toromanoff* [31].

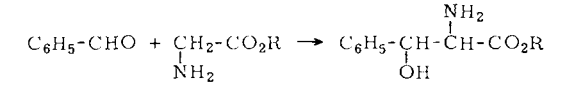
An example of this is the condensation of the magnesium enolate of phenylacetic acid with benzaldehyde where the



(17) *(18), threo*

intermediate state *(17)*, in which the remoteness of the two phenyl groups reduces steric interaction, is favored and leads to the *threo* compound *(18)* [32].

These concepts are applicable to condensations between aromatic aldehydes and glycine derivatives (sodium salts or esters) which yield derivatives of phenyl serine [33, 34, 35]. This type of condensation occurs in a synthesis of chloramphenicol [36, 37].



(19), threo

During our investigations on cyclic compounds *Valls* and *Toromanoff* analysed the stereochemistry of the attacks on cyclohexane enols and olefins already studied by *Corey* [38]. *Valls* and *Toromanoff* considered the conformations of the transition states according to the underlying steric, polar, and stereoelectronic interactions. It is well known that this study has led to the concept of "antiparallel" and "parallel" attack [1, 39]. These modes of attack play a part *e.g.* in the total synthesis of steroids, especially in the creation of the asymmetric centers at C-10 and C-13 [1].

The alkylation of the 13-position of D-homo-18-nor-steroidal structures, studied by *Johnson* during the "hydrochrysene synthesis", shows especially that its stereochemical course can be controlled by influencing the transition-state conformation. This effect is obtained by the introduction of a double-bond into ring C; the results are readily interpreted with the aid of the theoretical concepts proposed by *Bucourt* [1].

Toromanoff stressed that stereochemical control of the transition states in the case of reactions of α,β-ethylenic carbonyl functions is of still more importance, both when 1–4 and when 1–2 additions are involved [40, 41].

Such stereochemical control is evident in the 1,2-addition of hydride ion to 3,5-dimethyl-2-cyclohexen-1-one *(20)*, which leads to a preponderance of the *cis*-isomer (anti-parallel attack) [42], and in the 1,4-addition of methyl magnesium iodide to 5-methyl-2-cyclohexen-1-one *(21)* [43], where the perpendicular anti-parallel attack on the most stable envelope form [*]

[29] *W. G. Dauben* and *A. C. Ashcraft*, J. Amer. chem. Soc. *85*, 3673 (1963).

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[40] *E. Toromanoff*, Bull. Soc. chim. France *1962*, 708.

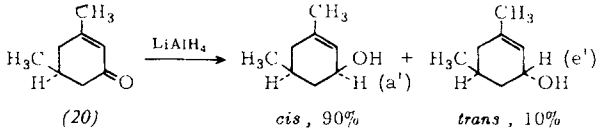
[41] *E. Toromanoff*, Bull. Soc. chim. France *1966*, 1445.

[42] *G. Asato*, Dissertation, Purdue University, 1961; Dissertation Abstr. *22*, 2186 (1962).

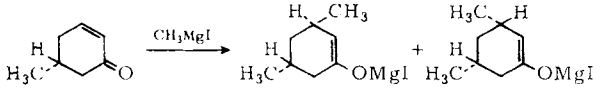
[43] *N. L. Allinger* and *C. K. Riew*, Tetrahedron Letters *1966*, 1269.

[*] For an explanation of "envelope form" see *H. H. Lau*, Angew. Chem. *73*, 423 (1961).

(CH_3 equatorial) favors access to an enolate in half-chair form. The steric aspects of a great number of angular alkylations of polycyclic derivatives of this type can be interpreted in a similar manner.



(20) cis, 90% trans, 10%



(21) 95% 5%

d) Stability of the Reaction Product

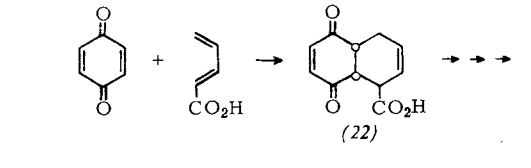
The action of various stereochemical factors at the site of the attacked conformation, the influence of approaching reagents, and the energy of transition states, lead to a primary product the steric structure of which is not necessarily in agreement with that of the thermodynamically most stable isomer. If the structure of this thermodynamic isomer differs from that of the primary "kinetic" product, one must take into account the conditions of the reaction. If a reversible reaction is possible and if the reaction conditions lead to an equilibrium, the "kinetic" product is converted to the "thermodynamic" isomer which can then be isolated.[1]. This aspect of the epimerization problem will be discussed in Section III.

e) Indirect methods

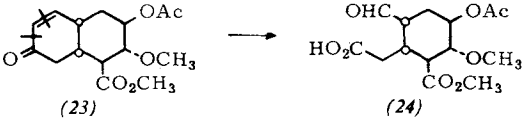
An ingenious method for the synthesis of a stereochemically complex molecule is that which involves the insertion of asymmetric carbon atoms into a rigid polycyclic system in which the supplementary rings are cleaved at a later, and suitable, time. This method is all the more avdantageous as some cyclization reactions are themselves highly stereoselective, for example the diene synthesis and the cyclization of polyenes.

Thus in the total synthesis of reserpine according to *Woodward*[20], the configurations of the five asymmetric centers of the monocyclic derivative *(24)*, the key product of the synthesis, have been obtained by transformation of the derivative *(22)* (obtained by diene synthesis) into *(23)*, followed by cleavage of the latter.

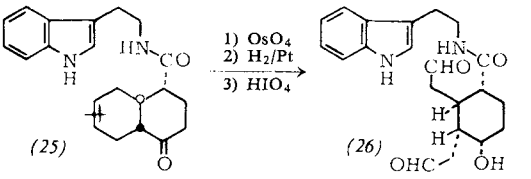
The same type of transformation is used in many other syntheses of alkaloids. In a synthesis of yohimbine by *Van Tamelen*[44] the intermediate *(26)* necessary for the formation of rings C, D and E has been obtained by oxidative cleavage of the derivative *(25)*.



(22)

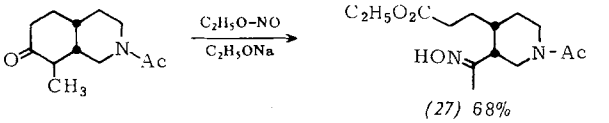


(23) (24)



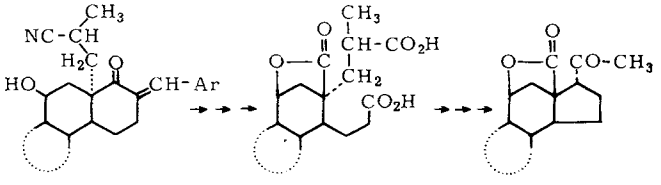
(25) (26)

The synthesis of quinine[45] affords another similar example of formation of a monocyclic compound *(27)* having two side chains in a *cis* configuration.



(27) 68%

In the steroid field this method has been used for the construction of the C,D-*trans*-hydrindan structure from the C,D-*trans*-decalin derivatives. *Johnson*'s "hydrochrysene synthesis" (cf. Section 1c)[1], and an aldosterone synthesis[46], in which a carbon atom of the chain introduced at 13α becomes part of the five-membered ring, serve as examples.



A similar example is the indirect method for the angular introduction of a carboxylic function in the synthesis of a derivative of podocarpanone[47].

II. Optical Resolution

In the synthesis of a natural product the main problem is the obtention of the desired compound in exactly the same structural form in which it occurs in nature.

Each of the three main methods of resolution have been used for preparative purposes (cf.[48–56]):

[44] *E. E. VanTamelen, M. Shamma, A. W. Burgstrahler, J. Wolinsky, R. Tamm*, and *P. E. Aldrich*, J. Amer. chem. Soc. *80*, 5006 (1958).

[45] *R. B. Woodward* and *W. von E. Doering*, J. Amer. chem. Soc. *67*, 860 (1945).

[46] *W. S. Johnson, J. C. Collins, R. Pappo*, and *M. B. Rubin*, J. Amer. chem. Soc. *80*, 2585 (1958).

[47] *R. F. Church, R. E. Ireland*, and *J. A. Marshall*, J. org. Chemistry *31*, 2526 (1966).

[48] *F. Ebel* in *K. Freudenberg*: Stereochemie. F. Deuticke, Leipzig-Vienna 1933, p. 553.

[49] *L. Velluz*, Substances Naturelles de Synthèse *9*, 119 (1954).

[50] *L. Eliel*: Stereochemistry of carbon compounds. McGraw-Hill, New York 1962, p. 31.

[51] *W. Theilacker* in Houben-Weyl: Methoden der Organischen Chemie. Georg Thieme Verlag, Stuttgart 1955, Vol. 1V-2, p. 505.

[52] *A. W. Ingersoll*, Org. Reactions *2*, 376 (1944).

[53] *J. P. Greenstein*: Advances Protein Chem. *9*, 121 (1954).

[54] *R. L. Shriner, R. Adams*, and *C. S. Marvel* in *H. Gilman et al.*: Organic Chemistry. Wiley, New York 1945, Vol. I, p. 214.

[55] *R. M. Secor*, Chem. Reviews *63*, 297 (1963).

[56] *M. Delépine* in *V. Grignard*: Traité de chimie organique. Masson & Cie, Paris 1935, Vol. 1, p. 843.

a) Methods without asymmetric agents.

b) Methods involving formation and separation of diastereoisomers.

c) Methods using selective reactions.

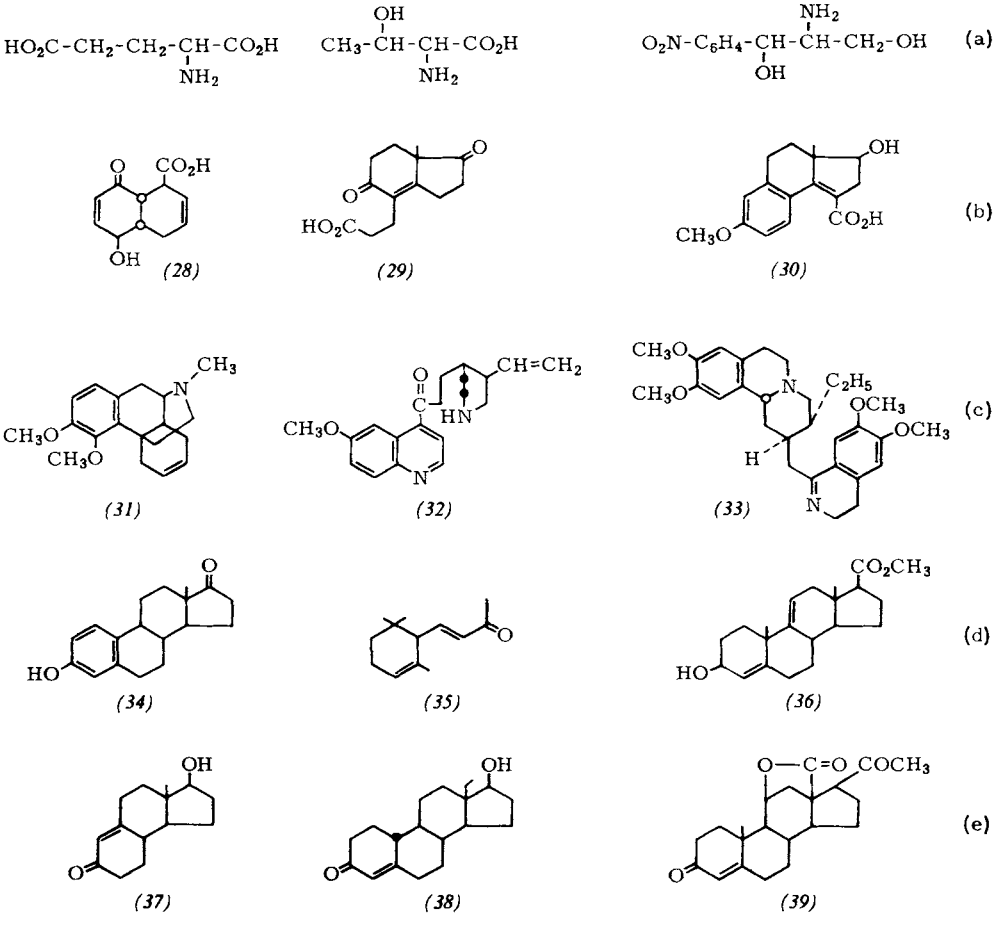
a) Methods without Asymmetric Agents

The method of selective crystallization has been used for the resolution of adrenaline[57] and histidine stereoisomers[58]. The entrainment method[*], which is insensitive to extraneous seed crystals, ensures a reliability and reproducibility that is not encountered in the inoculation method.

The method of entrainment is recommended by *Velluz*, *Amiard*, and *Joly* for the resolution of the racemic base of chloramphenicol[59]. In spite of some limitations relating to the solubility parameters of the products[60] this method has many interesting applications, such as in the resolution of threonine[61] and of other amino acids[62,63].

b) Methods Involving Formation and Separation of Diastereoisomers

Since the time of *Pasteur*, by far the most generally used methods of optical resolution have been those involving the formation and separation of diastereoisomers with the aid of optically active bases or acids. An example



Scheme 2. Examples of optical resolutions.

(a) Without auxiliary agent (seeding, coprecipitation).

(b) With basic reagent. *(28)* and *(29)*: Resolution with ephedrine; *(30)*: Resolution with L-(+)-*threo*-1-(*p*-nitrophenyl)-2-amino-1,3-propanediol.

(c) With acid reagent. *(31)*—*(33)*: Resolution with dibenzoyltartaric acid.

(d) With various derivatives. *(34)*: Resolution with menthoxyacetic acid; *(35)*: Resolution with menthyl carbazate; *(36)*: Resolution with digitonin.

(e) By microbiological means. *(37)*: Resolution with *Pseudomonas testosteroni*; *(38)*: Resolution with *Corynebacterium simplex*; *(39)*: Resolution with *Ophiobolus herpotrichus*.

[57] *E. Calzavara*, French Pat. 763374 (April 30, 1934); Chem. Abstr. *28*, 5472 (1934).

[58] *R. Duschinsky*, Chem. and Ind. *12*, 10 (1934); in: Festschrift Emil Barell, Hoffmann la Roche & Co., Basel 1936, p. 375.

[*] Description of the method: see [60].

[59] *L. Velluz*, *G. Amiard*, and *R. Joly*, Bull. Soc. chim. France *1953*, 342.

[60] *G. Amiard*, Experientia *15*, 38 (1959); Chem. Zbl. *1962*, 16972.

[61] *G. Amiard*, Bull. Soc. chim. France *1956*, 447.

[62] *K. Harada*, Nature (London) *206*, 1354 (1965); Bull. chem. Soc. Japan *38*, 1552 (1965).

[63] *T. Ogawa* and *T. Akashi*, Jap. Pat. 422/1956; Chem. Abstr. *51*, 5821i (1957).

of such a resolution is that which was carried out by *Pasteur* as long ago as 1853, when he resolved tartaric acid with the aid of the alkaloid base quinotoxine [64]. The underlying principle of this method has, during a century or more, given rise to countless variants currently used in both laboratory and industrial syntheses. Ephedrine and the intermediate base in the synthesis of chloramphenicol are especially valuable for the resolution of the intermediates *(28)–(30)* in the total synthesis of reserpine derivatives [65], and of steroid hormones [66,67], on a large scale (see Scheme 2).

Resolution with the aid of an active acid is based on the same principle; however, the occurrence in nature of active acids is much scarcer than that of alkaloids. Apart from tartaric acid, which for a long time permitted the resolution of cocaine [68] or adrenaline [69], the only acid which has found favor in optical resolution has been dibenzoyltartaric acid. This acid was chiefly used for the resolution of the intermediates *(31)–(33)* at the end of the total synthesis of morphine [70], of quinine [45], and of emetine [71]. β-Camphorsulfonic acid has been used for the resolution of sparteine [72] and of the free amine of chloramphenicol [36]. It is well known, however, that the use of these general methods is rarely devoid of difficulties.

With non salt-forming molecules diastereoisomeric compounds such as esters or hydrazones must be prepared. Thus synthetic estrone *(34)* has been resolved with the aid of menthoxyacetic acid [73]. Menthyl carbazate permits the resolution of α-ionone *(35)* [74]. α,β-Unsaturated carbonyl compounds can be converted into iminium salts that are stable enough to be resolved with camphorsulfonic acid [75]. Sometimes the formation of molecular complexes can be utilized; for example, those formed with digitonin, which have permitted the resolution of the synthetic steroid *(36)* [76].

[64] *L. Pasteur*, C. R. hebd. Séances Acad. Sci. *37*, 162 (1853).

[65] *L. Velluz, G. Muller, R. Joly, G. Nominé, J. Mathieu, A. Allais, J. Warnant, J. Valls, R. Bucourt*, and *J. Jolly*, Bull. Soc. chim. France *1958*, 673.

[66] *L. Velluz, G. Nominé, J. Mathieu, E. Toromanoff, D. Bertin, J. Tessier*, and *A. Pierdet*, C. R. hebd. Séances Acad. Sci. *250*, 1084 (1960).

[67] *L. Velluz, G. Nominé, G. Amiard, V. Torelli*, and *J. Cérède*, C. R. hebd. Séances Acad. Sci. *257*, 3086 (1963).

[68] *R. Willstätter, O. Wolfes*, and *H. Mäder*, Liebigs Ann. Chem. *434*, 111 (1923).

[69] *F. Flächer*, Hoppe-Seylers Z. physiol. Chem. *58*, 189 (1908).

[70] *M. Gates* and *G. Tschudi*, J. Amer. chem. Soc. *74*, 1109 (1952); *78*, 1380 (1956).

[71] *A. R. Battersby* and *J. C. Turner*, Chem. and Ind. *1958*, 1324; J. chem. Soc. (London) *1960*, 717.

[72] *N. J. Leonard* and *R. E. Beyler*, J. Amer. chem. Soc. *72*, 1316 (1950).

[73] *G. Anner* and *K. Miescher*, Helv. chim. Acta *31*, 2173 (1948).

[74] *H. Sobotka, E. Bloch, H. Cahnmann, E. Feldbau*, and *E. Rosen*. J. Amer. chem. Soc. *65*, 2061 (1943).

[75] *W. R. Adams, O. L. Chapman, J. B. Sieja*, and *W. J. Welstead jr.*, J. Amer. chem. Soc. *88*, 162 (1966).

[76] *R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler*, and *W. M. McLamore*, J. Amer. chem. Soc. *74*, 4223 (1952).

c) Methods Using Selective Reactions

Selective methods in which an enantiomer reacts either alone or at least in a predominant amount with an optically active reagent have found only few applications, although *Marckwald* [77] described, as early as early as 1899, the esterification of (–)-menthol with the dextrorotatory enantiomer of mandelic acid. The well-known specificity of enzymatic reactions has, however, been used in the steroid field to convert selectively only one of the two enantiomers of tricyclic intermediates such as *(37)* [78], as well as of tetracyclic derivatives such as *(38)* [79] or *(39)* [80].

III. Steric Correction

There are two kinds of steric correction; it may often be necessary to convert one diastereoisomer into another diastereoisomer (epimerization) or to recover the unwanted optical antipode after a resolution (racemization).

a) Epimerization

In the course of a synthesis, a diastereoisomer can be formed which differs in structure from the desired product in respect of the configuration of one or sometimes of several asymmetric centers. This drawback is often overcome with the aid of adequate steric corrections. Such epimerizations are easy in the case of reversible reactions if the product obtained under kinetically controlled conditions is to be converted into the thermodynamically more stable isomer (cf. Section 1d). This can be readily achieved under equilibrium conditions.

Epimerization generally involves the conversion of a tetragonal asymmetric carbon atom through an intermediate trigonal state back to a tetragonal state of the most stable configuration. This reaction sequence can be performed by keto-enol tautomerism, by oxidation-reduction, or by cleavage-condensation either directly on the "kinetic" product or indirectly on a simple derivative of the latter. Although these conversions lead nearly always to the most stable structure, the least stable epimer can sometimes be obtained from the stable one by selective inversion of a suitable derivative (cf. Section 1a).

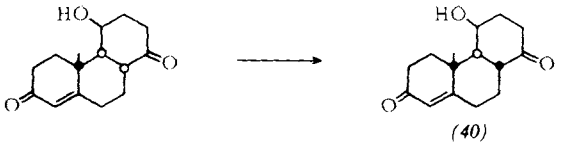
1. The epimerizations of substituents α to the carbonyl group by keto-enol tautomerism are classical methods which have been successfully applied to the total synthesis of steroids *(40)* [21] or alkaloids *(41)* [18].

[77] *W. Marckwald* and *A. McKenzie*, Ber. dtsch. chem. Ges. *32*, 2130 (1899).

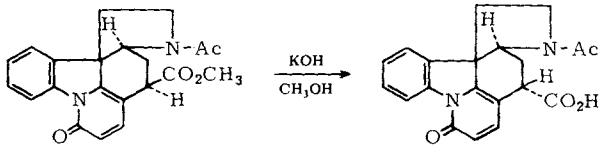
[78] *C. J. Sih* and *K. C. Wang*, J. Amer. chem. Soc. *85*, 2135 (1963).

[79] *G. Greenspan, L. L. Smith, R. Rees, T. Foell*, and *H. E. Alburn*, J. org. Chemistry *31*, 2512 (1966).

[80] *E. Vischer, J. Schmidlin*, and *A. Wettstein*, Experientia *12*, 50 (1956).



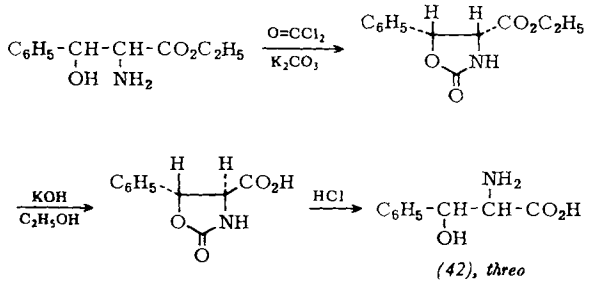
(40)



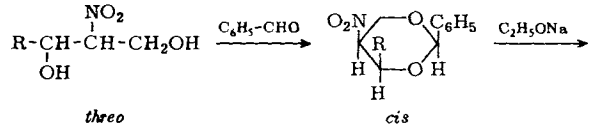
(41)

Similarly hydrogen atoms activated by an indole ring can give rise to equilibria. Thus alloyohimbane can isomerize into epialloyohimbane[81] or reserpine into 3 iso-reserpine[82]. A phenomenon of the same kind has been utilized in the synthesis of emetine in order to separate either of the two interconvertible diastereoisomers as insoluble salts[83].

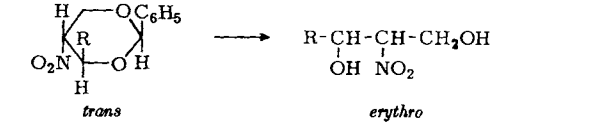
The indirect epimerization by keto-enol tautomerism of a simple derivative of the molecule involved has



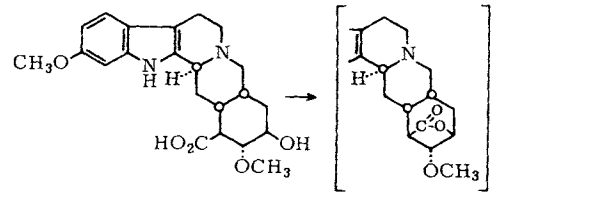
(42), *threo*

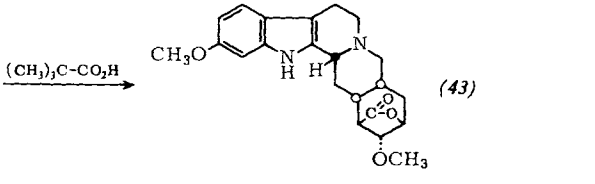


threo *cis*



trans *erythro*





(43)

been especially applied to phenylserine derivatives (*e.g.* intermediate *(42)* in the synthesis of chloramphenicol[84]), to a sphingosine synthesis described by *Grob*[85], and to the reserpine series at the intermediate lactone *(43)*[86].

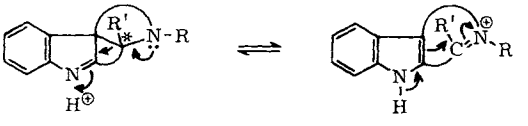
A more subtle epimerization, which in the case of α-substituted cyclohexanones allows the conversion of one epimer to the least stable isomer, takes advantage of the preferential conformation of an enamine intermediate with an axial α-substituent, the mild hydrolysis of which affords the least stable ketonic epimer. This type of epimerization has been utilized especially in the synthesis of antibiotics of the cycloheximide type (cf. Section 1a).

2. Reversible redox reactions are often the source of epimerization.

Thus, the reduction of a carbonyl group with aluminum alkoxide, by perpendicular attack on the most accessible side of the molecule, may yield the "kinetic" alcohol which can be converted into the "thermodynamic" alcohol. Similar equilibria are obtained with certain alcohols in the presence of a base, a ketonic intermediate being formed. This phenomenon has been known for a long time with regards to both acyclic and cyclic compounds. It has been applied to the synthesis of chloramphenicol, an L-*erythro* derivative being converted to the D-*threo* compound by permanganate oxidation followed by calcium borohydride reduction[87].

A well known example of its application in the cyclic series of compounds is, among others, the epimerization of yohimbine (axial 17-OH → equatorial 17-OH) on treatment with t-butoxide[88].

3. The reversibility of a few condensation reactions is also used for the creation of asymmetric centers that correspond to a more stable structural unit. The reversibility of the Mannich reaction enables equilibrations of the type *(44)* ⇌ *(45)*, especially in the alkaloid field, *e.g.* in the synthesis of strychnine[18], of akuammicine[89], and of aspidospermine[90].



(44) (45)

Similarly, the reversibility of the Micheal reaction often permits, as in the case of the synthesis of emetine[71], the epimerization of the primary "kinetic"

[81] *E. Wenkert* and *L. H. Liu*, Experientia *11*, 302 (1955).

[82] *H. B. MacPhillamy, C. F. Huebner, E. Schlittler, A. F. St. André*, and *P. R. Ulshafer*, J. Amer. chem. Soc. *77*, 4335 (1955).

[83] *J. H. Chapman, P. G. Holton, A. C. Ritchie, T. Walker, G. B. Webb*, and *K. D. E. Whiting*, J. chem. Soc. (London) *1962*, 2471.

[84] *T. Inui*, J. chem. Soc. Japan, pure Chem. Sect. (Nippon Kakagu Zasshi) *83*, 493 (1962).

[85] *C. A. Grob* and *F. Gadient*, Helv. chim. Acta *40*, 1145 (1957).

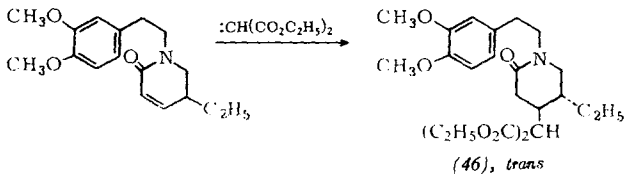
[86] *R. B. Woodward, F. E. Bader, H. Bickel, A. J. Frey*, and *R. W. Kierstead*, Tetrahedron *2*, 1 (1958).

[87] *L. Lévai, G. Fodor, K. Ritvay-Emandity, O. Fuchs*, and *A. Hajos*, Chem. Ber. *93*, 387 (1960).

[88] *A. Le Hir* and *E. W. Warnhoff*, C. R. hebd. Séances Acad. Sci. *246*, 1564 (1958).

[89] *G. F. Smith* and *J. T. Wrobel*, J.chem.Soc. (London) *1960*, 792.

[90] *G. Stork* and *J. E. Dolfini*, J.Amer.chem.Soc. *85*, 2872 (1963).

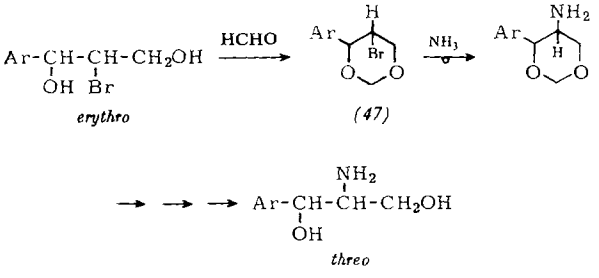


(46), trans

products (formed by 1,4- and 1,6-additions) to the more stable isomers such as *(46)* [91–93] in 76 % yield.

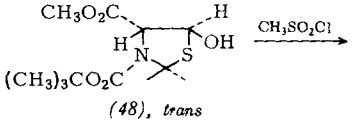
4. S_N2-substitution reactions can be considered as indirect methods for the inversion of an asymmetric center but it is beyond the scope of the present review to deal with this question as a whole. Only a few examples are given of the application of such reactions.

In the synthesis of chloramphenicol the *erythro*⟶*threo* conversion is achieved by an S_N2 substitution of a cyclic intermediate *(47)* [94,95] or otherwise by an intramolecular substitution obtained *via* cyclization and subsequent ring cleavage [96].

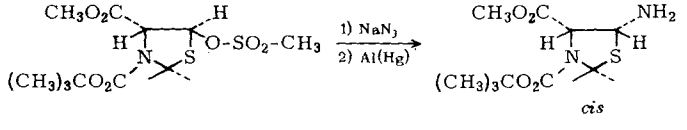


erythro *(47)* *threo*

Another example is *Woodward*'s recent synthesis of cephalosporin C, where the configuration of an asymmetric center of the intermediate *(48)* is changed by S_N2 substitution [97].



(48), trans

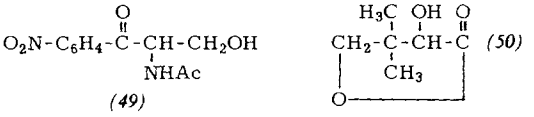


cis

b) Racemization

A study of the methods available for the racemization of a non-natural isomer is, of course, an essential feature of preparative total synthesis because it is theoretically possible for the total yield to be doubled with respect to the amount of starting material involved.

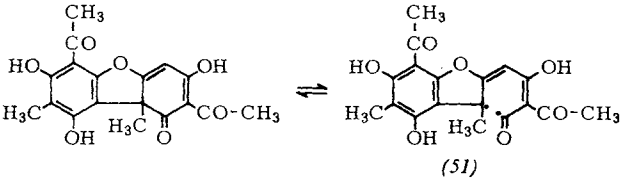
1. If the molecule possesses only one asymmetric carbon atom, racemization, like epimerization, is mostly achieved *via* an intermediary plane trigonal carbon atom (cf. Section IIIa). In the synthesis of chloramphenicol [98] or of pantothenic acid [99] intermediate products such as *(49)* or *(50)* are thus recovered by enolization.



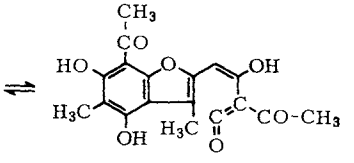
(49) *(50)*

The racemization of compounds by redox reactions especially in secondary alcohols, has been studied by *Doering* [100].

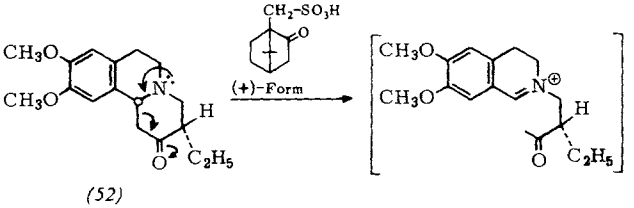
Racemizations are sometimes obtained by cleavage, followed by cyclization of an achiral intermediate; this is the case in the racemization of usnic acid *(51)* [101].



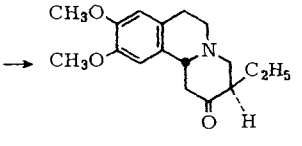
(51)



2. If the molecule possesses several asymmetric centers a racemization is rarely achieved. An example, however, is in the synthesis of emetine; a tricyclic intermediate *(52)* is formed which can be racemized quite successfully by cleavage and re-cyclization [102] (yield of optically active product 80 % referred to original racemate).



(52)



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[92] *M. Yanagita*, *S. Inayama*, *M. Hirakura*, and *F. Seki*, J. org. Chemistry *23*, 690 (1958).

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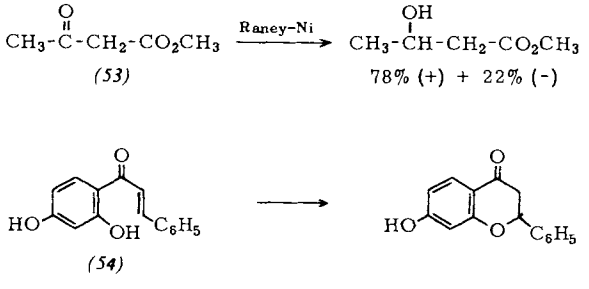
IV. Asymmetric Synthesis

Many organic chemists have investigated the problem of direct synthesis of optically active compounds without optical resolution [*], and interest in such a topic has been greatly enhanced by the progress that has been made in the total synthesis of natural products. Asymmetric synthesis may be defined as the creation of a chiral molecule from an achiral or prochiral molecule. This definition excludes the above mentioned selective reactions, which are carried out on antipodes already contained in a racemic product and which belong to the sphere of optical resolution (cf. Section II).

There are two types of method in use in asymmetric synthesis – direct methods and indirect methods. The direct methods involve the reaction of an asymmetric agent with a symmetric molecule. On the other hand the indirect methods require the preliminary attachment of an asymmetric link which must specifically induce the action of a symmetric agent. From an academic point of view, a poor yield of the desired product may be tolerated, but for a synthesis to be useful for preparative purposes it must ensure relatively good yields of a product of high optical purity.

a) Direct Asymmetric Syntheses

Stereospecific reactions with the aid of asymmetric catalysts have been attempted on several occasions. An example of this type of reaction is the catalytic hydrogenation of ketones such as *(53)* with Raney nickel pretreated with amino or hydroxy acids [112]. Camphorsulfonic acid induces asymmetry in the cyclization of a chalcone *(54)* [113].

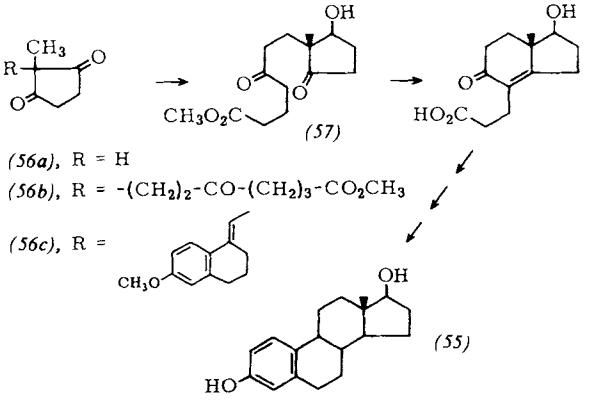


(53)

(54)

Another example is the use of quinine as a catalyst for the condensation of ketene with an alcohol, which at low temperature leads to the formation of optically active esters [114].

Worthy of special mention is enzymatic catalysis, which is highly selective and which is of especial use in the preparative reduction of carbonyl functions of achiral molecules. For example it can be used for the preparation of (–)mandelic acid from benzoylformic acid [115] and of L-malic acid from oxalacetic acid [116]. We have shown how the selective action [117] of enzymes on prochiral melecules may be used with advantage in the total synthesis of steroids [118]. It permits access to natural estradiol *(55)* from methylcyclopentanedione *(56a)* on a preparative scale and without optical resolution. The reduction of *(56b)* by *Rhizopus arrhizus* leads to an intermediate *(57)* having its two asymmetric centers in the configuration of natural steroids. A similar method using *Saccharo myces uvarum* for the reduction of an analogous prochiral derivative *(56c)* has been described [119].



Asymmetric reagents have been developed principally for the reduction of carbonyl derivatives. As early as 1946, *Vavon* obtained especially favorable results with various terpenic Grignard compounds [120, 121]. *Mosher* [122] extended the use of the method to simpler organomagnesium compounds such as the 2-methylbutylmagnesium halide. The transfer of the asymmetry of the Grignard compound to the carbonyl group must take place within a pseudocyclic transition state [123, 124].

[*] Many reviews have been devoted to this subject [103–111].

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[109] *C. Martinez Crespo*, Ion (Madrid) *17*, 253 (1957).

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[113] *H. Tatsuta*, Bull. chem. Soc. Japan *16*, 327 (1941); Chem. Abstr. *41*, 4488 (1947).

[114] *H. Pracejus*, Liebigs Ann. Chem. *634*, 9 (1960).

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[116] *P. Mayer*, Biochem. Z. *156*, 300 (1925).

[117] *V. Prelog*, Pure appl. Chem. *9*, 119 (1964).

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[119] *H. Gibian, K. Kieslich, H. J. Koch, H. Kosmol, C. Rufer, E. Schröder*, and *R. Vössing*, Tetrahedron Letters *1966*, 2321.

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[121] *G. Vavon* and *B. Angelo*, C. R. hebd. Séances Acad. Sci. *224*, 1435 (1947); Chem. Abstr. *41*, 6221 (1947).

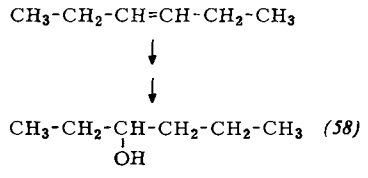
[122] *H. S. Mosher* and *E. LaCombe*, J. Amer. chem. Soc. *72*, 3994 (1950).

[123] *R. MacLeod, F. S. Welch*, and *H. S. Mosher*, J. Amer. chem. Soc. *82*, 876 (1960).

[124] *W. M. Foley, F. J. Welch, E. M. LaCombe*, and *H. S. Mosher*, J. Amer. chem. Soc. *81*, 2779 (1959).

The use of asymmetric alcoholates in the Meerwein-Ponndorf method also induces asymmetric reductions. The same is true for mixed alkoxyaluminum hydrides, which are obtained by the reaction of optically active alcohols with lithium aluminum hydride. According to *Cervinka* [125,126] however, only the use of amino alcohols gives good results.

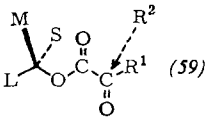
Another especially useful reagent has been prepared by *Brown* by the reaction of two molecules of α-pinene with diborane. The reaction of such a reagent on *cis*-3-hexene is highly stereoselective; after oxidation of the intermediate borane compound, the optical purity of the alcohol *(58)* obtained amounts to 90 % [127,128].



(58)

b) Indirect Asymmetric Synthesis

In the indirect methods an optically active link, which can be easily cleaved afterwards, must be attached to the molecule bearing the trigonal carbon atom. As early as 1904, McKenzie synthesized mandelic acid by esterification of benzoylformic acid with menthol followed by reduction with aluminum amalgam and subsequent hydrolysis [129]. This method has been extended to the condensation of Grignard compounds with α-keto esters of optically active alcohols. But it was the work of *Prelog* [130] that first permitted a rationalization of these results by assuming a selective attack of the molecule from the least hindered side of the conformation *(59)*.

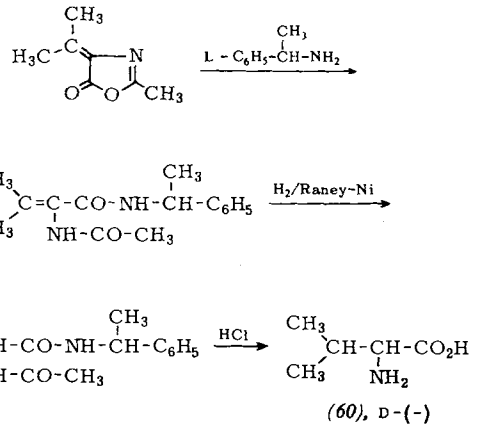


(59)

S = small, M = medium, L = large.

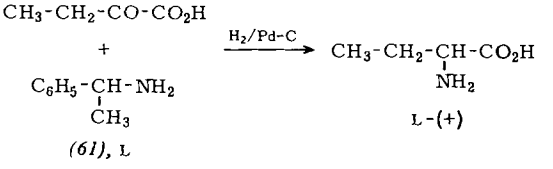
The optical yield varies with the asymmetry of the inducing alcohol; it attains 66 % in the case of 1-(2,4,6-tricyclohexylphenyl)ethanol.

The same general principle is also used for the preparation of optically active valine *(60)* from the corresponding azlactone [131].



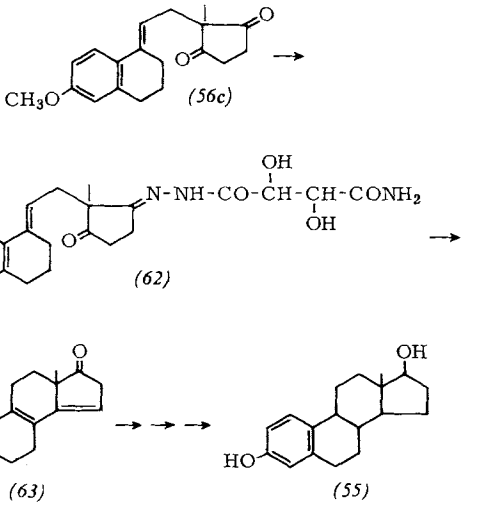
(60), D-(-)

An elegant synthesis of an amino acid involves the condensation of an α-keto acid with L-aminoethylbenzene followed by hydrogenation and hydrogenolysis [132].



(61), L

Finally, according to recent observations [133] one can utilize, in the total synthesis of an asymmetric steriod on a preparative scale, the preferential formation of one of the two compounds *(62)*, which arise in the reaction of a tartramic hydrazide with a carbonyl group of the prochiral compound *(56c)*. Cyclization and hydrolysis of *(62)* leads to the derivative *(63)*, which has a "natural" configuration and can be converted by conventional methods into estradiol *(55)*.



(56c) *(62)* *(63)* *(55)*

V. Linear versus Convergent Synthesis

From the point of view of the most economical use of raw materials, of reagents, and of man-power, two types of synthesis must be considered:

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[127] *H. C. Brown* and *G. Zweifel*, J. Amer. chem. Soc. *83*, 486 (1961).

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[131] *J. C. Sheehan* and *R. E. Chandler*, J. Amer. chem. Soc. *83*, 4795 (1961).

[132] *R. G. Hiskey* and *R. C. Northrop*, J. Amer. chem. Soc. *83*, 4798 (1961).

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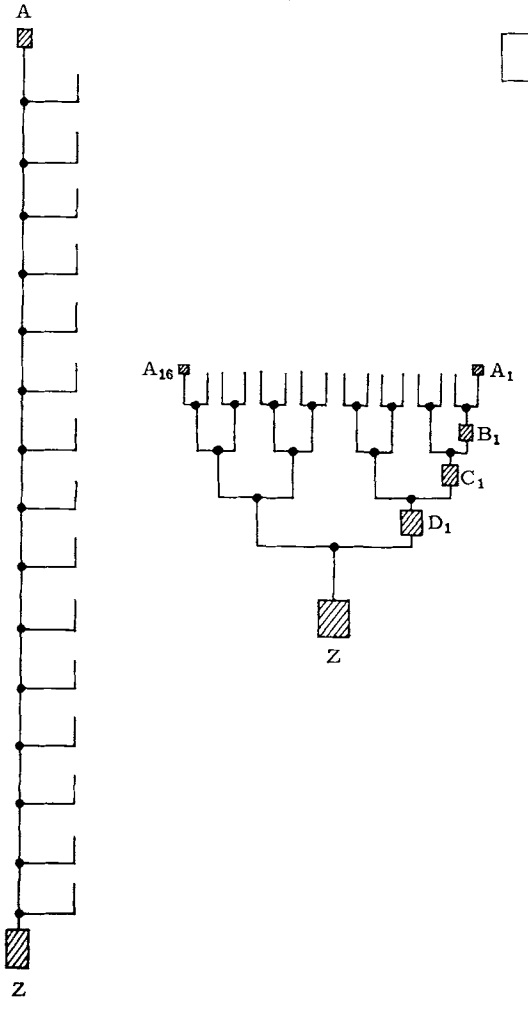
a) Linear syntheses (see Scheme 3, left) in which the starting product is gradually converted by the stepwise introduction of the elements of the final structure through a linear reaction sequence. Schemes of this nature are generally encountered in the partial syntheses of steroids, especially in the formation of cortisone-like structures.

b) Convergent syntheses (see Scheme 3, right) in which each product of the reaction sequence is obtained from two precursors. This type of synthesis is in frequent use in the preparation of peptides.

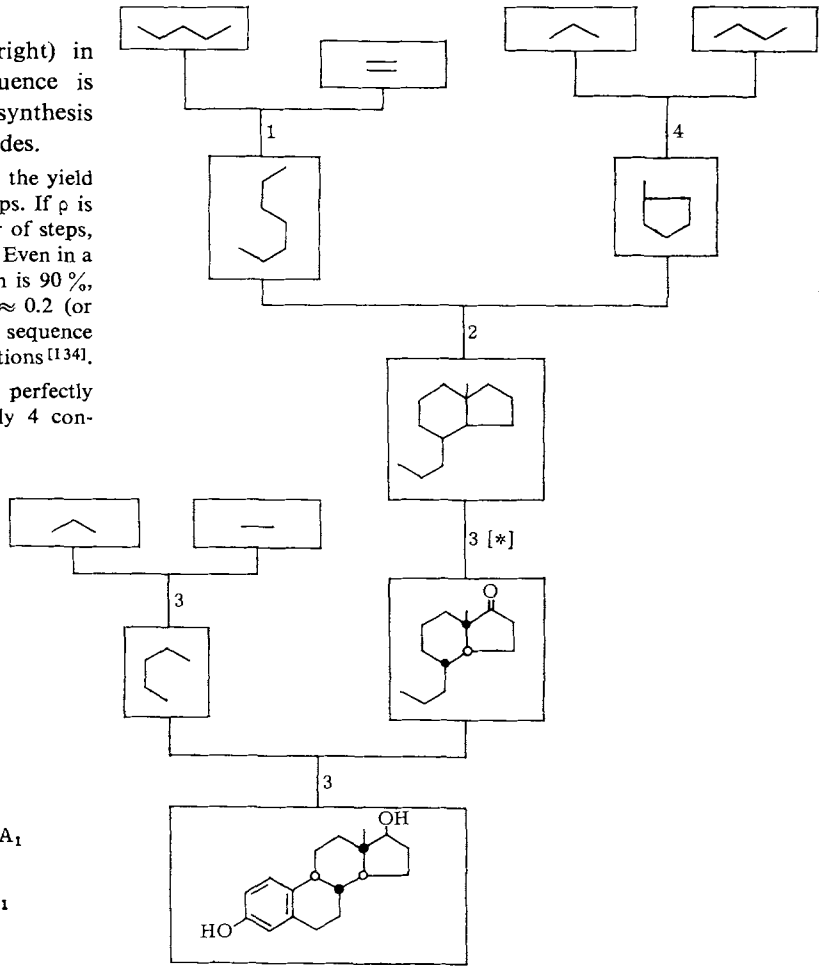
It is well known that in a given reaction sequence the yield R drops rapidly with the number of successive steps. If ρ is the mean yield of each reaction and n the number of steps, the over-all yield is given by the expression $R = \rho^n$. Even in a sequence in which the mean yield of each reaction is 90 %, the over-all yield after 15 steps drops to $(0.9)^{15} \approx 0.2$ (or 20 %). It is therefore desirable to split up the longest sequence as far as possible and to divide it into convergent sections [134].

If it were possible to arrange the 15 steps in a perfectly convergent pattern, the sections would have only 4 consecutive steps and the starting materials would be converted to the final product with a yield of $(0.9)^4 \approx 65$ %.

It is difficult to reach a perfect convergence; on the one hand the steps involving simple changes of intermediates are necessarily linear and on the other the requirement, on steric grounds, for a sort of asymmetric backbone on which achiral fragments can be grafted must be provided for.



Scheme 3. Left: Linear synthesis. Right: Convergent synthesis. A = Starting materials, Z = end product.



Scheme 4. Total synthesis of estradiol, schematic. The figures between the individual stages indicate the number of reaction steps.

[*] Optical resolution here.

An example of a compromise between all these requirements is shown in the total synthesis of estradiol, which was recently carried out by *Velluz, Nominé, Amiard et al.* [67] (Scheme 4). Six starting products require a total of twenty reaction steps (exclusive of the resolution). Five steps are condensation reactions and fifteen are simple intermediate changes. The convergence is obvious since the longest sequence includes only three condensation steps and ten consecutive steps involving simple reactions.

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Translated by *J. Wohlgemuth*

[134] *L. Velluz*, L'industrie nationale *1959*, 71.

The Active Species in Homogeneous Ziegler-Natta Catalysts for the Polymerization of Ethylene[**]

BY G. HENRICI-OLIVÉ AND S. OLIVÉ [*]

Cp_2TiCl_2 and $Cp_2TiEtCl$ (Cp = cyclopentadienyl, Et = ethyl), in combination with aluminum alkyls, have been studied as model catalyst systems for the polymerization of ethylene in toluene. The activity of these systems resides in the presence of a complex molecule involving an alkylated Ti(IV) and an alkylated Al species, linked together by chlorine bridge bonds. The environment of the Ti is of octahedral symmetry with one vacant site available for the coordination of ethylene. The bridged Al-alkyl causes a destabilization of the Ti-alkyl bond ("trans effect"), thus rendering it active for polymerization. The reduction Ti(IV) → Ti(III), inevitable in these systems, involves the irreversible change from octahedral to tetrahedral symmetry with loss of the catalytic activity. Polymerization and reduction are supposed to occur at the same catalyst site. Magnetic methods (susceptibility and EPR) as well as the kinetics of polymerization were used in the investigation of these catalyst systems.

Introduction

The first "mixed catalysts" developed by *Ziegler* [1] for the low pressure polymerization of ethylene and the stereospecific polymerization of α-olefins are insoluble in the reaction medium. For some time it was taken for granted that the "catalytic surface", *i.e.* heterogeneity, is essential for the extraordinary catalytic activity.

In the meantime, however, it has been shown, especially from the work of *Natta et al.* [2] as well as by that of *Breslow* and his co-workers [3], that certain soluble complex catalysts are well able to accomplish at least part of the numerous tasks of the heterogeneous catalysts. Of course such homogeneous systems are very attractive from the point of view of polymerization kinetics, since they allow one to bypass serious problems inherent in heterogeneous systems, such as particle size and surface quality of the catalytic species, stirring, and mass-transport phenomena. The prospects of elucidation of the mechanism of this type of coordinative polymerization is certainly greater with soluble systems. The results of such an investigation may allow one to draw conclusions about the technically more interesting heterogeneous systems.

The complex Ziegler-Natta catalysts are in general composed of a transition metal salt (or chelate) and an organometallic (reducing) compound containing a Group I–III metal. (In some cases combinations of two transition metal compounds of different valency and (or) ligand environment have been found useful [4].)

The most frequently used transition metal compound in soluble systems is bis(cyclopentadienyl)titanium dichloride (Cp_2TiCl_2). Fig. 1 shows schematically how the four ligands are arranged in an approximately tetrahedral fashion, around the central titanium atom [5,6], the cyclopentadienyl rings being π-bonded to the metal.

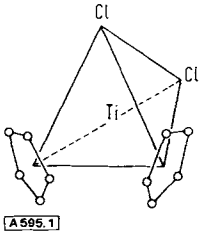


Fig. 1. The structure of bis(cyclopentadienyl)titanium dichloride.

A catalyst for the polymerization of ethylene is formed from this Ti-compound in combination with aluminum alkyls. The basic question of the present work is the following: In which way do the two components of the complex catalyst interact in order to yield an active species, and what is its configuration? Magnetic measurements, namely those of magnetic susceptibility and of electron paramagnetic resonance (EPR), are particularly suited to answer this kind of question, if used in combination with polymerization kinetic data.

[*] Dr. G. Henrici-Olivé and Dr. S. Olivé
Monsanto Research S.A.
Binzstr. 39
CH-8045 Zürich (Switzerland)

[**] Extended version of a lecture delivered at the "Makromolekulares Kolloquium", Freiburg, in March 1967.

[1] *K. Ziegler, E. Holzkamp, H. Breil,* and *H. Martin,* Angew. Chem. *67,* 541 (1955).

[2] a) *G. Natta, P. Pino, G. Mazzanti,* and *V. Giannini,* J. Amer. chem. Soc. *79,* 2975 (1957).

b) *G. Natta, G. Mazzanti, A. Valvassori, G. Sartori,* and *D. F. Umani,* J. Polymer Sci. *51,* 411 (1961).

[3] *D. S. Breslow* and *N. R. Newburg,* J. Amer. chem. Soc. *79,* 5072 (1957); *81,* 81 (1959).

[4] *L. A. Rodriguez* and *H. M. van Looy,* J. Polymer Sci. A 1, *4,* 1951. 1971 (1965).

[5] *F. A. Cotton* and *G. Wilkinson*: Advanced Inorganic Chemistry. Interscience, New York 1962.

[6] *J. C. W. Chien,* J. physic. Chem. *67,* 2477 (1963).

In Section I of this Paper the system $Cp_2TiCl_2/EtAlCl_2$ (Et = ethyl) in toluene is dealt with. Valency and ligands of the Ti in the active species are determined. This investigation leads to the recognition of the system $Cp_2TiEtCl/EtAlCl_2$ as especially suitable for a mechanistic study of the catalytic process. This is reported in Section II. The combination of all data obtained with both systems allows an interpretation of the reasons for catalytic activity and the proposal of a mechanism (Section III). Finally the homogeneous systems are compared with the technically more important heterogeneous catalysts (Section IV).

I. The System $Cp_2TiCl_2/EtAlCl_2$ in Toluene

a) Valency of Titanium in the Active Species

Aluminum alkyls are reducing agents, and therefore a reduction Ti(IV) → Ti(III) inevitably takes place if the two components Cp_2TiCl_2 and $EtAlCl_2$ are brought together. The first question to be answered is: what is the valency of the titanium in the catalytically active species? This question can easily be investigated by means of magnetic-susceptibility measurements since Ti(III), with the electronic configuration $3d^1$, is paramagnetic, whereas Ti(IV) is diamagnetic ($3d^0$). The course of the reduction Ti(IV) → Ti(III) may therefore be followed by measuring the susceptibility of the reaction solution as a function of time. The concentration of Ti(III) is calculated from the experimental volume susceptibility, $\varkappa$, and the molar susceptibility, χ_m (for one unpaired electron per molecule $\chi_m = 1270\times10^{-6}$ emu, corresponding to a magnetic moment of 1.73 B.M.), according to

$$[Ti(III)] = \varkappa/\chi_m. \qquad (1)$$

The concentration of Ti(III) is represented, in Fig. 2, as a function of time. The relatively high titanium concentration of 20×10^{-3} mol/l used in this experiment allows susceptibility measurements to be carried out with a satisfactory degree of accuracy. The solubility of Cp_2TiCl_2 is not high enough to prepare solutions in toluene of such concentrations; however, it becomes more soluble by complex formation with the aluminum alkyl. A certain excess of the latter is necessary to dissolve the Ti compound in a reasonable time. Therefore a ratio of Al/Ti = 2 was chosen. Preliminary trials had shown that the polymerization of ethylene is also optimal at this ratio (compare also reference [7]).

Fig. 2 shows that reduction occurs initially with a relatively high rate, but slows down after some 30 hours, when roughly one half of the Ti(IV) has been reduced, thus indicating the parallel occurence of at least two reactions. We shall come back to this point in Section Ib. For the moment, the curve will be used only to determine the actual concentrations of Ti(III) and Ti(IV) after different times. About 90 % of the titanium is present as Ti(III) after some 400 hours; complete reduction is obtained only after some thousand hours. A greater excess of $EtAlCl_2$ does not increase the rate of reduction.

[7] *W. Long*, J. Amer. chem. Soc. *81*, 5312 (1959).

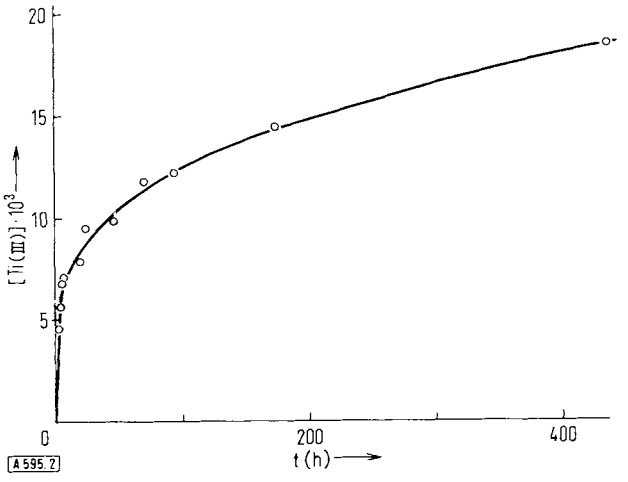


Fig. 2. Concentration of Ti(III) in the mixture $Cp_2TCl_2/EtAlCl_2$ as a function of time. $[Ti(IV)]_0 = 20\times10^{-3}$ mole/l; Al/Ti = 2; T = 20 °C; t = 0 at the moment of mixing of the catalyst components.
Ordinate: $[Ti(III)]\times10^3$ (mol/l).

Catalyst solutions identical with those used for the magnetic measurements (Fig. 2) have been used, after different times of aging, in the polymerization of ethylene. Data obtained from these polymerization runs are shown graphically in Fig. 3.

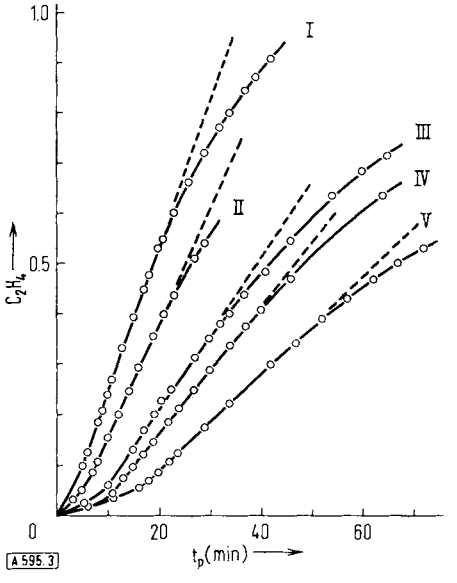


Fig. 3. Polymerization of ethylene at different aging times, t_a, of the catalyst solution. I: t_a = 0; II: t_a = 2h; III: t_a = 16h; IV: t_a = 20h; V: t_a = 66 h.
Ethylene pressure 710 mm Hg; aging temperature T_a = 20 °C; polymerization temperature T_p = 0 °C; polymerization time t_p.
Ordinate: Ethylene consumption in mole/l.

The polymerization rate clearly decreases with increasing aging time. Since the Ti(III) concentration has increased with aging (Fig. 2), this finding precludes Ti(III) species from being responsible for catalytic activity.

On the other hand, it may be seen from Figures 2 and 3 that the polymerization rate is higher when more Ti(IV) is present. The initial rate of polymerization, as obtained from the linear parts of the curves in Fig. 3, proves to depend in an approximately linear manner on the actual concentration of unreduced Ti(IV), which can easily be computed as

$$[Ti(IV)]_t = [Ti(IV)]_0 - [Ti(III)]_t \quad (2)$$

Therefore, the first question may be answered: The catalytic species must contain the titanium as Ti(IV).

b) EPR Spectra of the Catalyst Solution

The magnetic susceptibility cannot be used to distinguish between different paramagnetic species. EPR however supplies complementary information. Since this method is sensitive to variations in the environment of the paramagnetic ion, it is sometimes possible to observe several paramagnetic compounds simultaneously, and to measure changes in their concentrations.

The EPR signal of the catalyst solution, after different aging times, is given in Fig. 4. Two different Ti(III) species may be distinguished. One six-line signal is present from the very beginning, first superimposed by the signal of another substance, then finally almost pure (Fig. 4, left).

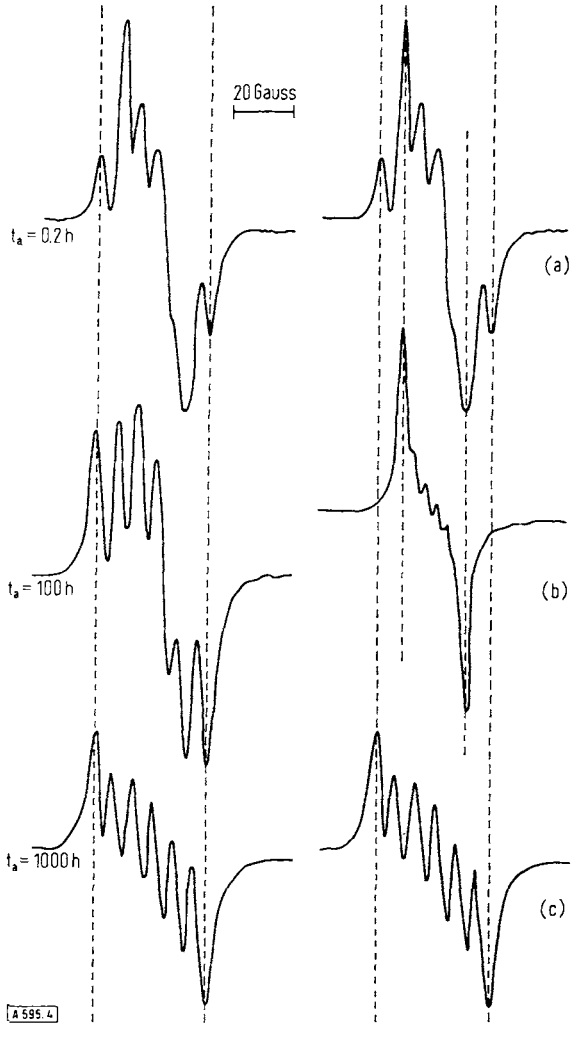
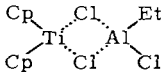


Fig. 4. Left: EPR signal of the system $Cp_2TiCl_2/EtAlCl_2$ represented in Fig. 2, at different t_a. Right: Identification of the components of the spectra shown. (a) Spectrum immediately after mixing of the components; (b) spectrum of compound *(1)*; (c) spectrum of compound *(2)*.

The top of the right-hand side of Fig. 4 shows the EPR spectrum of the catalyst solution immediately after mixing. Below these spectra are shown the signals of compounds *(1)* and *(2)* (taken from the literature [8, 12]).



(1)



(2)

The six lines seen in the spectrum of *(2)* result from the interaction of the unpaired electron of the Ti(III) with the magnetic nucleus of the aluminum (nuclear spin I = 5/2). A control experiment with a crystalline sample of this compound, prepared according to *Natta et al.* [9], shows, in toluene solution, an identical EPR signal (g = 1.9748, a_{Al} = 6.9 gauss).

The bridged structure of this complex was determined by *Natta et al.* [10] by means of X-ray structural analysis. The electron-deficient, three-center bonds Ti...Cl...Al required by this structure plausibly explain why no interaction of the unpaired electron of the Ti(III) with the chlorine atoms (nuclear spin I = 3/2) is to be observed in EPR: The molecular orbital responsible for the interaction of the unpaired electron with the Al nucleus can presumably be represented as a linear combination of the lowest vacant orbitals of the three-center bonds with a suitable Ti orbital. The lowest vacant orbital of a three-center bond has a node at the central atom [11]. Therefore no spin density (or very low spin density) is to be expected at the Cl nuclei.

The signal in the middle of Fig. 4 was ascribed by *Maki* [12] to the Ti(III)/Al complex *(1)*. The six Al-hyperfine lines of the EPR signal of this complex have come so close together that they cannot be fully resolved. The distance of these lines is a measure of the density of the unpaired spin at the nucleus of the aluminum atom. It is remarkable that this density is diminished by the introduction of an electron donating substituent at the Al. This may be interpreted as the consequence of "electron pressure" in the direction Ti ← Cl ← Al ← Et, which counteracts the delocalization of the unpaired Ti(III) electron. This idea was first postulated by *Adema et al.* [8]: "It is as if the alkyl groups push the unpaired electron away from the Al atom". Consistently, the introduction of a second ethyl group at the Al leads to a further narrowing of the signal. The complex with two ethyl groups at the Al shows only a single-line EPR signal with about one half of the line width of that for the complex with one Et [8].

This EPR-evidenced concept of increasing "electron pressure" as a consequence of increasing substitution of Cl by ethyl groups will be used later on in this paper.

The EPR signals in Fig. 4 are characterized not only by number, distance, and width of the lines, but also by their situation in the magnetic field (g-value). The dotted lines connect corresponding parts of the spectra. Thus the attribution of the two superimposed signals in the EPR spectrum of the original catalyst solution to the complexes *(1)* and *(2)* may be regarded as satisfactory and reliable.

At the beginning of the reduction, the concentrations of both complexes increase. The course of this increase

[8] *H. J. M. Bartelink, H. Bos, J. Smidt, C. H. Vrinssen,* and *E. H. Adema,* Recueil Trav. chim. Pays-Bas *81*, 225 (1962).

[9] *G. Natta, P. Pino, G. Mazzanti,* and *U. Gianni,* J. inorg. nuclear Chem. *8*, 612 (1958).

[10] a) *G. Natta, P. Corradini,* and *I. W. Bassi,* J. Amer. chem. Soc. *80*, 755 (1958).
b) *G. Natta* and *G. Mazzanti,* Tetrahedron *8*, 86 (1960).

[11] *F. A. Cotton*: Chemical Applications of Group Theory. Interscience, New York 1963.

[12] *A. H. Maki* and *E. W. Randall,* J. Amer. chem. Soc. *82*, 4109 (1960).

may be estimated from the changes of the EPR spectrum with time – see Figure 5. Although the absolute values of the concentrations given in this figure should not be stressed too much, the simultaneous increases in the concentrations of both complexes indicate clearly the simultaneous presence of two Ti(IV) complexes from which the two Ti(III) compounds originate.

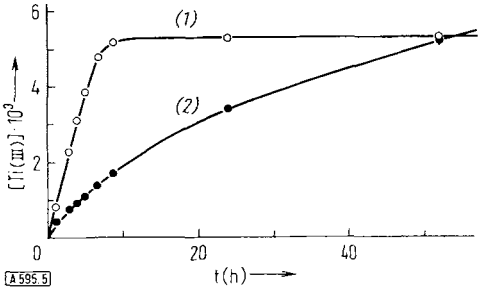


Fig. 5. Changes of the concentrations of the two Ti(III)/Al complexes $Cp_2TiCl_2AlEtCl$ *(1)* and $Cp_2TiCl_2AlCl_2$ *(2)*, as estimated from the changes of the EPR signal with time.
(Ordinate: [Ti(III)]× 10^3 in mole/l).

After some 10 hours, the concentration of the complex $Cp_2TiCl_2AlEtCl$ *(1)* does not increase further, but shows a slight decrease. Presumably this complex is transformed, in a very slow reaction, to the more stable $Cp_2TiCl_2AlCl_2$ *(2)* by substitution of $EtAlCl_2$ by $AlCl_3$. This is in agreement with the EPR spectra of Fig. 4. After *ca.* 1000 h practically pure $Cp_2TiCl_2AlCl_2$ *(2)* is found.

c) Configuration of the Active Complex

The reaction scheme represented in Fig. 6 shows how the simultaneous formation of the two observed Ti(III) complexes may be envisaged.

If Cp_2TiCl_2 is brought together with $EtAlCl_2$, instantaneous complex formation takes place. This follows from an immediate color change (red → brown-green),

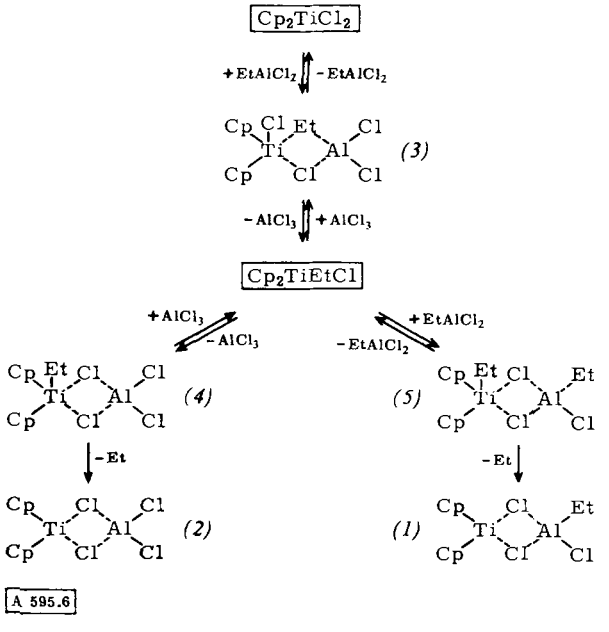


Fig. 6. Reaction scheme for complex formation and reduction in the system $Cp_2TiCl_2/EtAlCl_2$ in toluene at 20 °C.

and from the disappearance of the absorption band of Cp_2TiCl_2 at 515 nm. Although these Ti(IV)/Al complexes have not been isolated, it seems highly probable that the two metal atoms are also linked by bridge bonds, the tendency of both metals to form electron-deficient bonds being known [*]. Possibly the first complex contains two chlorine atoms in the bridge positions and the ethyl group on the aluminum. It is certain that the complex is in equilibrium with its parent substances, Cp_2TiCl_2 and $EtAlCl_2$, although the optical evidence indicates that the equilibrium concentration of the original Ti(IV) compound is rather low.

Part of the complex will doubtlessly be present in the form *(3)* represented in the scheme. In this configuration, it could decompose with loss of $AlCl_3$ to give $Cp_2TiEtCl$. This substance, whose intermediate formation we now postulate (further evidence see below) will play a key role in our further argument.

If $Cp_2TiEtCl$ reacts with $AlCl_3$, the complex *(4)*, in which the ethyl group is bonded to the titanium, may be formed; reaction with another $EtAlCl_2$ yields the doubly ethylated complex *(5)*.

Sinn and *Patat* [14] have shown, by means of ^{14}C-labeled aluminum alkyls, that the reduction of the titanium in similar complexes occurs by elimination of an exocyclic ethyl group on the titanium. Thus only at this stage of the reaction does the reduction process become feasible (and not from compound *(3)* or its analogues with the ethyl group in one of the bridges). Reduction leads to $Cp_2TiCl_2AlCl_2$ *(2)* (left hand route of scheme), and to $Cp_2TiCl_2AlEtCl$ *(1)* (right hand route of scheme); both Ti(III) complexes were found in the system and were identified by means of their EPR signals.

Thus the EPR evidence has guided us to the detection of the simultaneous presence of several Ti(IV)/Al complexes. Knowing that the catalytically active species is a Ti(IV) complex, the immediate question is, which of these complexes is the catalyst?

The answer comes from the "key substance", $Cp_2TiEtCl$. This compound can be prepared in crystalline form [15]. Without an Al-component it is stable in solution, and not catalytically active. If $EtAlCl_2$ is added to such a solution, only the right hand route of the scheme (Fig. 6) becomes feasible; addition of $AlCl_3$ allows the left hand route, and possibly permits the above equilibrium.

The latter system has practically no activity as a polymerization catalyst. In the absence of ethylene a relatively slow reduction (some 7 % in 24 hours) leads exclusively to the Ti(III)/Al complex which shows the six line EPR signal.

However, *via* the right hand route, one obtains a polymerization catalyst $Cp_2TiEtCl/EtAlCl_2$ *(5)* whose

[*] Bridge bonds in a Ti(IV) complex have been reported, by *Watenpaugh* and *Caughlan* [13], for the crystalline dimer of $TiCl_2(OC_6H_5)_2$. In this case the bridges are formed by oxygen.

[13] *K. Watenpaugh* and *C. N. Coughlan*, Inorg. Chem. *5*, 1782 (1966).

[14] *H. Sinn* and *F. Patat*, Angew. Chem. *75*, 805 (1963); Angew. Chem. internat. Edit. *3*, 93 (1964).

[15] *W. P. Long* and *D. S. Breslow*, J. Amer. chem. Soc. *82*, 1953 (1960).

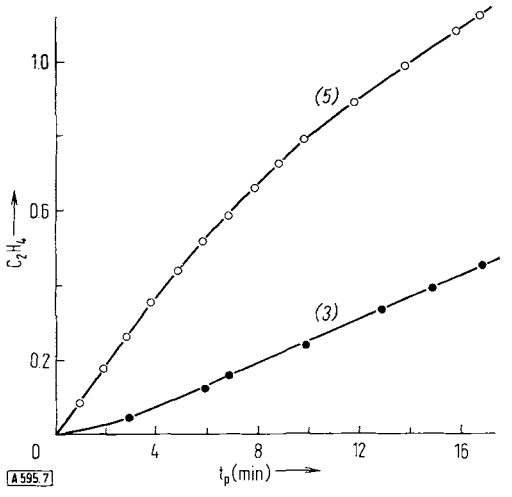


Fig. 7. Time—conversion curves of the polymerization of ethylene with $Cp_2TiEtCl/EtAlCl_2$ *(5)* and $Cp_2TiCl_2/EtAlCl_2$ *(3)*. $[Ti(IV)]_0 = 20\times10^{-3}$ mole/l; ethylene pressure = 720 mm Hg; Al:Ti = 2:1; $t_a = 0$; $T_p = 0$ °C. Ordinate: Ethylene uptake in mole/l.

activity is considerably greater than that of the original system $Cp_2TiCl_2/EtAlCl_2$ (referred to equal titanium concentration). Fig. 7 compares the rate of ethylene uptake in both systems.

From this result we can draw the following conclusion: Only the Ti(IV)/Al complex *(5)* with two ethyl groups, (one exocyclic on the Ti, the other on the Al) is active as polymerization catalyst. In the original system, the possibility of the inactive left hand route (Scheme 6) reduces the catalytic efficiency of the titanium.

II. The System $Cp_2TiEtCl/EtAlCl_2$ in Toluene

a) Second-Order Reduction Ti(IV) → Ti(III)

The investigations reported in Section I have shown that the catalyst combination $Cp_2TiEtCl/EtAlCl_2$ has a unique position inasmuch as it promises a simple, clear-cut, one-way reaction mechanism. This system is therefore expecially suited for mechanistic and kinetic studies of the reduction process as well as of the polymerization activity.

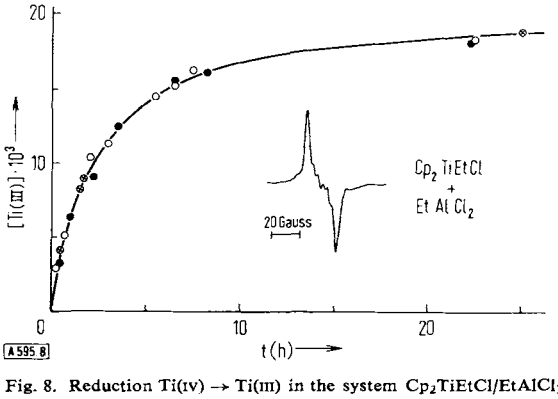


Fig. 8. Reduction Ti(IV) → Ti(III) in the system $Cp_2TiEtCl/EtAlCl_2$ in toluene.
$[Ti]_0 = 20\times10^{-3}$ mole/l; Al:Ti = 2:1; $T = 20$ °C. ●: Concentration of Ti(III) as determined from magnetic susceptibility. o ⊗: Concentration of Ti(III) as determined from EPR spectrum (two parallel runs). Ordinate: $[Ti(III)]\times10^3$ in mole/l.

When $Cp_2TiEtCl$ and $EtAlCl_2$ are mixed together in toluene in the absence of monomer, a relatively rapid reduction (compared with the system described in Section I) occurs. This reduction has been followed by magnetic susceptibility (Fig. 8). In the EPR spectrum only one signal is observed, namely that of the complex $Cp_2TiCl_2AlEtCl$ *(1)*, which increases in parallel with the magnetic susceptibility. Since the signal shape does not change with time, the signal height, h_S, can be taken as a measure of the concentration of the Ti(III) complex (setting $h_{S,\infty} = [Ti(IV)]_0$). These data are also included in the curve of Fig. 8.

This reduction occurs with a remarkable precision and up to some 80 % conversion, according to second-order kinetics. This observation precludes the reduction Ti(IV) → Ti(III) by a spontaneous monomolecular ejection of the ethyl radical, but rather suggests a bimolecular, mutual deactivation of two catalyst molecules (see Section IIc.). The second-order rate constant of this reaction is found to be:

$$k_{II} = 5.0\times10^{-3} \quad (\text{l mole}^{-1}\,\text{sec}^{-1}) \qquad (3)$$

b) Parallelism between the Rates of Reduction and of Polymerization

As already indicated, the $Cp_2TiEtCl/EtAlCl_2$ system is not only the better polymerization catalyst, but also is more rapidly reduced than $Cp_2TiCl_2/EtAlCl_2$. This parallel trend of both types of reaction holds also for other combinations: The system $Cp_2TiEtCl/AlCl_3$ reduces extremely slowly and shows practically no polymerization activity (compare Section Ic). The system Cp_2TiCl_2/Et_2AlCl, on the other hand, reduces and polymerizes very rapidly. Presumably both phenomena have a certain mechanistic correlation.

The four systems compared are summarized in Fig. 9. The Ti(III)/Al complexes observed in the EPR spectrum are also given in the legend.

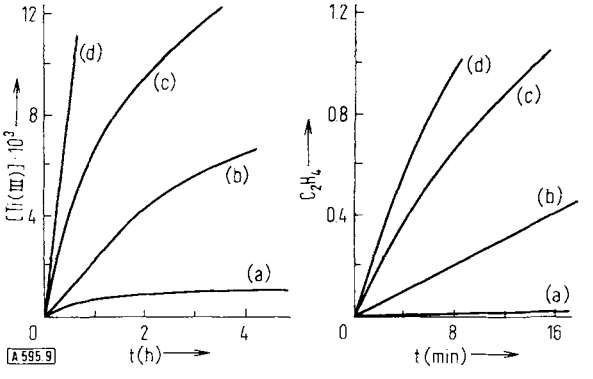


Fig. 9. Comparison of the rates of reduction Ti(IV) → Ti(III) (left) and rates of polymerization (C_2H_4) (right) for different Ti/Al systems. $[Ti]_0 = 20\times10^{-3}$ mole/l; Al:Ti = 2:1. Ordinates: mole l^{-1}.

System	Ti(IV) compound	Al compound	Ti(III)/Al complexes observed in the EPR spectrum
(a)	$Cp_2TiEtCl$	$AlCl_3$	$Cp_2TiCl_2AlCl_2$ *(2)*
(b)	Cp_2TiCl_2	$EtAlCl_2$	$Cp_2TiCl_2AlCl_2$ *(2)* + $Cp_2TiCl_2AlEtCl$ *(1)*
(c)	$Cp_2TiEtCl$	$EtAlCl_2$	$Cp_2TiCl_2AlEtCl$ *(1)*
(d)	Cp_2TiCl_2	Et_2AlCl	$Cp_2TiCl_2AlEtCl$ *(1)* + $Cp_2TiCl_2AlEt_2$

c) Polymerization Kinetics

The polymerization with the catalyst system $Cp_2TiEtCl/EtAlCl_2$ (system (c)) begins without a noticeable induction period (see Fig. 7, upper curve). With system b, on the other hand, induction periods are always observed (see Fig. 7, lower curve, and Fig. 3). From the reaction scheme in Fig. 6 this becomes understandable: In system b the catalytic species *(5)* can be supplied after the beginning of the polymerization, *via* the various equilibria involved, thus giving rise to an increase of polymerization rate until chain termination (see below) begins to dominate. In system c, however, the clear-cut beginning of the polymerization indicates that all available catalyst is transferred to growing chains from the very beginning of the reaction. Thus, in this system the relationship

$$[P^*]_0 = [Ti(IV)]_0 \qquad (4)$$

($[P^*]_0$ = concentration of active sites at times $t = 0$) is assumed to hold. A kinetic evaluation of the polymerization mechanism becomes possible on the basis of this equation. A preliminary estimate, based on the data represented in Fig. 7 (upper curve), is given below.

The polymerization rate can be obtained by graphical differentiation of the time-conversion curve.

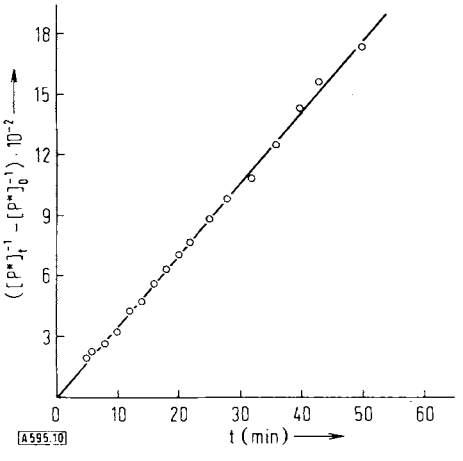


Fig. 10. Polymerization of ethylene with $Cp_2TiEtCl/EtAlCl_2$ at T_p = 0 °C. Second-order kinetics for the disappearance of growing chains. (Ordinate: $[P^*]_t^{-1}-[P^*]_0^{-1}$ in l·mole^{-1}).

The observed decrease of the polymerization rate with time must be ascribed to a chain-termination reaction. The kinetics of this reaction may be determined with the aid of the general equation for the overall polymerization rate:

$$R_p = -\frac{d[M]}{dt} = k_p\,[P^*]\,[M] \qquad (5)$$

([M] = concentration of monomer; k_p = rate constant of chain propagation.)

Taking into account eq. 4, the concentration of P* at any time can be calculated as

$$[P^*]_t = \frac{R_{p,t}}{R_{p,0}}\,[Ti(IV)]_0 \qquad (6)$$

Fig. 10 shows that the disappearance of growing chains follows second-order kinetics, indicating a bimolecular mutual deactivation of growing chains. From the slope of the straight line, the rate constant of this deactivation is obtained:

$$k_t \approx 0.6 \text{ (l mol}^{-1} \text{ sec}^{-1}) \qquad (7)$$

This is an astonishingly high value for this constant (at 0 °C) in comparison with the second-order rate constant of the mutual deactivation of the catalyst complexes in the absence of ethylene ($k_{II} = 5{\cdot}0\times10^{-3}$, at 20 °C; eq. 3).

A check of the concentration of paramagnetic Ti(III) species at the end of the run represented in Fig. 10, *i.e.* after 17 minutes of polymerization, shows that also considerably more Ti(III) has been formed than in the comparable run without ethylene. From the EPR signal height after polymerization and the information given in Fig. 8, it may be concluded that the following relationship holds:

$$[P^*]_t + [Ti(III)]_t \approx [Ti(IV)]_0 \qquad (8)$$

i.e. the chain termination reaction is accompanied by the reduction of the Ti in the active species. (For a mechanistic interpretation of this finding see Section IIIc.)

The kinetic study also allows an estimate to be made concerning the rate constant of chain propagation. From eq. 4 and 5 it follows that:

$$R_{p,0} = k_p\,[P^*]_0[M] = k_p\,[Ti(IV)]_0[M] \qquad (9)$$

The concentration of the monomer (ethylene) in the reaction solution (ethylene pressure = 710 mm Hg, 0 °C) has been determined as [M] = 0.065 mole/l. Thus it follows from eq. 9 with $R_{p,0} \approx 8\times10^{-3}$.

$$k_p \approx 6 \text{ (l mol}^{-1} \text{ sec}^{-1}) \qquad (10)$$

Kinetic measurements of the polymerization of ethylene with a similar catalyst system, Cp_2TiCl_2/Me_2AlCl (Me = methyl), have been carried out by *Chien* [16], who used radioactive tracer techniques as an analytical tool. Although the data published by this author indicate that a complicated mechanism analogous to that shown in Fig. 8 may be involved (induction periods), similar values were reported for the rate constants of chain propagation and chain termination (at 0 °C: $k_p = 1.5$, $k_t = 0.5$).

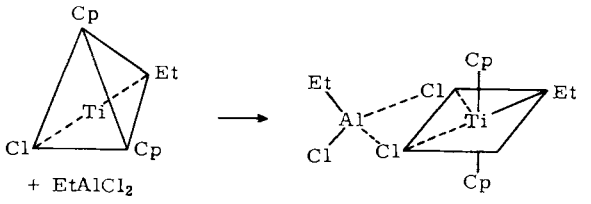
III. Interpretation of Catalytic Activity

a) The Reactive Site in the Complex

The information given in Sections I and II will now be combined in order to derive a spatial picture of the catalytic complex and of the reasons for polymerization activity.

[16] *J. C. W. Chien*, J. Amer. chem. Soc. *81*, 86 (1959).

In Cp_2TiCl_2, as well as in $Cp_2TiEtCl$, the titanium is present in an approximately tetrahedral environment [5,6]. Since we have seen that catalytic activity requires a titanium-ethylated species we shall consider only $Cp_2TiEtCl$ (Fig. 11).



A 595.11

Fig. 11. Change from tetrahedral to octahedral environment of titanium on complex formation.

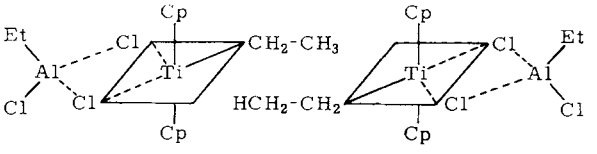
On complex formation with an aluminum alkyl, one of the ligands of the Al also requires a place in the coordination sphere of the Ti. We propose that this requirement forces the Ti into an octahedral environment (only tetrahedral and octahedral complexes of Ti have so far been reported [5,17]). By this procedure the Ti–Et bond comes under the *trans*-influence of the bridged aluminum (Fig. 11), and presumably suffers weakening. This weakening, in our opinion, is responsible for the two plenomena, polymerization and reduction.

We now come back to the EPR-evidenced "electron pressure" in the direction Ti← Cl← Al← Et (Section Ib). It may easily be imagined that the higher the electron density at the Ti, the lower the stability of the Ti–Et bond. If all ligands at the Al were chlorines, no such "pressure" would be experienced; the Ti–Et bond would be relatively stable. This is indeed observed in the left hand route of the scheme, Fig. 6, which corresponds to system (a) in Fig. 9. The introduction of one or two ethyl groups leads to an increased destabilization of the Ti–Et bond, and consequently to the observed increase in the rates of polymerization and reduction (systems (b)–(d) in Fig. 9) [*].

This parallel course of polymerization and reduction is, in our opinion, strong evidence that both reactions occur in the same complex configuration and at the same site, namely at the exocyclic Ti–Et bond.

b) Reduction

In the absence of ethylene only the reduction reaction has to be taken into account. The octahedral complex, as represented in Fig. 11, has one coordination site empty. A β-hydrogen atom of the ethyl group of a second complex unit may occupy this site, as shown in Fig. 12. Subsequent transfer of this hydrogen to the other ethyl group would lead to the formation of ethane and ethylene, as has been observed experimentally [14,9]. As a consequence the titanium is reduced to Ti(III).



A 595.12

Fig. 12. Proposed configuration for the bimolecular mutual reduction of two complex units.

Experiments with a comparable Zr complex during which an intermediate compound $\rangle Zr-CH_2-CH_2-Zr\langle$ could be isolated, prompted *Sinn et al.* [18] to formulate the reduction mechanism in a similar manner to that given in Fig. 12. Bimolecular deactivation was also postulated by *de Vries* [19]. We feel that our kinetic data (second-order reduction rate) strongly corroborate such a formulation.

c) Polymerization

Under polymerization conditions, ethylene can coordinate to Ti at the sixth, so far empty, coordination site. The importance of this coordination, which is indispensable for the polymerization of ethylene, has been thoroughly discussed [20]. The most convincing ideas have been forwarded by *Cossee* [21,22], and are adopted with slight changes, in the present discussion.

Ethylene has an especially suitable electronic configuration for complexing with a transition metal. Fig. 13 represents the *x-y* plane of the octahedral complex *(6)*. The bonding π-orbital of the ethylene has σ-symmetry with respect to the *x*-axis of the complex, and therefore matches the $d_{x^2-y^2}$ (vacant) σ-orbital of the Ti. Also the antibonding π*-orbital of the olefin finds a symmetry match within the complex, namely the (also vacant) d_{xy} π-orbital of the Ti (π-symmetry with respect to the *x*-axis).

Part of the electron density will be transferred from the bonding π-orbital of the ethylene to the metal, thus weakening the ethylene double bond and making it susceptible to polymerization.

If, however, a higher transition metal were considered, the d_{xy} orbital could be filled; in this case a "back-donation" of electron density from the Ti to the ethylene could be achieved. The metal-olefin complex may then become so stable that no polymerization occurs. This is probably one of the reasons why useful catalysts for ethylene and α-olefins are found only on the left side of the Periodic Table (Ti, V, Cr), where the d_π orbital is found vacant or only partially filled. This concept also explains why the type of Ziegler-Natta catalysis discussed here is suitable for ethylene and α-olefins, whereas certain vinyl monomers with electron attracting substituents (*e.g.* vinylchloride, tetrafluoroethylene) do not polymerize. The electron density in the bonding π-orbital of the vinyl monomer is reduced by

[17] *F. A. Cotton*, J. chem. Educat. *41*, 466 (1964).

[*] With Et_3Al the reduction rate at room temperature is already too high; no polymerization is observed, presumably because of lack of Ti(IV).

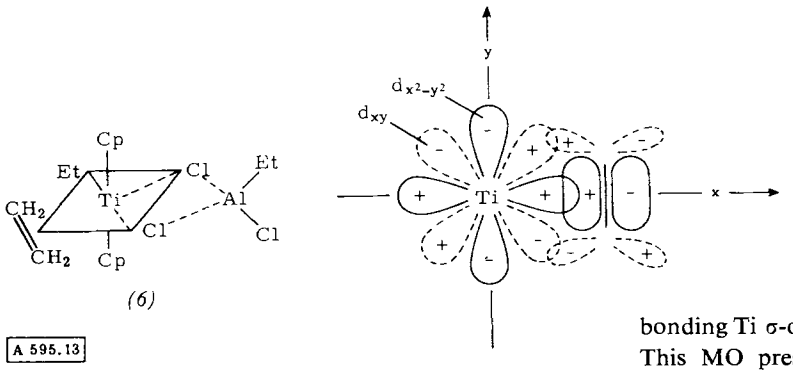
[18] *H. Sinn* and *E. Kolk*, J. organometallic Chem. *6*, 373 (1966).

[19] *H. de Vries*, Recueil Trav. chim. Pays-Bas *80*, 866 (1961).

[20] *J. P. Kennedy* and *A. W. Langer*, Fortschr. Hochpolymeren-Forsch. *3*, 508 (1964) and references therein.

[21] *P. Cossee*, J. Catalysis *3*, 80 (1964).

[22] *P. Cossee*, Recueil Trav. chim. Pays-Bas *85*, 1151 (1966).



A 595.13

Fig. 13. Left: The octahedral complex of $Cp_2TiEtCl \cdot EtAlCl_2$ with ethylene; right: schematic representation of the relevant orbitals in the *x-y* plane of the complex.

such substituents, the tendency to coordinate to the metal decays, and thus one of the most important conditions for this type of catalysis is not satisfied.

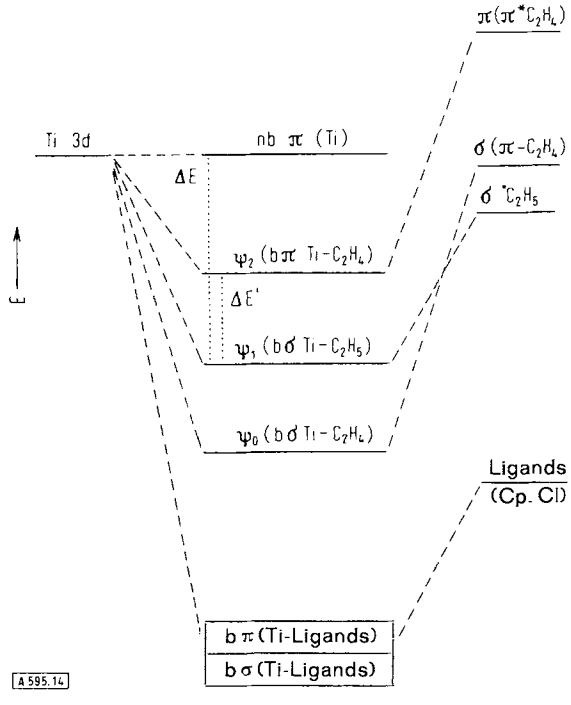
The coordination of ethylene also has a destabilizing influence on the Ti–Et bond – a further factor favoring polymerization. This effect is best elucidated by a qualitative, simplified molecular orbital (MO) description of the coordination process.

The five-coordinate complex (one vacancy) possesses a number of stable, filled σ- and π-bonding orbitals, which unite the titanium with the ligands Cp and Cl (bσ and bπ in Fig. 14). The highest occupied orbital is assumed to be the destabilized (*trans* effect, "electron pushing") bonding σ–MO, ψ_1, which is responsible for the Ti–Et bond. (The ψ_0 and ψ_2 MO's are not present in the pentacoordinated complex, see below.) Furthermore, the Ti has one non-bonding σ-orbital (due to the vacancy), and also non-bonding π-orbitals.

When an ethylene molecule approaches the vacancy, its bonding π-orbital overlaps with the as yet non-bonding Ti σ-orbital to form the bonding σ–MO (ψ_0). This MO presumably has a lower energy than the destabilized ψ_1 [*].

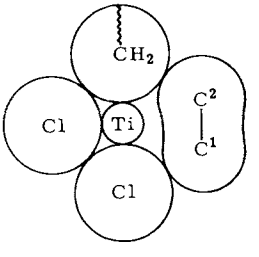
The formation of the π-MO (ψ_2) from a so far non-bonding titanium π-orbital and the antibonding ethylene π*-orbital (compare also Fig. 13) makes available a vacant MO which is energetically favorable for an electron transition $\psi_1 \rightarrow \psi_2$. Whereas before the coordination of the ethylene the energy ΔE was necessary to promote, by thermal exitation, an electron from ψ_1 to the next vacant orbital, now only the energy $\Delta E'$ is required to make the ethyl group available as a radical. (The concept of stabilization and destabilization of transition metal-alkyl bonds by influencing the energy gap between highest occupied and lowest vacant MO was first put forward by *Chatt* and *Shaw* [24].)

The schematic picture of the atomic orbitals in Fig. 13 does not give a clear impression of sizes and distances. Fig. 15 gives a further representation of the *x-y* plane, the diameters of the ligands and of the metal being drawn approximately to scale (according to *Cossee* [21])



A 595.14

Fig. 14. Simplified qualitative MO representation of the influence of ethylene coordination on the stability of the Ti–Et bond (antibonding MO's omitted).



A 595.15

Fig. 15. *x-y* plane of the complex *(6)* represented in Fig. 13, with diameters of metal and ligands drawn approximately to scale (according to *Cossee* [21]).

This representation emphasizes that this arrangement of the ligands, possible only in the octahedral (and not in the tetrahedral) complex, is specially favorable for a "*cis*-migration" of the ethyl-group (or a growing chain) to the coordinated monomer. Only a small "in-plane" displacement of the CH_2-group, which may be possible within the normal vibrational modes, brings it into a position of considerable overlap with

[*] Since *Cossee* [21] did not take into account bridge bonds to the aluminum, but supposed the Al compound to be necessary only to alkylate the Ti, his assignment of the energies of the MO's ($\psi_1 > \psi_0$) was perhaps not quite justified. This was criticized by *Scrocco* [23]. In our opinion the destabilizing influence of the bridge might well be a sufficient reason for postulating that the energy of ψ_1 is higher than that of ψ_0.

[23] *E. Scrocco*, note in reference [21], p. 87.

[24] *J. Chatt* and *B. L. Shaw*, J. chem. Soc. (London) *1959*, 705.

the olefin. (This point of view has been carefully discussed on a qualitative quantum mechanical basis by *Cossee* [22].) The weakened olefinic double bond breaks, a new bond Ti–C_1 is formed, and the ethyl group (or growing chain) bonds to C_2. After the insertion, the coordination site where the ethyl group was situated becomes free. Since this position has the same configuration, with respect to the Al-bridge, as the one where the olefin was coordinated, the process of chain growth can begin again (cf. *(6)*, Fig. 13).

It therefore follows that three influences are cooperative in the catalysis discussed:

1. Destabilization of the titanium-alkyl bond by the alkylated Al bridge, and by the coordination of the monomer (Fig. 14);

2. Destabilization of the olefin double bond by partial electron transfer from the bonding π-orbital to the titanium (Fig. 13);

3. Suitable steric arrangement for the "*cis*-migration" of the ethyl group, or growing chain (Fig. 15).

Presumably the concerted action of all three conditions is only possible in an octahedral environment.

In the presence of ethylene, the bimolecular mutual deactivation of the catalyst complexes has also to be taken into account, as shown in Section IIc. It can be imagined in a similar manner to that depicted in Fig. 12, if one hydrogen of each CH_3 group is replaced by a polyethylene chain. In terms of polymerization kinetics, this mutual deactivation represents a case of a true chain termination reaction, since the reduced (tetrahedral) complex cannot be reactivated. The reaction gives one polymer molecule with a vinyl end group, and one saturated molecule.

It has been shown in Section IIc that mutual deactivation (reduction) occurs considerably faster in the presence of ethylene than in the monomer-free system. The reason could reside, at least in part, in the smaller dissociation energy for a C–H bond in a $>CH_2$ group as compared with a $-CH_3$ group ($\Delta E \simeq 3$ kcal/mol [25]). This difference is known to cause considerable differences in rate constants and activation energies of other hydrogen-abstraction reactions (*e.g.* the free radical hydrogen abstraction, by the polystyryl radical, from toluene or ethylbenzene, $k_{EtB}/k_{Tol} = 4.3$ at 80 °C, $\Delta E_A \simeq 3$–4 kcal/mol [26]). Possibly the β-position of the decisive $>CH_2$ group (growing chain) or $-CH_3$ (ethyl group) to the metal can strengthen this effect considerably.

Summarizing, it may be said that the experimental data of the polymerization are also consistent with the proposed mechanism, which postulates the combination of the exocyclic alkyl group on the titanium and the vacancy as the site of reaction for the polymerization as well as for the reduction.

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IV. Comparison with Heterogeneous Systems

It has been stated in the previous sections that the catalytically active species in the treated homogeneous systems contain the titanium exclusively as Ti(IV). Reduction to Ti(III) renders the compounds inactive. On the other hand, some of the most efficient and versatile technical catalysts for the polymerization of ethylene and α-olefins are based on $TiCl_3$.

This apparent contradiction finds its explanation in symmetry considerations. In the present Ti(IV) compounds (Cp_2TiCl_2, $Cp_2TiEtCl$) the four ligands are located tetrahedrally around the titanium. Only by complex formation with the Al-alkyl is an octahedral environment achieved; reduction brings the Ti/Al complex again into an inactive tetrahedral configuration. The various crystalline modifications of $TiCl_3$ (α, β, and γ), however, have the common property that the Ti atoms are located in octahedral interstices of the Cl-lattice [27]. At surface defects, and especially at the lateral faces of hexagonal crystals of, for example, α-$TiCl_3$, titanium atoms are to be found which, because of electroneutrality requirements, exhibit incomplete coordination. The presence of titanium atoms, in which four octahedral sites are occupied by chlorine (two chlorine vacancies) can result in complex formation with an Al-alkyl (bridge) and alkylation of the titanium in an analogous fashion to that described in Figure 6 for Cp_2TiCl_2. (Only the two Cp groups have to be thought of as being replaced by chlorines.) In our opinion these titanium centers having two vacancies are essentially responsible for the activity of the heterogeneous Ziegler-Natta catalysts on the basis of $TiCl_3$. (Cf. also reference [4].) In contrast to the soluble systems dealt with in the present work, the octahedral arrangement of the ligands of titanium in heterogeneous catalysts is guaranteed at the outset by crystal structure.

This comparison of the homogeneous and heterogeneous systems emphasizes that the symmetry requirements for catalytic activity are rather severe, whereas the valency of the titanium seems to be of less importance.

V. Experimental

Cp_2TiCl_2 (Fluka) was recrystallized from methylene chloride several times; $Cp_2TiEtCl$ was prepared according to *Long* and *Breslow* [15]. The aluminum alkyls used were supplied by Schering, Bergkamen. Catalyst preparation and aging, as well as magnetic measurements, were carried out *in vacuo* or under argon. Magnetic susceptibility was determined on a Gouy balance. A Varian V-4502 spectrometer, with 100 kHz field modulation, has been used for the EPR measurements. The rate of polymerization of ethylene was determined at constant pressure; the equipment was essentially that described by *Schnecko et al.* [28].

The authors are grateful to Mr. W. Hess for able and conscientious technical help.

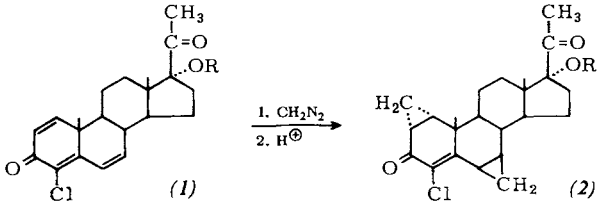
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4-Chloro-1α,2α:6β,7β-bismethylene-steroids

By *R. Wiechert* [*]

1,4,6-Triolefinic 3-keto-steroids add diazomethane selectively to the 1,2-double bond, even if the diazomethane is in excess, to yield 1α,2α-pyrazoline derivatives [1]. If these products are cleaved thermally or by Lewis acids, they afford 4,6-diolefinic 1α,2α-methylene-3-keto-steroids.

However, 4-chloro-3,20-dioxo-1,4,6-pregnatrien-17α-yl acetate *(1a)* (m.p. 213.5–214 °C; prepared by chlorination of 3,20-dioxo-1,4,6-pregnatrien-17α-yl acetate with chlorine in dimethylformamide/propionic acid) adds two equivalents of diazomethane. Cleavage of the labile crude bispyrazoline with catalytic amounts of perchloric acid in acetone at room temperature leads to the 4-chloro-1α,2α:6β,7β-bismethylene compound *(2a)* (yield 16%), m.p. 278.5–279 °C; UV: ε_{274} = 12600 (methanol); $[\alpha]_D^{26} = -48.1°$ (c = 1.03 in $CHCl_3$); NMR: no olefinic proton, 19-CH_3 at δ = 1.12 (tetramethylsilane as internal standard in $CDCl_3$).



(a), R = CO-CH_3
(b), R = H

Addition of diazomethane in the δγ-position of an enone system has not been described previously. In *(1a)* it is made possible by the 4-chloro substituent (electron deficiency at C-7.

Compound *(2a)* is also formed by direct methylenation of *(1b)* [m.p. 199–201 °C; formed from *(1a)* by hydrolysis] by the method of *Corey* [2] and *Franzen* [3] with dimethylsulfoxonium methylide [giving a 28% yield of *(2b)*, m.p. 246–250 °C; UV: ε_{274} = 12400 (methanol)] with subsequent acetylation. Because of steric hindrance of the C-1/C-2 bond by the angular methyl group on C-10, attack at the rear side must be assumed, leading to the 1α,2α-methylene group, whereas the β-position of the 6,7-methylene group follows from the position of the NMR signal of the methyl group on C-13 [shift of −0.17 ppm compared with *(1)*].

In animal experiments *(2a)* has an extremely strong gestational and ovulation-blocking activity.

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[*] Dr. R. Wiechert
Hauptlaboratorium der Schering AG
Müllerstr. 170–172
1 Berlin 65 (Germany)

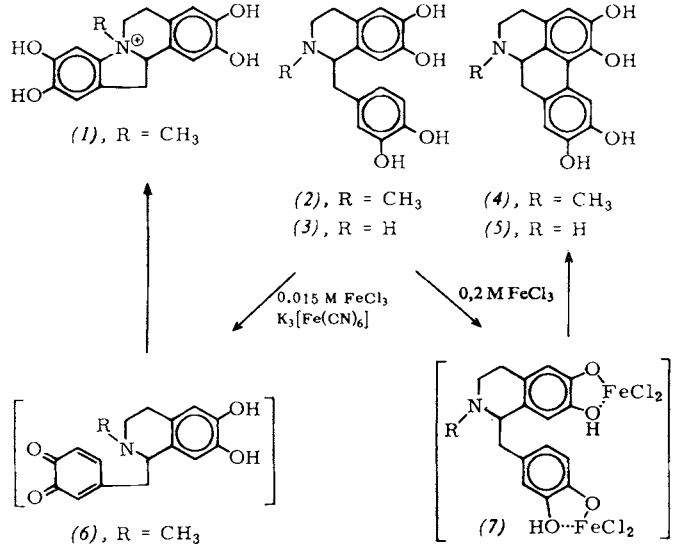
[1] *R. Wiechert* and *E. Kaspar*, Chem. Ber. *93*, 1711 (1960).
[2] *E. J. Corey* and *M. Chaykovsky*, J. Amer. chem. Soc. *84*, 867 (1962).
[3] *V. Franzen* and *H. E. Driesen*, Tetrahedron Letters *1962*, 661.

Aporphines from Laudanosoline and Norlaudanosoline [1]

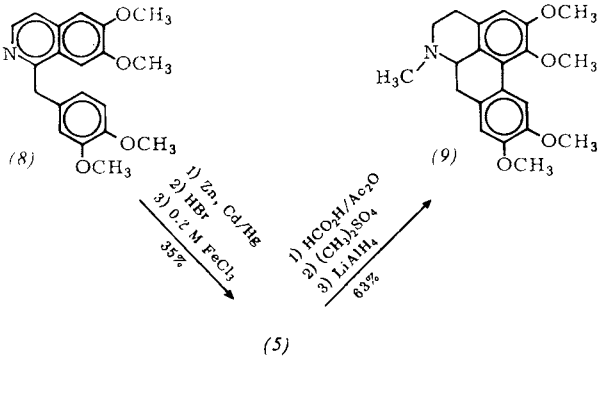
By *B. Franck* and *L.-F. Tietze* [*]

The biogenetic-type preparation of the basic structure of the numerous aporphine alkaloids, *e.g. (4)*, by oxidative condensation of derivatives of laudanosolines *(2)* is a much-studied problem of alkaloid chemistry [2–4]. Laudanosoline *(2)* [3,4] and norlaudanosoline *(3)* [5] yielded solely dibenzopyrrocoline derivatives *(1)* when treated with various oxidizing agents. Progress in this field was made when we [6], and subsequently other authors [8], were able to show that laudanosoline and related compounds undergo oxidative condensation to aporphines when their nitrogen groups are protected by quaternization.

We have now found that laudanosoline *(2)* and norlaudanosoline *(3)* may be converted into aporphines surprisingly simply and in good yields if the formation of an *o*-quinone intermediate *(6)* [3] during oxidation is hindered by complex formation with the pyrocatechol OH groups. This may be accomplished with concentrated solutions of iron(III) chloride, which converts the laudanosoline derivatives into deep green, water-soluble, weak complexes *(7)* and simultaneously acts as oxidizing agent. After reaction of *(2)* or *(3)* with 2.5 equivalents of $FeCl_3$ in 0.2 M solution at 20 °C for 48 h, and subsequent concentration of the reaction mixture, the aporphine *(4)* or *(5)*, respectively, is obtained in 63 or 52% yield as crystals of the hydrochloride. Condensation products of the type *(1)* could not be detected. On the other hand, when the reaction is carried out with the same amount of $FeCl_3$ in very dilute solution (0.015 M), or with $K_3[Fe(CN)_6]$ [3], insufficient complex formation takes place and the chloride of *(1)*, m.p. 305 °C [3], is formed (yield in excess of 70%) *via* the *o*-quinone intermediate *(6)*.



The hydrochloride of *(4)*, $C_{17}H_{17}NO_4 \cdot HCl$ (m.p. 243 °C), gives a UV spectrum [in methanol, λ_{max} = 281 (ε = 13800) and 360 (ε = 13970) nm] that is typical of aporphine alkaloids of the glaucine type *(9)*. The NMR spectrum shows three 1-proton singlets at δ = 6.23, 6.44, and 7.66 (D_2O/NaOD,



DSS[**] = O). The mass spectrum shows the characteristic main peak of tertiary aporphines (M − CH_2=N−CH_3) at *m/e* = 256[9]. The hydrochloride of *(5)* ($C_{16}H_{15}NO_4$·HCl, m.p. 280 °C) was identified similarly. Furthermore, *N*-formylation, methylation, and subsequent reduction of the formyl group yielded the naturally abundant alkaloid glaucine *(9)*. Thus the compound *(5)*, which may be obtained in three steps from papaverine *(8)*, provides the simplest route to glaucine yet discovered.

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[*] Prof. Dr. B. Franck and Dipl.-Chem. L.-F. Tietze
Institut für Organische Chemie der Universität
Neue Universität
23 Kiel (Germany)

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[5] *J. Harley-Mason*, J. chem. Soc. (London) *1953*, 1465.

[6] *B. Franck* and *G. Schlingloff*, Liebigs Ann. Chem. *659*, 123 (1962); *B. Franck, G. Blaschke*, and *G. Schlinghoff*, Angew. Chem. *75*, 957 (1963); Angew. Chem. internat. Edit. *3*, 192 (1964).

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[**] DSS signifies sodium 2,2-dimethyl-2-silapentane-5-sulfonate.

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Catalysed Synthesis of *cis*-1,2-Divinylcyclobutane

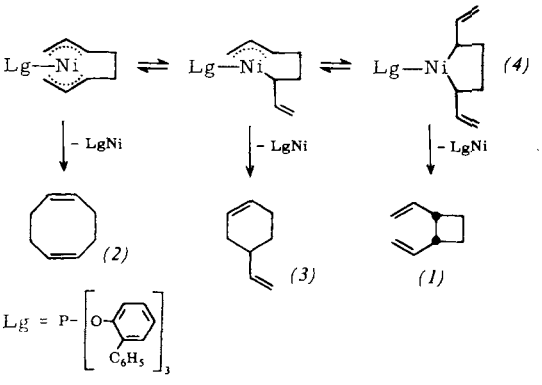
By *P. Heimbach*[**] and *W. Brenner*[*]

cis-1,2-Divinylcyclobutane *(1)* was first prepared by *Vogel*[1], using a many-stage synthesis. *Vogel*'s description of the Cope rearrangement of this four-membered ring system to *cis,cis*-1,5-cyclooctadiene (COD) *(2)* supported his hypothesis that thermal formation of *(2)* from butadiene[2] proceeds by way of *(1)*. The *cis*-compound *(1)* is also formed (8–17%) in admixture with, *inter alia*, *trans*-divinylcyclobutane in the photosensitized dimerization of butadiene[3]. Butadiene can by cyclodimerized faster in the presence of complexes of zerovalent nickel that contain *e.g.* tris-(2-biphenylyl) phosphite as ligand (Ni:P = 1:1), the rate being *ca.* 1 kg per g of nickel in the catalyst per h at atmospheric pressure and 80 °C, and the reaction yielding *(2)* (97%) and, by a side reaction, 4-vinylcyclohexene *(3)* (2.7%)[4].

If the reaction is carried out in liquid butadiene to incomplete conversion of butadiene, yields of up to 40% of *(1)*, together with *(2)* and *(3)*, are obtained. The table shows the dependence of the yields on conversion of butadiene (catalyst: $Ni^0(COD)_2$[5] + tris-(2-biphenyl) phosphite, molar ratio 1:1).

	Conversion of butadiene (20 °C)			
	30%	85%	95%	100%
(1), yield	36%	36%	14%	–
(3), yield	2.0%	2.0%	2.2%	2.4%
(2), yield	61%	61%	83%	97%

We presume that, with high concentrations of butadiene, the coordination positions on nickel that become free on conversion of π-allyl groups into σ-allyl groups become occupied by butadiene (not taken into account in the formulae given here) and that the synthesis of *(2)* is thus transformed into a synthesis of *(1)*. The product *(1)* is probably formed from the bis-σ-allyl form *(4)*.



The rate of synthesis of *(1)* depends markedly on the nature of the ligand. With short reaction times (*e.g.* 0.5 h), yields exceeding 30% of *(1)* can be achieved even at 80 °C, although thermal rearrangement of *(1)* to *(2)* has then already begun[6]. Pure *(1)* is obtained by distillation under vacuum: b.p. 8 °C/9 mm, $n_D^{20} = 1.4562$[1]. Substituted butadienes can also be converted catalytically into cyclobutanes in good yields[7].

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[*] Dr. P. Heimbach and Dipl.-Chem. W. Brenner
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz
433 Mülheim (Germany)

[**] Paper read by *P. Heimbach* at Sheffield (Symposium on Allylic and Olefinic Complexes of Metals) on April 11th, 1967.

[1] *E. Vogel*, Liebigs Ann. Chem. *615*, 1 (1958).

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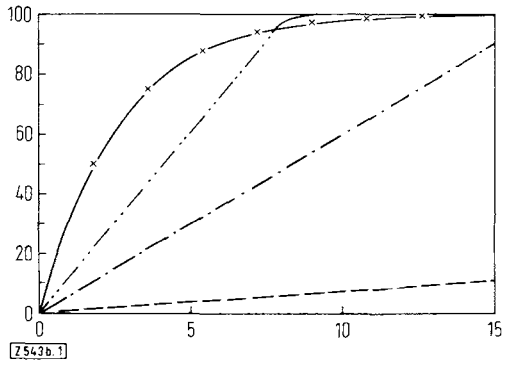
[7] Note added in proof (July 27th, 1967): Further investigations have shown that cyclooctadiene and *cis*-1,2-divinylcyclobutane are probably formed *via* the bis-π-allyl form.

Catalysed Cope Rearrangement of *cis*-1,2-Divinylcyclobutane

By *P. Heimbach*[**] and *W. Brenner*[*]

The yield of *cis*-1,2-divinylcyclobutane obtained on catalysed dimerization of butadiene depends markedly on the extent of conversion[1]. This suggested that the first product *(1)* was further catalytically altered. Our first experiments showed that predominately *cis,cis*-1,5-cyclooctadiene *(2)*, with little 4-vinylcyclohexene *(3)*, is formed from *(1)*. The rate of the catalysed rearrangement of *(1)* could be determined at 24 °C by following the volume contraction and the change of refractive index during the reaction, as well as by gas-chromatographic analysis. The concentration of catalyst in the solution was 0.2 or 0.1 molar (Ni:ligand = 1:1). The rate is directly dependent on the Ni concentration and the nature of the ligand up to *ca.* 97% conversion of *(1)*.

Fig. 1 shows the rate of the catalysed (24 °C) and also of the thermal (uncatalysed) rearrangement (80 °C) of *(1)* to *(2)*.



—×—×— Thermal conversion of *(1)* at 80 °C.

····· ·· Catalysed rearrangement, 24 °C, 0.2 M solution; ligand, tris-(2-biphenylyl) phosphite. · · · Catalysed rearrangement, 24 °C, 0.1 M solution; ligand, tris-(2-biphenylyl) phosphite. — — — Catalysed rearrangement, 24 °C, 0.2 M solution; ligand, triphenylphosphine.

Ordinate: % rearranged *(1)*.

Abscissa: Time (hours).

The latter is a first-order reaction whereas the catalysed rearrangement is a zeroth-order reaction with respect to *(1)*. However, the marked dependence of the composition of the product on the nature of the ligand [tris-(2-biphenylyl) phosphite, 0.5 % of *(3)*, 99 % of *(2)*; triphenylphosphine, 31 % of *(3)*, 60 % of *(2)*; tricyclohexylphosphine, 33 % of *(3)*, 55 % of *(2)*] confirms the assumption that the reactivity of the bis-π-allyl form *(4)* increases with marked back-donation of the nickel to the free d orbitals of the phosphorus (phosphite), but that the reactivity of the π-allyl-σ-allyl form *(5)* is greater when there is weak back-donation (phosphine) [2, 3].

Trebellas et al. [8] recently described the first Cope rearrangement that is induced by transition-metal compounds and yet occurs stoichiometrically. The catalysed Cope rearrangement of *(1)* and the fact the bis-allyl complexes formed as intermediates therein can react with further components are phenomena of a new type. We are engaged in analogous studies of other 1,5-dienes with nickel and other transition-metal catalysts.

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[*] Dr. P. Heimbach and Dipl.-Chem. W. Brenner
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz
433 Mülheim (Germany)

[**] Paper read by *P. Heimbach* at Sheffield (Symposium on Allylic and Olefinic Complexes of Metals) on April 11th, 1967.

[1] *P. Heimbach* and *W. Brenner*, Angew. Chem. *79*, 813 (1967); Angew. Chem. internat. Edit. *6*, 800 (1967).

[2] *G. Wilke* and *P. Heimbach*, unpublished.

[3] Paper read by *P. Heimbach* at the GDCh Conference, Bonn, September 1965.

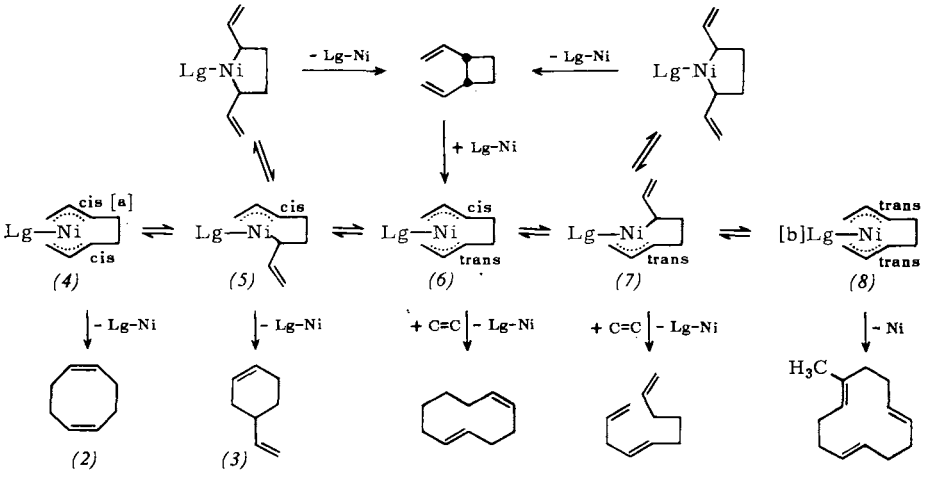
[4] *B. Bogdanovic, M. Kröner*, and *G. Wilke*, Liebigs Ann. Chem. *699*, 1 (1966).

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[a] The prefixes *cis* and *trans* refer to the configuration of the allyl groups between the C-atoms 2 and 3, or 6 and 7.

[b] In this case, Lg = isoprene.

The α-ω-allyl C_8 chain that is formed from *(1)* as intermediate on the $Ni^{(0)}$-Lg system apparently exists in equilibrium with various other forms.

Only the forms *(4)* and *(5)* react in the catalysed rearrangement of *(1)* to *(2)* and *(3)*. If ethylene is added to the reaction mixture [*ca.* 45 atm, 20 °C, Lg = $P(C_6H_5)_3$], of *cis,trans*-1,5-cyclodecadiene [from *(6)* + ethylene] (73 %) and *trans*-1,4,9-decatriene [from *(7)* + ethylene)](1 %) are formed, as well as *(2)* and *(3)*. Isoprene reacts with *(1)* in the presence of, *e.g.*, cyclododecatrienenickel(0) [4] with formation of *trans, trans, trans*-1-methyl-1,5,9-cyclododecatriene [from *(8)* and isoprene]. These reactions support the assumption that a C_8 chain is formed as intermediate in the synthesis of eight- [5], ten- [6], and twelve-membered rings [7] on complexes of nickel(0) [2].

Structure of Alkali Metal t-Butoxides

By *E. Weiss, H. Alsdorf*, and *H. Kühr* [*]

According to X-ray powder studies, the t-butoxides of potassium, rubidium, and cesium are tetrameric. They have cubic lattices, each unit cell containing one tetrameric formula-equivalent [space group $P\bar{4}3m$, a_0 = 8.47$_5$ Å (K), 8.610 (Rb), 8.902 (Cs)]. The tetrameric structural units have T_d symmetry, the metal and oxygen atoms occupying alternate corners of an only slightly distorted cube with the four t-butyl groups lying on the extended diagonals (see Fig. 1).

The following atomic distances were obtained for the potassium compound: K–O 2.56; C–O 1.39; C–CH_3 1.56 Å; bond angle O–C–CH_3 112.1 °. The non-metallic atoms could not be precisely located in the rubidium or cesium compound. Sodium t-butoxide crystallizes in a lattice of lower symmetry and as yet undefined structure.

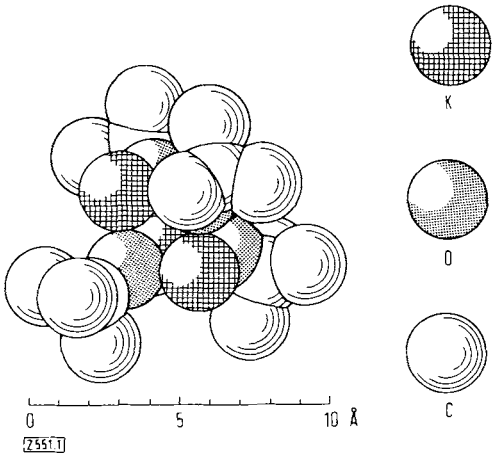


Fig. 1. Structure of potassium t-butoxide.

The following information about internal rotations was obtained from ^{1}H–NMR spectra (broad line resonance): the second moment (S_2)[1] is almost constant (2.4 ± 0.3 G^2) between +20 and −20 °C, rises rapidly between −20 and −50 °C, and at −80 °C reaches a value of 8.0 ± 0.5 G^2; we interpret this as freezing of the rotation of the t-butyl groups about their three-fold axes in the temperature range −20 to −50 °C. As the temperature falls further, the rotation of the individual methyl groups also becomes increasingly hindered as shown by the further increase in S_2, particularly in the region −130 to −160 °C. An end value of about 40 G^2 is reached at −190 °C.

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[*] Prof. Dr. E. Weiss, Dipl.-Chem. H. Alsdorf, and Dipl.-Chem. H. Kühr
Institut für Anorganische Chemie der Universität Papendamm
2 Hamburg 13 (Germany)

[1] The second moment is defined as $S_2 = \int_{-\infty}^{+\infty} f(H)\Delta H^2 dH / \int_{-\infty}^{+\infty} f(H)dH$. The unit G denotes gauss.

Preparation of Organoboron Halides from Halogenoalkenes and Organoboron Hydrides

By *R. Köster* and *W. Fenzl*[*]

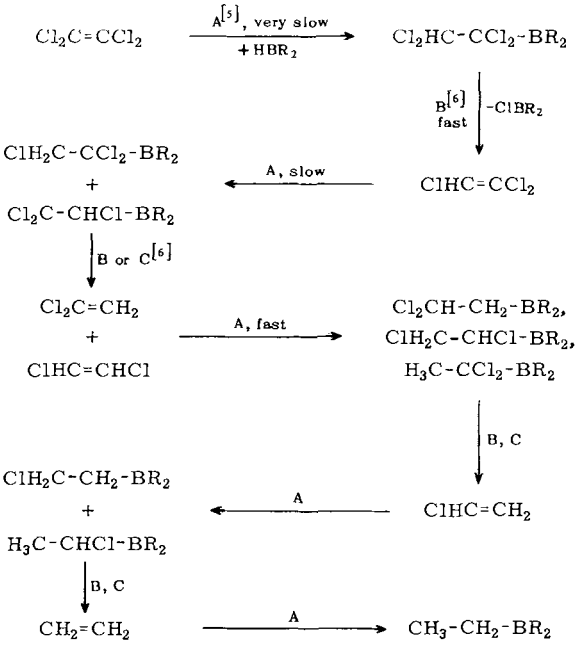
Alkenes and cycloalkenes that are chlorinated or brominated in the vinyl or allyl position can be completely dehalogenated by boron hydrides. Whereas vinyl chlorides[1–4] and vinylidene dichlorides react even at room temperature, it is only above 150 °C that reasonably rapid exchange of chlorine for hydrogen occurs with trichloroethylene, tetrachloroethylene, or analogous compounds (*e.g.* perchloropropylene).

Organoboron chlorides are also obtained in high yield from perchlorocycloalkenes (*e.g.* perchlorocyclopentadiene) or perchlorodienes (perchlorobutadiene) and organoboron hydrides.

Sodium borohydride reacts in the presence of trialkylboranes in the same way as organoboron hydrides (*e.g.* tetraalkyldiboranes, which are always present in equilibrium with dialkylboron hydrides). For the reaction

$$5(C_2H_5)_2BH + Cl_2C{=}CCl_2 \rightarrow 4\ ClB(C_2H_5)_2 + (C_2H_5)_3B$$

hydroboration of the perchlorinated ethylene is the rate-determining step. Partially chlorinated ethylenes do not occur in the product mixture. The hydroborations and removals of Cl–BR$_2$ that constitute successive stages of the reaction lead to boranes with halogen-free alkyl groups (see reaction scheme). They are not catalysed by organoboron chlorides or aluminum chloride.



Experimental

66.4 g (0.4 mole, 55.4 g of Cl on C) of tetrachloroethylene and 151.7 g (2.0 BH equiv.) of tetraethyldiborane (13.29 ‰ of H$^\ominus$) are heated in a 500-ml autoclave at 190–225 °C for 18 h. After cooling, 15.15 l (NTP) of gas (=20 g; C_2H_6 93 %; CH_4 4.8 %; C_2H_4 0.9 %; C_4H_{10} 0.6 %) were released. Distillation of the brown liquid, which is formed in the reaction, gives 146 g of ethylboron chlorides (b.p. 73–92 °C). Yield: 37.7 g of Cl on B (68.1 %). Working up of the residue (52 g) gives, as well as boranes of higher chlorine content and unreacted tetrachloroethylene, 6 g of organocarboranes (b.p. 41–47 °C/10^{-3} mm), which contain mainly 1,3,5,6,7-pentaethyl-2,4-dimethyl-2,4-dicarbaclovoheptaborane(7) (mol. wt. 254).

Alkenes with chlorine in the allyl position are also completely dehalogenated. Thus the organoboron chlorides obtained from perchloropropene and ethyldiboranes contain also propyl groups on the boron. The reactions are clean so long as no boranes more highly chlorinated than diorganoboron monochlorides are formed. It is therefore advantageous to add an excess of trialkylborane to the reaction mixture, particularly when using sodium borohydride as source of B–H.

$$3\ NaBH_4 + 3\ (C_2H_5)_3B + 3\ C_2Cl_3H \rightarrow 9\ (C_2H_5)_2BCl + (C_2H_5)_3B$$

If the concentration of boron hydrides is too high, organocarboranes[7] are formed above 180 °C by condensation (loss of alkane, H_2). Since hexachlorocyclopentadiene is relatively easily hydroborated by tetraethyldiborane, it can be rapidly dehalogenated even at 170 °C.

$$3\ C_5Cl_6 + 24\ (C_2H_5)_2BH \xrightarrow{+\ \rangle BH} 18\ (C_2H_5)_2BCl + 4\ (C_2H_5)_3B + B_2(C_5H_8)_3$$

Experimental

52.8 g (0.196 mole) of hexachlorocyclopentadiene and 124.9 g (1.56 BH equiv.) of tetraethyldiborane (12.5 ‰ of H$^\ominus$) are shaken in a 500-ml autoclave at 170 °C for 2 h. After cooling, and release of 660 l (NTP) of ethane (containing a little CH_4

and traces of H_2 and C_4H_{10}), the 169 g of crude product (21.6 % of Cl on B, corresponding to 89 % of the Cl on C used) affords on distillation 135.6 g of diethylboron chloride and triethylborane (b.p. 79–83 °C; 26.7 % of Cl). There remains 33 g of a brownish viscous liquid (9.6 % of B), which contains, *inter alia*, bisboronated cyclopentane.

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[*] Dr. R. Köster and Dr. W. Fenzl
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1
433 Mülheim-Ruhr (Germany)

[1] *M. F. Hawthorne* and *J. A. Dupont*, J. Amer. chem. Soc. *80*, 5830 (1958).

[2] *M. F. Hawthorne*, J. Amer. chem. Soc. *82*, 1886 (1960); *D. J. Pasto* and *S. R. Snyder*, J. org. Chemistry *31*, 2773, 2777 (1966).

[3] *T. Wartik* and *R. K. Pearson*, J. inorg. nucl. Chem. *1958*, 250.

[4] *R. Köster*, *G. Griasnow*, *W. Larbig*, and *P. Binger*, Liebigs Ann. Chem. *672*, 1 (1964); *P. Binger* and *R. Köster*, Tetrahedron Letters *1961*, 156.

[5] A: Hydroboration.

[6] B: *cis*-1,2-Elimination [1,2,4]; C: transfer reaction [2].

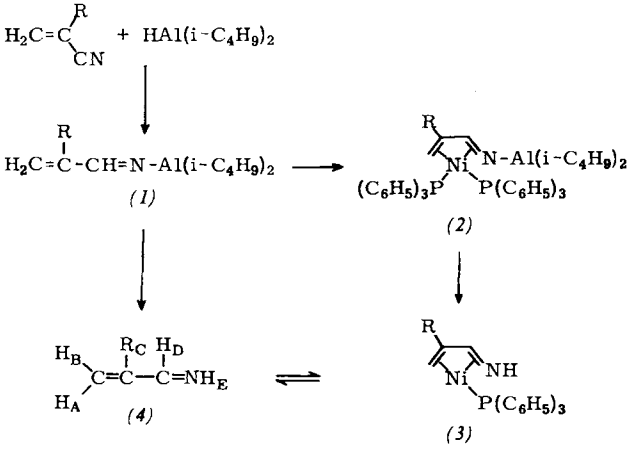
[7] *R. Köster*, *W. Larbig*, and *G. Rotermund*, Liebigs Ann. Chem. *682*, 21 (1965).

Acraldehyde Imine and 2-Methylacraldehyde Imine

By *B. Bogdanović* and *M. Velić* [*]

It was reported earlier [1] that dialkylaluminum *N*-alkylideneamides obtained by addition of dialkylaluminum hydrides to nitriles react with equivalent amounts of acetylacetone, with cleavage of the Al–N bond, to yield aldimines and dialkylaluminum acetylacetonates. This reaction is suitable for synthesis of aldimines on a preparative scale provided that the rather unstable aldimines can be separated from the organoaluminum compounds.

From diisobutylaluminum hydride and acrylonitrile (molar ration 1:1, in pentane at 20 °C) we obtained diisobutylaluminum *N*-allylideneamide *(1a)* as a pale yellow liquid, b.p. 105–110 °C/10^{-4} mm, in 58 % yield. This compound is dimeric in benzene. It reacts with acetylacetone in the molar ratio 1:1 in toluene at −5 °C, yielding acraldehyde imine *(4a)* which is proved to be present in the high-vacuum distillate (0 °C) by conversion into the π-complex *(3a)* on reaction with bis(triphenylphosphine)ethylenenickel [2] (yield 30 %). Solutions of free acraldehyde imine thus obtained are always contaminated by small amounts of diisobutylaluminum acetylacetonate and/or ammonia.



(a), R = H
(b), R = CH_3

Pure acraldehyde imine is isolated in higher yield as follows: *(1a)* reacts with bis(triphenylphosphine)ethylenenickel [2] with removal of ethylene to give high yields of the sparingly soluble, orange (acraldehyde diisobutylaluminoamide)bis-(triphenylphosphine)nickel *(2a)* [3]. The latter reacts with acetylacetone in the same way as *(1a)*, but in this case the imine can be separated from the soluble diisobutylaluminum acetylacetonate as the well crystalline, deep red complex *(3a)* (yield 84 %). The IR spectrum of the products obtained *via* both routes (*(1a)* → *(4a)* → *(3a)* and *(1a)* → *(2a)* → *(3a)*) showed that the compounds are identical. Acraldehyde imine *(4a)* can be removed from the π-complex *(3a)* by means of triphenyl phosphite, being obtained as distillate in pure, solvent-free form in yields of *ca.* 50 %. Yields of *ca.* 65 % are obtained if the imine is separated from *(3a)* in toluene solution and then distilled in a high vacuum.

Acraldehyde imine is a colorless liquid at −80 °C; its mass spectrum shows the molecular ion at *m/e* = 55. The ^{1}H–NMR spectrum of a perdeuteriotoluene solution (50 %) at −70 °C accords with structure *(4a)*: τ = 4.55 (H_A, doublet), τ = 4.47 (H_B, doublet), τ = 3.43 (H_C, multiplet), τ = 1.95 (H_D, double doublet), τ = −1.22 (H_E, doublet) with J_{DE} = 16 Hz; the signal for H_E is found only when the spectrum of the solvent-free compound is measured at −70 °C; the doublet structure is no longer recognizable from −40 °C upwards [4]. From the ^{1}H–NMR spectrum it can be shown that the pure compound is altered within a few hours even at −70 °C [**]; apparently polymerization or oligomerization occurs. In dilute solution, however, polymerization of the compound requires several days.

The aluminoamide *(1b)* (colorless crystals, b.p. 125–130 °C/10^{-4} mm; 98 % yield) was prepared analogously by addition of diisobutylaluminum hydride to methacrylonitrile. Reaction with bis(triphenylphosphine)ethylenenickel afforded the complex *(2b)* (89 % yield). In this case treatment with acetylacetone in the molar ratio 1:1 surprisingly did not lead to complete protolysis of the Al–N bond; a molar ratio of 3:1 was required for quantitative cleavage of the Al–N bond; the sparingly soluble aluminum trisacetylacetonate was then formed thus hindering isolation of the complex *(3b)*. This difficulty was overcome by cleaving *(2b)* with water. The aldimine π-complexes *(3a)* and *(3b)* are stable to hydrolysis. 2-Methylacraldehyde imine *(4b)* is obtained, like acraldehyde imine, by displacement from the π-complex with triphenyl phosphite (yield in toluene, 84 %). ^{1}H–NMR spectrum of *(4b)* in perdeuteriotoluene (50 %) at −70 °C: τ = 4.88 and 4.63 (H_A and H_B, singlets), τ = 8.06 ($CH_{3,C}$ singlet), τ = 2.12 (H_D, doublet), τ = 0.08 (H_E, doublet), J_{DE} = 16 Hz. The mass spectrum shows the molecular ion at *m/e* = 69.

The compounds *(4a)* and *(4b)*, not hitherto isolated, have been discussed as possible intermediates in the ammonoxidation of propene and isobutene to acrylonitrile and methacrylonitrile, respectively [5].

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[*] Dr. B. Bogdanović and Dipl.-Ing. M. Velić
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1
433 Mülheim/Ruhr (Germany)

[**] We thank Dr. *E. G. Hoffmann*, Dr. *D. Henneberg*, and their co-workers for measurement and discussion of the ^{1}H–NMR and mass spectra.

[1] *B. Bogdanović*, Angew. Chem. *77*, 1010 (1965); Angew. Chem. internat. Edit. *4*, 954 (1965).

[2] *G. Wilke* and *G. Herrmann*, Angew. Chem. *74*, 693 (1962); Angew. Chem. internat. Edit. *1*, 549 (1965); *G. Herrmann*, Dissertation, Technische Hochschule Aachen, 1963.

[3] The nickel complexes of types *(2)* and *(3)* will be described in detail in later publications.

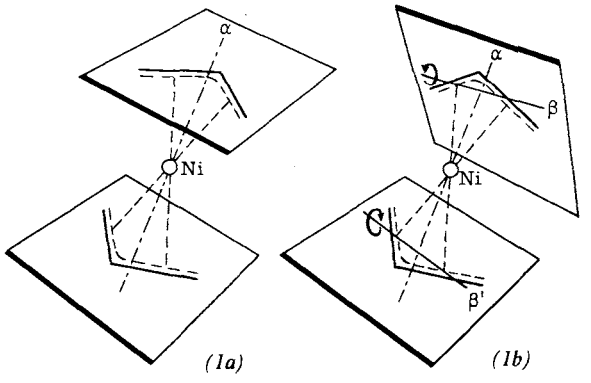
[4] Similar effects were observed for ketimines by *J. B. Lambert*, *W. L. Oliver*, and *J. D. Roberts*, J. Amer. chem. Soc. *87*, 5086 (1965).

[5] *D. J. Hadley*, Chem. and Ind. *1961*, 238; *W. F. Brill* and *J. H. Finley*, Ind. Engng. Chem. Prod. Res. Dev. *3*, (2) 89 (1964).

cis- and *trans*-Bis-(π-allyl)nickel Systems [1]

By *H. Bönnemann*, *B. Bogdanović*, and *G. Wilke* [*]

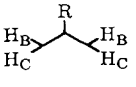
In 1961 we reported on bis-(π-allyl)nickel *(1)* [2], the first "pure" [3] allyl derivative of a transition metal. From the ^{1}H–NMR spectrum it could be shown that this complex exists in *cis-trans*-isomeric forms *(1a)* and *(1b)* [2b]. X-ray structure analysis [5] has proved that bis-(π-methallyl)nickel *(2)* [6] exists as *trans*-isomer [cf. *(1a)*] in the single crystal.



(1a) *(1b)*

The ^{1}H–NMR spectra of *(1)* and *(2)* are independent of temperature, within experimental error, from −70 to +30 °C, *i.e.* the proportions of the isomers in *(1)* (3:1) and *(2)* (2.3:1) remain substantially constant. The same proportions are found if the crystalline complexes are dissolved at −70 °C and their NMR spectra are measured immediately. For the time being, the groups of signals in the ^{1}H–NMR spectra [7] can be assigned to the *cis*- and *trans*-forms only on the basis of the following considerations of models.

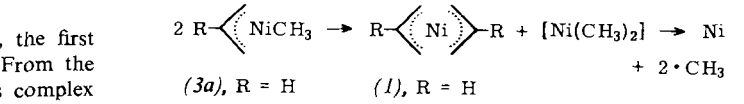
Measurement of atomic distances on a scale model shows that on transition of the *trans*- *(1a)* into the *cis*-form *(1b)* (180 ° rotation of the allyl groups around the "σ-bond axis") the most favorable steric arrangement is obtained if the allyl groups are also twisted by about 10 ° around the axes β and β′ [see arrows in *(1b)*]. The *anti*-protons (H_C) are farther from



(1), R = H_A
(2), R = CH_3

the nickel (less shielded) in *(1b)* than in *(1a)*, while the *syn*-protons (H_B) and the *meso*-substituent approach the nickel somewhat more closely (increased shielding); the assignments given in the table then follow.

We obtained products with different proportions of isomers in the following way: (π-Allyl)- *(3a)* [8] and (π-methallyl)-methylnickel *(3b)* [1] disproportionate quantitatively above −78 °C as follows:



(3a), R = H *(1)*, R = H
(3b), R = CH_3 *(2)*, R = CH_3

The $Ni(CH_3)_2$ decomposes at once to give CH_3 radicals and elemental nickel. The bis-(π-allyl)nickel compounds *(1)* and *(2)* obtained in this way can be isolated in crystalline form at −100 °C. The crystals were dissolved in deuteriotoluene at −78 °C and the ^{1}H–NMR spectra of the solutions were measured as the temperature increased (the samples were thawed over a period of 5 hours). The following proportions of isomers were calculated from the spectra.

Temp. (°C)	*(1a)* : *(1b)*	*(2a)* : *(2b)*
−70	7.8 : 1	0.5 : 1
−50	3.1 : 1	1.2 : 1
−30	3 : 1	2.3 : 1
+30	3 : 1	2.3 : 1
−70	3 : 1	2.3 : 1

From these results it follows that:

1. Bis-(π-allyl)nickel *(1)* and bis-(π-methallyl)nickel *(2)* occur as mixtures of *cis-trans*-isomers.

2. The *trans*-form is favored.

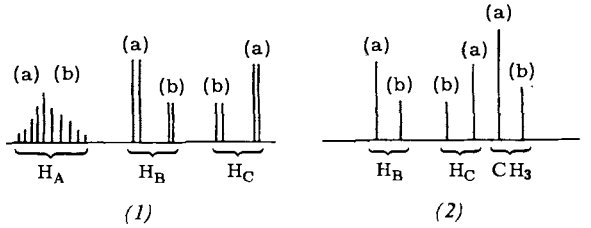
3. (π-Allyl)methylnickel *(3a)* decomposes largely stereospecifically to the *trans*-isomer (*trans*:*cis* = 7.8:1 instead of 3:1) at −75 °C, whereas under similar conditions the (π-methallyl)methylnickel *(3b)* affords the *cis*-form preferentially (*trans*:*cis* = 0.5:1 instead of 2.3:1).

4. At low temperatures the energetically favored equilibrium of *cis*- and *trans*-forms is established only slowly from these mixtures – with *(2)* more slowly than with *(1)*.

Final proof of the configuration of *(2b)* is currently being sought by X-ray structure analysis of the crystalline bis-(π-methallyl)nickel obtained by disproportionation.

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	τ H_A	τ H_B	τ H_C	τ CH_3	Intensity ratio *trans* : *cis*
$Ni(C_3H_5)_2$					
(1a), *trans*	5.02	6.09	8.25	—	3.0:1
(1b), *cis*	5	6.32	7.81	—	
$Ni(C_4H_7)_2$					
(2a), *trans*	—	6.34	8.21	8.36	2.3:1
(2b), *cis*	—	6.49	7.81	8.61	



(1)

(2)

[*] Dr. H. Bönnemann, Dr. B. Bogdanović, and Prof. G. Wilke
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1
433 Mülheim-Ruhr (Germany)

[1] *H. Bönnemann*, Dissertation, Technische Hochschule Aachen. 1967.

[2] [a] *G. Wilke* and *B. Bogdanović*, Angew. Chem. *73*, 756 (1961).
[b] *B. Bogdanović*, Dissertation, Technische Hochschule Aachen, 1962.

[3] Newcomers to the field [4] have recently introduced the term "isoleptic"; however, we feel that the use of this term is not philologically sound.

[4] *J. K. Becconsall*, *B. E. Job*, and *S. O'Brien*, J. chem. Soc. (London) *1967 A*, 423, report that the proportion of the isomers is temperature-dependent between −40 °C [3:1 in $CDCl_3$] and +60 °C [2.2:1 in benzene].

[5] *H. Dietrich* and *R. Uttech*, Z. Krist. *122*, 112 (1965).

[6] [a] *G. Wilke*, Angew. Chem. *75*, 10 (1963); p. 19; Angew. Chem. internat. Edit. *2*, 105 (1963), p. 114.
[b] *W. Keim*, Dissertation, Technische Hochschule Aachen, 1963.

[7] The spectra were measured on a Varian A 60 spectrometer for solutions in deuteriotoluene at 30 °C with tetramethylsilane as internal standard. We thank Dr. *E. G. Hoffmann* and his collaborators for measurement and discussion of the spectra.

[8] *B. Bogdanovic*, *H. Bönnemann*, and *G. Wilke*, Angew. Chem. *78*, 591 (1966); Angew. Chem. internat. Edit. *5*, 582 (1966).

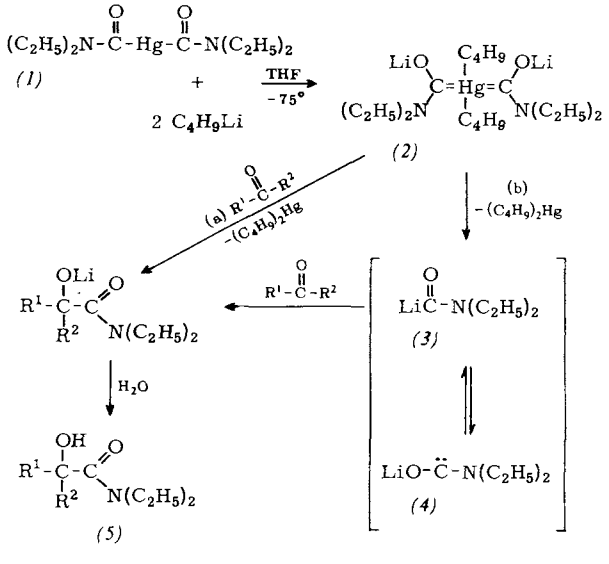
Preparation of Diethylcarbamoyllithium [(Diethylamino)lithiooxycarbene] from Bis(diethylcarbamoyl)mercury

By *U. Schöllkopf* and *F. Gerhart* [*]

In organic chemistry, a reagent for one-stage nucleophilic introduction of carboxyl groups [1] would prove very useful. Alkali-metal compounds of formic acid derivatives should be most suitable for this purpose but are apparently unstable [2]. We are at present studying whether they can be prepared at low temperatures and whether they can be stabilized, perhaps in their tautomeric carbene forms, by complex formation with heavy-metal atoms [3].

When we treated bis(diethylcarbamoyl)mercury *(1)* [4] in tetrahydrofuran at *ca.* −75 °C with two equivalents of n-butyllithium we obtained diethylcarbamoyllithium *(3)*, or an equivalent reagent *(4)* (cf. below), which on reaction with carbonyl compounds gave α-hydroxy-*N*,*N*-diethylcarboxamides *(5)* and with tributyltin chloride gave tributyl(diethylcarbamoyl)tin [b.p. 118 °C/0.1 mm; IR spectrum: $\nu_{C=O}$ 1570 cm^{-1}, NMR spectrum (in CCl_4): N–CH_2– at τ = 6.66 (quartet) and 6.17 (quartet)]. In dilute HCl the compound evolves CO.

The reactions may begin by addition of the butyllithium to the mercury atom of *(1)* to form the dibutylmercury-(diethylamino)lithiooxycarbene complex *(2)*. We cannot yet decide whether this complex reacts directly with the electrophile (*e.g.* the carbonyl compound) (route a) or whether reaction takes place *via* a tautomer [*i.e.* (diethylcarbamoyl)lithium *(3)* or (diethylamino)lithiooxycarbene *(4)*] (route b).



Electrophile	Product (after hydrolysis)	Yield (%)
Benzaldehyde	*N*,*N*-Diethylmandelamide	71
Acetophenone	*N*,*N*-Diethylatrolactamide	66
Benzophenone	*N*,*N*-Diethyldiphenylglycolamide	75
Benzoyl chloride	*N*,*N*-Diethylphenylglyoxylamide	65
Ethyl benzoate	*N*,*N*-Diethylphenylglyoxylamide [a]	31
Methanol	*N*,*N*-Diethylformamide	54
[O–D]-Methanol	*N*,*N*-Diethyldeuterioformamide	51
Methyl iodide	*N*,*N*-Diethylacetamide	23
Mercury(II) chloride	Bis(diethylcarbamoyl)mercury	68
Tributyltin chloride	Tributyl(diethylcarbamoyl)tin	74

[a] As well as α-hydroxy-α-phenylmalonic acid bis(diethylamide).

N,N-Diethylatrolactamide: A 1.4 M solution (25 ml) of n-butyllithium in pentane is added to a suspension of very finely powdered *(1)* [4] (7 g, 17.5 mmoles) in anhydrous tetrahydrofuran (70 ml) at −70 to −78 °C over a period of 15 min with vigorous stirring. The bright yellow solution is then added to a solution of acetophenone (4.2 g, 35 mmoles) in anhydrous THF at −70 °C. The solvent is distilled off in a rotary evaporator under vacuum and the residue is treated with water (25 ml) and extracted with ether. The ether extract is then worked up as usual. Distillation affords dibutylmercury (3.91 g; b.p. 47 °C/0.1 mm) and *N*,*N*-diethylatrolactamide [5.10 g; b.p. 115–116 °C/0.3 mm, m.p. 90 °C (from petroleum ether boiling range 70–80 °C)].

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[*] Prof. U. Schöllkopf and Dipl.-Chem. F. Gerhart
Organisch-Chemisches Institut der Universität
34 Göttingen (Germany)

[1] For experiments on the introduction of carboxyl groups by means of metalated orthothioformic esters see *D. Seebach*, Angew. Chem. *79*, 468 (1967); Angew. Chem. internat. Edit. *6*, 442 (1967).

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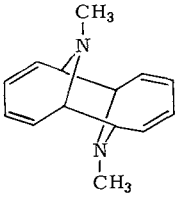
[3] For metal-carbene complexes see *E. O. Fischer* and *A. Maasböl*, Chem. Ber. *100*, 2445 (1967); *U. Schöllkopf* and *F. Gerhart*, Angew. Chem. *79*, 578 (1967); Angew. Chem. internat. Edit. *6*, 650 (1967); *P. W. Yolly* and *R. W. Pettit*, J. Amer. chem. Soc. *88*, 5044 (1966).

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X-ray Structure Analysis of a Dimer of 1-Methylazepine

By *G. Habermehl* and *S. Göttlicher* [*]

On reduction of 1-azepinecarboxylic esters with lithium tetrahydridoaluminate *Hafner* and *Mondt* [1] obtained 1-methylazepine, which dimerized very rapidly above 0 °C to afford two isomers melting at 171 and 66 °C respectively. On the basis of spectroscopic data and its dipole moment, the compound of m.p. 171 °C was assigned the structure of a 13,14 - dimethyl - 13,14 - diazatricyclo[6.4.1.1^{2,7}]tetradeca-3,5,9,11-tetraene *(1)*.



(1)

We have carried out an X-ray structure analysis of the hydrobromide (m.p. 240 °C) of this compound in order to prove the assigned structure and configuration.

The hydrobromide crystallizes, from 50 % methanol, in the triclinic form containing two molecules of water. The space group is P $\bar{1}$; the lattice constants are a = 8.14 Å; b = 8.77 Å; c = 7.15 Å; α = 94.5 °; β = 94.0 °; γ = 125.0 °. The unit cell contains one centrosymmetrical molecule.

Two and three-dimensional electron-density determinations by the heavy-atom method showed that the structure given by *Hafner* and *Mondt* is correct. Refinements were carried out by Fourier difference syntheses and by least-squares calculations. Bond distances and valence angles accord with the theoretical values.

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[*] Priv.-Doz. Dr. G. Habermehl and Dr. S. Göttlicher
Institut für Organische Chemie und Zintl-Institut für anorganische und physikalische Chemie der Technischen Hochschule
Schlossgartenstrasse 2
61 Darmstadt (Germany)

[1] *K. Hafner* and *J. Mondt*, Angew. Chem. *78*, 823 (1966); Angew. Chem. internat. Edit. *5*, 839 (1966).

10-Chloro-9-fluorobicyclo[6.2.0]deca-2,4,6,9-tetraene and 3-Chloro-2-fluorobicyclo[2.2.0]hexa-2,5-diene

By *G. Schröder* and *Th. Martini* [*]

We are currently studying the behavior of cyclooctatetraene towards reagents that can undergo 1,2-cycloaddition and we report here its reaction with 1,1-dichloro-2,2-difluoroethylene.

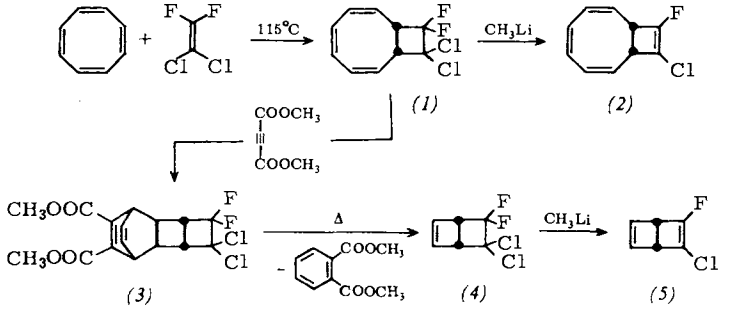
When 30 g of cyclooctatetraene is heated in an ampoule with 40 g of 1,1-dichloro-2,2-difluoroethylene for 70 h at *ca.* 115 °C, 4.7 g of the cycloadduct $C_{10}H_8Cl_2F_2$ *(1)* [1], b.p. 53 °C/0.05 mm, is formed and can be separated from unchanged starting materials by fractional distillation. The spectral data [2] of *(1)* are: UV spectrum, λ_{max} = 246 nm (ε = 1800); NMR spectrum, two multiplets centered at τ = 4.2 and 6.3 (relative intensities 3:1).

Like other derivatives of cyclooctatriene [3], the adduct *(1)* reacts smoothly with dienophiles. This behavior and the general views concerning 1,2/1,2-cycloaddition [4] indicate the *cis*-configuration for the two bridgehead H atoms.

The adduct *(1)* (6.5 g) reacts smoothly with CH_3Li (from 15 g CH_3I and 1.5 g Li) in ether (250 ml) at *ca.* −20 °C, to yield 10-chloro-9-fluorobicyclo[6.2.0]deca-2,4,6,9-tetraene *(2)*. The mixture is treated at 0 °C with aqueous NH_4Cl, the ethereal phase is separated and dried, and the ether is distilled off in a rotatory evaporator at not more than 0 °C and at a pressure of *ca.* 1 mm [crude yield of *(2)*, 70 %]. Column chromatography [basic Al_2O_3, petroleum ether (b.p. 30 to 35 °C)] at 0 °C yields pure *(2)*. The structure of compound *(2)* follows from (i) the assumption that the C skeleton of *(1)* remains intact on dehalogenation by CH_3Li and (ii) the spectral data [2]: UV spectrum, pronounced shoulder at 246 nm (ε = 2400); NMR spectrum, multiplet with little fine structure at τ = 4.3 and a broad multiplet with well-developed fine structure between τ = 6.1 and τ = 7.1 (relative intensities 3:1).

Compound *(2)* is a colorless thermolabile liquid. Its half-life can be determined by means of NMR spectroscopy and amounts to *ca.* 8 h in CCl_4 at 20 °C. When kept at room temperature, 1–2 g of *(2)* rearranges almost explosively with loss of hydrogen halide, to 1-chloro- and 1-fluoro-naphthalene [5].

Gentle warming of a solution of *(2)* in, *e.g.*, CCl_4 affords the same end products in about the same proportions (8 parts of 1-chloro- and 1 part of 1-fluoro-naphthalene, determined by gas chromatography). We suggest that 1,9-dihalogeno-9,10-dihydronaphthalenes are formed *via* 2-chloro-1-fluoro[10]annulene [6] and afford the end products by elimination of HF or HCl.



With dimethyl acetylenedicarboxylate, the adduct *(1)* undergoes a Diels-Alder reaction.

Dimethyl acetylenedicarboxylate (3.8 g) is warmed with *(1)* (5 g) in benzene (40 ml) in an ampoule at 80 °C for 45 h. After removal of the solvent by distillation and recrystallization of the residue from petroleum ether/tetrahydrofuran, the adduct has the composition $C_{16}H_{14}Cl_2F_2O_4$ [1] (yield 80 %; m.p. 82–83 °C). Its spectral data (NMR, IR, and UV) are in accord with structure *(3)*. At 150–160 °C it decomposes into dimethyl phthalate [5] and the derivative *(4)* of bicyclo[2.2.0]-hexene [1] [yield of *(4)*, 65 % after purification by gas chromatography] in accord with the Alder-Rickert mechanism. The NMR spectrum [2] of *(4)* includes a signal, only slightly split, at τ = 3.65 and a triplet with fine structure at τ = 6.3 (relative intensities 1:1).

3-Chloro-2-fluorobicyclo[2.2.0]hexa-2,5-diene *(5)* is obtained from the product *(4)* (2.5 g) and CH_3Li (from 8.5 g CH_3I and 0.6 g Li) in ether (150 ml) at *ca.* −20 °C. The mixture is treated with aqueous NH_4Cl at *ca.* 0 °C and the ethereal phase is separated, dried, and concentrated to *ca.* one tenth of its original volume in a vacuum through a reflux column. The ethereal solution enriched in *(5)* is separated into its components by preparative gas chromatography [yield of pure *(5)*, 70 %]. The NMR spectrum [2] of *(5)* contains only a slightly split signal at τ = 3.50 (relative intensity 1) and two doublets of doublets (relative intensity 1) centered at τ = 6.30 and τ = 6.45. When *(5)* is warmed it gives pure *o*-chlorofluorobenzene [5], the half-life, determined by NMR spectroscopy, being three weeks in CCl_4 at 20 °C [7].

The reaction path *(1)* → *(3)* → *(4)* → *(5)* not only proves the structure of *(1)*, but also provides a convenient route to the "Dewar benzene" *(5)* from cyclooctatetraene. Pure *(5)* is a colorless liquid. It is sensitive to shock and explodes violently on gentle warming, and even when kept at 20 °C. It is advisable to handle the undiluted substance only in small quantities (*ca.* 50 mg).

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[*] Priv.-Doz. Dr. G. Schröder and Dipl.-Chem. Th. Martini
Institut für Organische Chemie der Technischen Hochschule
Richard-Willstätter-Allee
75 Karlsruhe (Germany)

[1] Satisfactory C,H analyses were obtained for this compound.

[2] The UV spectra were measured with a Beckman DK-2 instrument for solutions in n-hexane or cyclohexane; the NMR spectra were recorded with a Varian A-60 apparatus for solutions in CCl_4 or CS_2 with tetramethylsilane as internal standard.

[3] The Diels-Alder reaction is preceded by valence isomerization of the cyclooctatriene; see, *e.g.*, *G. Schröder* and *W. Martin*, Angew. Chem. *78*, 117 (1966); Angew. Chem. internat. Edit. *5*, 130 (1966); *A. C. Cope et al.*, J. Amer. chem. Soc. *74*, 4867 (1952).

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[5] Identification was by comparison of the IR and UV spectra with those of authentic material.

[6] Unsubstituted [10]annulene was recently described as a species that exists only at low temperature: *E. E. van Tamelen* and *T. L. Burkoth*, J. Amer. chem. Soc. *89*, 151 (1967).

[7] *E. E. van Tamelen* and *S. P. Pappas*, J. Amer. chem. Soc. *85*, 3297 (1963), give two days as the half-life of unsubstituted "Dewar benzene" in pyridine at room temperature.

Synthesis and Structure of Dialkylgallium Fluorides

By *H. Schmidbaur*, *H. F. Klein*, and *K. Eiglmeier* [*]

In view of the distinctive position of dialkylaluminum fluorides [1–4] among dialkylaluminum halides, investigation of the corresponding gallium compounds appeared desirable [5–7].

We have found that the treatment of trimethyltin fluoride with trialkylgallium or trialkylgallium-ether complexes yields the desired compounds in good yields (85–95 %) and in high purity; the tetraalkyltin that is formed as by-product is readily separable.

$$(CH_3)_3Ga{\cdot}O(C_2H_5)_2 + (CH_3)_3SnF \rightarrow (C_2H_5)_2O + (CH_3)_4Sn + (CH_3)_2GaF \quad (1)$$

$$(C_2H_5)_3Ga + (CH_3)_3SnF \rightarrow (CH_3)_3SnC_2H_5 + (C_2H_5)_2GaF \quad (2)$$

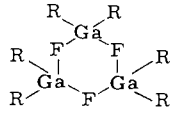
Trimethylsilicon fluoride does not react with a trialkylgallium, although it does react with a trialkylaluminum[3].

Compounds *(1)* and *(2)* are colorless, viscous liquids that crystallize when cooled (m.p. 20–22 °C and −19 to −18 °C, respectively) and can be distilled without decomposition in a vacuum (b.p. 75 °C/20 mm and 92–94 °C/1 mm, respectively). They are very soluble, without decomposition, in diethyl ether, petroleum ether, cyclohexane, benzene, methylene chloride, and water (!). Cryoscopic molecular-weight determinations in benzene give the triple formula weight in each case.

Both benzene and aqueous solutions of *(1)* show only one ^{1}H–NMR signal for all the methyl groups, namely a singlet, $\delta CH_3 = +37$ or +17.5 Hz at 60 MHz (tetramethylsilane as external standard). The ^{1}H–NMR spectrum of *(2)* in the same solvents and referred to the same standard shows an A_3B_2 multiplet with J(HCCH) ≈ 7 Hz and $\delta CH_3 = +37.5$, $\delta CH_2 = -3$, or $\delta CH_3 = -66$, $\delta CH_2 = -25$ Hz.

The IR spectra contain very few absorption bands in the 4000–400 cm^{-1} region; for *(1)* there are, *inter alia*, the following bands: 613 s, 552 w, 538 m (νGaC$_2$), and 490 s, 420 s (νGaF) cm^{-1} [6]. The corresponding bands for *(2)* are at 597 sh, 582 vs, 525 m (νGaC$_2$) and 487 s, 425 s (νGaF) cm^{-1} [8].

From these spectra and the molecular weights we conclude that *(1)* and *(2)* have a symmetrical six-membered ring structure with coordinatively bivalent fluorine atoms.



(1), R = CH_3
(2), R = C_2H_5

Dimethyl-[3,4] and diethyl-aluminum fluoride[2], on the contrary, are tetrameric and form eight-membered rings. In the ^{1}H-NMR spectrum of dimethylaluminum fluoride $[(CH_3)_2AlF]_4$ containing traces of $(CH_3)_3Al$ we found a 1:2:1 triplet signal, $J(^1H-C-Al-^{19}F) = 4.65$ Hz, proving the presence of coordinatively bivalent fluorine. No comparable triplet signal is found in the spectra of *(1)* and *(2)*; it is presumably eliminated by rapid exchange processes[9].

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*] Prof. H. Schmidbaur, Dr. H. F. Klein, and Dr. K. Eiglmeier
Institut für Anorganische Chemie der Universität
Röntgenring 11
87 Würzburg (Germany)

[1] *K. Ziegler* and *R. Köster*, Liebigs Ann. Chem. *608*, 1 (1957); *K. Ziegler, E. Holzkamp, R. Köster*, and *H. Lehmkuhl*, Angew. Chem. *67*, 213 (1955).

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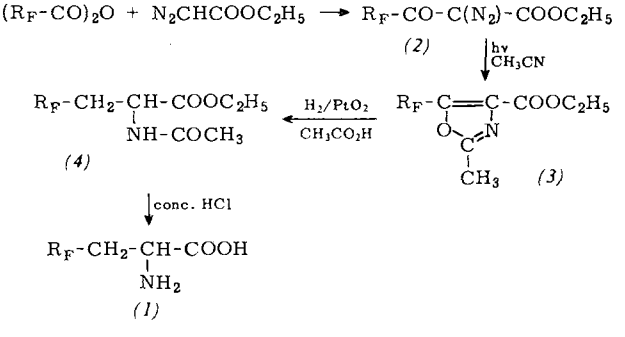
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A General Method for the Preparation of β-Perfluoroalkylalanines

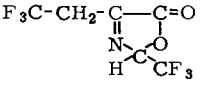
By *W. Steglich, H.-U. Heininger, H. Dworschak*, and *F. Weygand*[*]

We recently reported the synthesis of *C*-perfluoroalkylglycines[1] and now describe a general process for the preparation of β-perfluoroalkylalanines *(1)*. Starting materials are the perfluoroacyldiazoacetic esters *(2)* that are readily accessible by treatment of perfluoro carboxylic anhydrides with ethyl diazoacetate. If these esters *(2)* are illuminated in acetonitrile solution (concentration 0.3 mole/l) with a quartz immersion lamp (Hanau TQ 81, 70 W) for 10 h, 60 to 70 % yields of 2-methyl-5-perfluoroalkyl-4-oxazolecarboxylic esters *(3)* are formed[2], which on catalytic hydrogenation in glacial acetic acid in the presence of PtO_2 afford *N*-acetyl-β-perfluoroalkylalanine ethyl esters *(4)* (yield 75–85 %). The amino acids *(1)* are obtained therefrom in about 80 % yields by hydrolysis with conc. HCl (18 h, 90 °C).



	R_F	*(2)*, B.p. (°C/mm)	*(3)*, B.p. (°C/mm)	*(4)*, M.p. (°C)	*(1)*, M.p. (°C)
(a)	CF_3	[2]	80/1.1	88–89	260–265 [3]
(b)	C_2F_5	75–77/10	67–69/2.2	86–87	215 (decomp., subl.)
(c)	C_3F_7	80–81/10	68–70/0.9	49–50	202 (decomp., subl.)

For conversion into the L-form, DL-2-amino-4,4,4-trifluorobutyric acid *(1a)* was first *N*-trifluoroacetylated (*N*-trifluoroacetyl-*(1a)*, 80 %, m.p. 135–136 °C) and cyclized by dicyclohexylcarbodiimide to 4-(2,2,2-trifluoroethyl)-2-(trifluoromethyl)oxazol-5(2*H*)-one *(5)* (70 %), b.p. 58 °C/12 mm. Treatment of the oxazolone with dimethyl L-glutamate in tetrahydrofuran gave a dimethyl *N*-(2-trifluoroacetamido-4,4,4-trifluorobutyryl)-L-glutamate containing 83 % of the L-L- and



(5)

17 % of the D-L-diastereoisomer (determined by gas chromatography[4]). Assignment of configuration to the diastereoisomers follows from the rule that treatment of 2-trifluoromethyl-2*H*-oxazolones with optically active amino esters always give preferentially the diastereoisomer that has the same absolute configuration at both asymmetric centers[5].

After three recrystallizations from ether, pure (gas chromatography) L-L-*N*-(trifluoroacetyl)dipeptide dimethyl ester (m.p. 96 °C, $[\alpha]_{546}^{25} = -4.1°$, $c = 9.6$ in ethyl acetate) was isolated in 33 % yield. Hydrolysis with conc. HCl and removal of the glutamic acid with Amberlite IR 45 gave L-*(1a)* in 87 % yield (m.p. 189.5–190.5 °C, $[\alpha]_{546}^{25} = -6.3°$, $c = 16.4$ in 1 N HCl). To prove that the hydrolysis did not involve any racemization, the product was benzyloxycarbonylated [Cbo-L-*(1a)*, 90 %, m.p. 121 °C] and converted by dicyclohexylcarbodiimide and dimethyl L-glutamate into dimethyl *N*-[2-(benzyloxycarbonylamino)-4,4,4-trifluorobutyryl]-L-glutamate (m.p. 99–100 °C). The ester obtained by removal of the Cbo group and subsequent *N*-trifluoroacetylation shows only the peak of the L-L-diastereoisomer in its gas chromatogram.

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[*] Priv.-Doz. Dr. W. Steglich, Dipl.-Chem. H. U. Heininger, Dr. H. Dworschak, and Prof. Dr. F. Weygand
and Prof. Dr. F. Weygand
Organisch-Chemisches Institut der Technischen Hochschule
Arcisstr. 21
8 München 2 (Germany)

[1] *F. Weygand, W. Steglich, W. Oettmeier, A. Maierhofer*, and *R. S. Loy*, Angew. Chem. *78*, 640 (1966); Angew. Chem. internat. Edit. *5*, 600 (1966); *F. Weygand, W. Steglich, W. Oettmeier*, and *F. Fraunberger*, Chem. Ber., in press.

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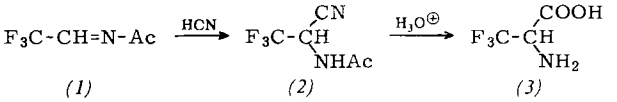
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A Simple Synthesis of 3,3,3-Trifluoroalanine [1]

By *F. Weygand, W. Steglich*, and *F. Fraunberger* [*]

Although treatment of *N*-acyltrifluoroacetaldimines *(1)* with cyanides yields ethylene derivatives with elimination of fluoride [2], anhydrous hydrogen cyanide reacts smoothly with *(1)* to form 2-acylamino-3,3,3-trifluoropropionitriles *(2)*.



(1) *(2)* *(3)*

(2a), Ac = C_6H_5CO-, yield 81 %, m.p. 127.5–128.5 °C

(2b), Ac = $C_6H_5-CH_2O-CO-$, yield 98 %, m.p. 106–107 °C

The nitriles *(2)* can be hydrolysed to 3,3,3-trifluoroalanine *(3)* by boiling HCl (6 N to 10 N) containing a little glacial acetic acid. Thus boiling *(2b)* for 5 h with 6 N HCl gives an 81 % yield of *(3)*, whose properties correspond to those of a product obtained by a different route [3]. Boiling *(2a)* for only 4 h with 1 N HCl hydrolyses it partially to *N*-benzoyl-3,3,3-trifluoroalanine [3] (65 % yield). Since *N*-acyltrifluoroacetaldimines are readily accessible from *N*-acyl-1-chloro-2,2,2-trifluoroethylamines [4], relatively large quantities of *(3)* can be conveniently prepared in this way.

Experimental

(2b): *N*-Benzoyloxycarbonyl-1-chloro-2,2,2-trifluoroethylamine [4,5] (5 g) in anhydrous tetrahydrofuran (THF) is treated with triethylamine (2.6 ml). The triethylamine hydrochloride is filtered off with exclusion of moisture and washed with THF. The filtrate is cooled to −50 °C and HCN (from 20 g of KCN and 50 % H_2SO_4, dried over P_2O_5) is passed in. The cooling bath is removed, the mixture is left overnight, and the excess of HCN is then removed at 60 °C in a stream of nitrogen. Evaporation of the THF leaves 4.7 g (98 %) of *(2b)*, m.p. 102–104 °C; the m.p. is 106–107 °C after recrystallization from chloroform/petroleum ether.

(3): The compound *(2b)* (14.5 g) is heated under reflux with 6 N HCl (300 ml) and glacial acetic acid (50 ml) for 5 h. After evaporation of the solvent the residue is taken up in water and the solution evaporated, this process being repeated three times. Finally the residue is dried by addition of toluene and subsequent removal thereof under vacuum. The residue is then covered with chloroform (100 ml); most of it dissolves when triethylamine (20 ml) is added with stirring, and the insoluble part (ammonium chloride) is filtered off. Addition of glacial acetic acid precipitates the product *(3)* (yield 6.5 g, 81 %).

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[*] Prof. F. Weygand, Dr. W. Steglich, and
Dipl.-Chem. F. Fraunberger
Organisch-Chemisches Institut der Technischen Hochschule
Arcisstr. 21
8 München 2 (Germany)

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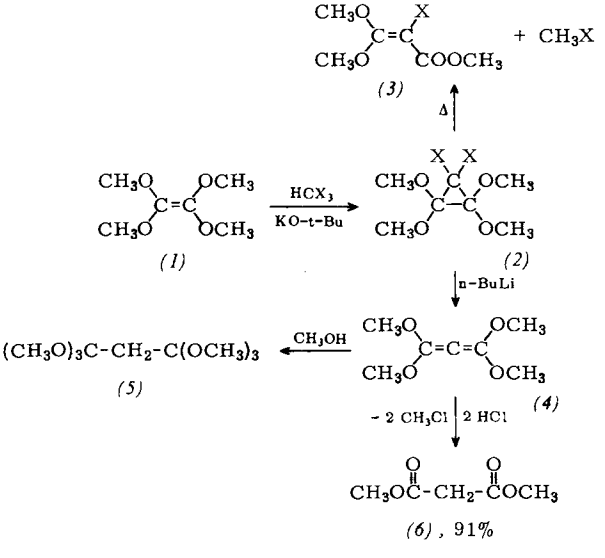
[4] *F. Weygand, W. Steglich, I. Lengyel, F. Fraunberger, A. Maierhofer*, and *W. Oettmeier*, Chem. Ber. *99*, 1944 (1966).

[5] Firma Dr. Th. Schuchardt, München.

Tetramethoxyallene, the Diacetal of Carbon Suboxide

By *R. W. Hoffmann* and *U. Bressel* [*]

1,1-Dihalogenotetramethoxycyclopropanes *(2)* [2], which are obtained from tetramethoxyethylene *(1)* [1] by the action of a haloform and potassium t-butoxide, undergo exothermic reaction at 80–110 °C [3] to afford methyl 2-halogeno-3,3-dimethoxyacrylates *(3)* [4]. Treating *(2b)* with n-butyllithium [5] gives tetramethoxyallene *(4)* in 72 % yield; the same product is obtained on treatment of *(2a)* with n-butyllithium.



Compound	M.p. (°C)	B.p. (°C/mm)	Yield (%)	NMR (τ)	IR (cm^{-1})
(2a), X = Cl	46–48		40	6.47 singlet ($CDCl_3$)	
(2b), X = Br	63–65		47	6.52, singlet ($CDCl_3$)	
(3a), X = Cl		62/1	91	6.04 singlet, 6.18 (1:1:1), 6.28 (CCl_4)	1715,1615, 1290-1310, 1200,1095
(3b) X = Br		92/1	89	as *(3a)*	1710,1595, 1280,1090
(4)	65–67		72	6.54, singlet (CCl_4)	1920,1215, 955
(5)		70–71/1	81	6.80 singlet, 7.92 (9:1) (CCl_4)	

In contrast to unsubstituted allene[6], the product *(4)* is protonated on the central carbon atom owing to the influence of the four methoxy groups, as is shown by the formation of dimethyl malonate *(6)* on treatment of *(4)* with anhydrous HCl. As a double ketene acetal, *(4)* is readily hydrolysed, again affording *(6)*. Addition of methanol to *(4)* leads to hexamethyl orthomalonate *(5)*.

1,1-Dibromotetramethoxycyclopropane (2b):

A suspension of potassium t-butoxide (2.87 g, 25.6 mmoles) in anhydrous petroleum ether (25 ml) is added dropwise to a solution of tetramethoxyethylene (3.78 g, 25.6 mmoles)[1] and bromoform (6.47 g, 25.6 mmoles) in anhydrous petroleum ether (10 ml) at −10 °C, with stirring, under a N_2 atmosphere. After one hour's stirring at 25 °C, enough water is added to dissolve the salts. On extraction with petroleum ether, drying over $MgSO_4$, and concentration, *(2b)* is obtained; recrystallization from petroleum ether gives 3.84 g (47 %) of product, m.p. 63–65 °C.

Tetramethoxyallene (4):

A 1.45 M solution (24 ml) of n-butyl-lithium in pentane is added dropwise over 1 h to a stirred solution of *(2b)* (8.37 g, 26.2 mmoles) in anhydrous petroleum ether (40 ml) at −80 °C under nitrogen. When all the butyl-lithium has reacted, the mixture is filtered at −80 °C under nitrogen through a sintered-glass filter. The residue is washed with three portions each of 50 ml of anhydrous petroleum ether. Concentration of the last 100 ml of wash liquor under nitrogen affords the product *(4)* (3.05 g, 72 %), m.p. 65–67 °C.

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[*] Doz. Dr. R. W. Hoffmann
Institut für Organische Chemie der Technischen Hochschule
Schlossgartenstr. 2
61 Darmstadt (Germany)
Dipl.-Chem. U. Bressel
Organisch-Chemisches Institut der Universität
Tiergartenstr.
69 Heidelberg (Germany)

[1] *R. W. Hoffmann* and *H. Häuser*, Tetrahedron *21*, 891 (1965).

[2] All the new compounds prepared gave satisfactory analytical results.

[3] *(2b)* decomposes slowly at 25 °C.

[4] Cf. the rearrangement of 1,1-dichloro-2,2-diethoxycyclopropane: *S. M. McElvain* and *P. L. Weyna*, J. Amer. chem. Soc. *76*, 2579 (1959).

[5] *L. Skattebøl*, Acta chem. scand. *17*, 1683 (1963), where further references are given.

[6] *K. Griesbaum*, Angew. Chem. *78*, 953 (1966); Angew. Chem. internat. Edit. *5*, 933 (1966).

X-ray Structure Analysis of Neophorbol

By *W. Hoppe*, *F. Brandl*, *I. Strell*, *M. Röhrl*, and *I. Gassmann*[*] and *E. Hecker*, *H. Bartsch*, *G. Kreibich*, and *Ch. v. Szczepanski*[**]

In 1966, phorbol *(2)*, the parent alcohol of the tumor promoting compounds from croton oil, was assigned the structure of a 4,9,12,13,20-pentahydroxy-1,6-tigliadien-3-one[1]. The relative configuration of seven of the eight asymmetric centers was established[1,2]. We have now been able to grow suitable single crystals of a derivative of phorbol, neophorbol 13,20-diacetate 3-*p*-bromobenzoate *(1)* [m.p. 216–217 °C, λ_{max} = 245, (282)nm, ε_{max} = 21100, (880) (in CH_3OH)], for X-ray structure analysis. X-ray analysis results[3] indicated the relative configuration shown in Fig. 1 (crystal data: space grouping $P2_1$, $Z = 2$, unit cell dimensions a = 12.31 Å, b = 12.91 Å, c = 9.87 Å, γ = 111.29 °). The site of the *p*-bromobenzoyl residue was determined by means of the convolution-molecule method. A series of successive

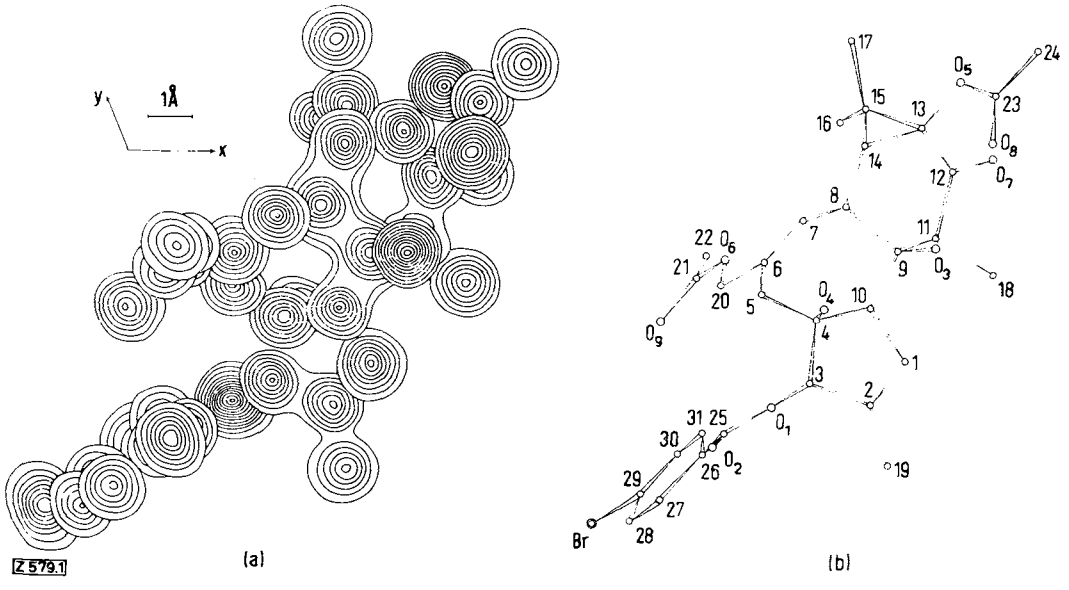
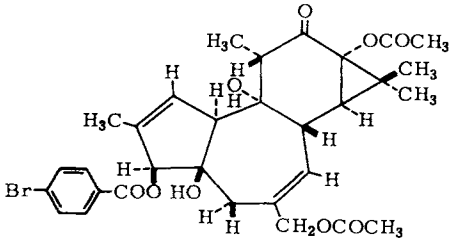


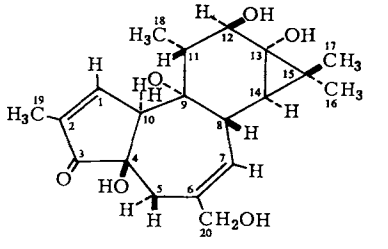
Fig. 1. (a) Fourier synthesis of neophorbol-13,20-diacetate-3-*p*-bromobenzoate. Light atoms: line distance 1e/Å^3; Bromine: 1 line 2e/Å^3; Distance of remaining high lines 5e/Å^3.

(b) Perspective representation of neophorbol-13,20-diacetate-3-*p*-bromobenzoate. Direction of the *z*-axis perpendicular to the *x*/*y* plane.

Fourier syntheses yielded a structure which, referred to H-14, has the configuration 3-*trans*-4-*trans*-9-*cis*-13-*cis*. An automatic structure analysis by the phase-correction method [4] led to the same result. Following our first communications [1–3] a further confirmation of the constitution and



(1)



(2)

relative configuration of phorbol was obtained by X-ray structure analysis of a phorbol 20-(5-bromofuroate) [5].

The absolute configuration of *(1)* was determined by calculation and measurement of approximately 200 selected Bijvoet pairs. It corresponds to the mirror image of the first discussed absolute configuration of phorbol [2] and is (incidentally) the same as the relative configuration referred to in reference [3] and shown in Fig. 1.

On the basis of X-ray structure analysis the absolute configuration of phorbol is represented by *(2)*, in which the reference atom H-14 is situated on the underside of the molecule (α-side). Phorbol is, therefore, a 4,9,12β,13,20-pentahydroxy-1,6-tigliadien-3-one. Accordingly the asymmetry center C-14 has (*R*)-chirality and tiglian [6] has the absolute configuration of a (1a*S*), 1,1,3 ξ,6 ξ,8*c*-pentamethyl-(1a*r*H, 1b*t*H, 4a*t*H, 7a*c*H, 7b*c*H, 9a*c*H)-tetradecahydro-1*H*-cyclopropa[3,4]benz[1,2-*e*]azulene.

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[*] Prof. W. Hoppe, Dr. F. Brandl, Dr. I. Stell, Dipl.-Chem. M. Röhrl, and Dr. J. Gassmann
Abteilung für Röntgenstrukturforschung am Max-Planck-Institut für Eiweiß- und Lederforschung
Schiller-Str. 46
8 München (Germany)

[**] Prof. E. Hecker, Dipl.-Chem. H. Bartsch, Dipl.-Chem. G. Kreibich, and Dr. Ch. v. Szczepanski
Biochemisches Institut
am Deutschen Krebsforschungszentrum
Berliner Str. 23
69 Heidelberg (Germany)

[1] *E. Hecker*, Naturwissenschaften *54*, 282 (1967); cf. Nachr. Chem. Techn. *15*, 245 (1967).

[2] *E. Hecker, H. Bartsch, H. Bresch, M. Gschwendt, E. Härle, G. Kreibich, H. Kubinyi, H. U. Schairer, Ch. v. Szczepanski*, and *H. W. Thielmann*, Tetrahedron Letters *1967*, 3165.

[3] *A. Amit, F. Brandl, N. Brodherr, A. Gieren, E. Hädicke, W. Hoppe, R. Huber*, and *M. Röhrl*, Lecture at the 9. Diskussionstagung der Sektion für Kristallkunde der Deutschen Mineralogischen Gesellschaft, 24–27 April 1967, Bonn and Jülich, Report p. 53–55.

[4] *W. Hoppe, R. Huber*, and *J. Gassmann*, Acta crystallogr. *16*, A 4 (1963); *J. Gassmann, ibid. 21*, A 6 (1966); *W. Hoppe*, Angew. Chem. *78*, 289 (1966); Angew. Chem. internat. Edit. *5*, 267 (1966), *J. Gassmann* and *W. Hoppe*, Acta crystallogr., in press.

[5] *R. C. Pettersen* and *G. Ferguson* and *L. Crombie, M. L. Games*, and *D. J. Pointer*, Chem. Commun. *1967*, 716.

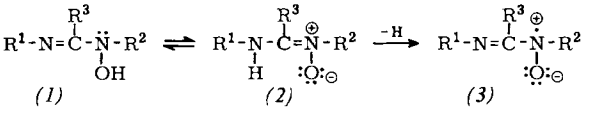
[6] The asymmetry centers of the saturated hydrocarbon tiglian exhibit, according to [2], the same configuration as in phorbol.

CONFERENCE REPORTS

ESR Spectroscopic Studies of Nitroxide Radicals that are Capable of Mesomerism

By *H. G. Aurich* [*]

N,N'-Substituted *N*-hydroxyamidines have been prepared by various methods. Spectroscopic results suggest that these compounds exist in the tautomeric α-amino nitrone form. Their oxidation leads to nitroxide radicals in which delocalization of the unpaired electron over the azomethine group is possible. ESR spectra provide information about the extent of this delocalization.



(1) *(2)* *(3)*

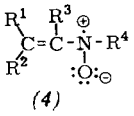
(a): $R^1 = R^2 = R^3 =$ aryl
(b): $R^1 = R^2 =$ aryl, $R^3 =$ t-butyl
(c): $R^1 = R^2 =$ aryl, $R^3 = H$
(d): $R^1 =$ t-butyl, $R^2 =$ aryl, $R^3 = H$
(e): $R^1 =$ aryl, $R^2 =$ t-butyl, $R^3 = H$
(f): $R^1 = R^2 =$ t-butyl, $R^3 = H$

Exact analysis of the complicated ESR spectra of the nitroxide radicals *(3a)* to *(3e)* is possible only after the introduction of t-butyl groups into various positions of the phenyl groups. The coupling constants found for the nitroxide- and the azomethine-nitrogen can be used as an approximate measure of the spin density on the nitroxide group and on the azomethine-nitrogen.

	Coupling constants (in gauss)	
	^{a}N(nitroxide)	^{a}N(azomethine)
(3a)	9.8–10.1	0.87
(3b)	10.1–10.3	0.86–0.88
(3c)	7.40–7.46	2.94–3.02
(3d)	8.21–8.30	2.61–2.70
(3e)	8.24	3.49
(3f)	9.25	3.20

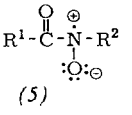
As shown by comparison of the coupling constants, the spin density on the azomethine-nitrogen is substantially smaller for the radicals *(3a)* and *(3b)*, with R^3 = aryl or t-butyl, than for the radicals *(3c)* to *(3f)*, with $R^3 = H$. From this it is concluded that in *(3a)* and *(3b)* the nitroxide group is twisted with respect to the azomethine group, so that delocalization of the unpaired electron over the azomethine group is hindered. For steric reasons, groups R^1 and R^3 would then be expected to assume an orientation in the *anti*-position. When $R^3 = H$ a *syn*-arrangement of R^1 and R^3 at the azomethine group is possible, and the nitroxide group with R^2 can be almost coplanar with the azomethine group; this leads to an increase of the spin density on the azomethine group and a decrease of that on the nitroxide group.

For nitroxide radicals with vinyl or acyl groups that can undergo mesomerism, only the coupling constants of the nitroxide-nitrogen (and the phenyl-protons of the neighboring phenyl nucleus) are available for comparison. As



(4)

R^1 to R^4 = aryl or
$R^1 = R^3 = R^4$ = aryl, R^2 = CN



(5)

R^1 = aryl or methyl
R^2 = aryl

would be expected from the steric relations, the coupling constants of the vinyl-nitroxide radicals *(4)* studied are comparable with those of the azomethine-nitroxide radicals *(3a)* and *(3b)*, and those of the acyl-nitroxide radicals *(5)* are comparable with those of the azomethine-nitroxide radicals *(3c)*.

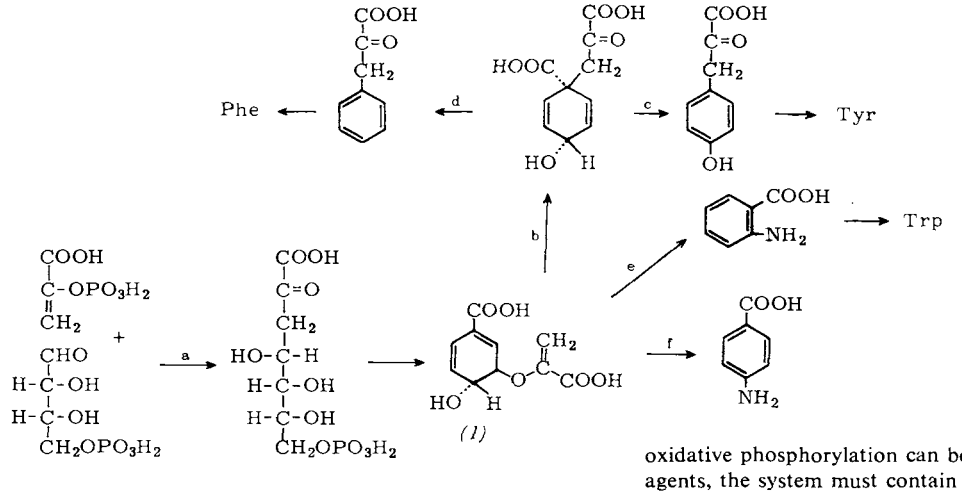
Lecture given at Marburg (Germany) on April 28th, 1967 [VB 79 IE]
German version: Angew. Chem. 79, 825 (1967)

[*] Doz. Dr. H. G. Aurich
Chemisches Institut der Universität
Bahnhofstr. 7
355 Marburg/Lahn (Germany)

The Biosynthesis of Aromatic Amino Acids and its Control

By *F. Lingens*[*]

The biosynthetic pathway to aromatic amino acids branches at chorismic acid *(1)*. By studying the control mechanism of this biosynthesis by yeast (*Saccharomyces cerevisiae*), the following enzymes could be detected and concentrated: 3-deoxy-2-oxo-*arabo*-heptonic acid 7-phosphate synthetase (DAHP synthetase) (a), chorismate mutase (b), prephenate dehydrogenase (c), prephenate dehydratase (d), anthranilate synthetase (e), and *p*-aminobenzoate synthetase (f).



(1)

DAHP synthetase could be separated chromatographically into three isoenzymes, one of which was allosterically inhibited by phenylalanine (Phe) and a second by tyrosine (Tyr); the third is not inhibited by phenylalanine, tyrosine, or tryptophan (Trp). Chorismate mutase consists of two isoenzymes, both of which are inhibited by tyrosine; tryptophan induces and activates this enzyme. Prephenate dehydrogenase is inhibited by tyrosine; phenylalanine causes both induction and activation. Prephenate dehydratase is inhibited allosterically by phenylalanine and repressed in its biosynthesis. Anthranilate synthetase is inhibited allosterically by tryptophan and repressed. *p*-Aminobenzoate synthetase can be induced by simultaneous addition of phenylalanine, tyrosine, and tryptophan (multivalent induction)[1].

Corresponding studies with an alkaloid-producing strain of *Claviceps paspali* gave the following results. The DAHP synthetase could be separated into three isoenzymes, which are inhibited by phenylalanine, tyrosine, and tryptophan, respectively. The last named isoenzyme shows 60 % of the total activity. The concentrated chorismate mutase is inhibited by phenylalanine or tyrosine; tryptophan activates it. Prephenate dehydrogenase and dehydratase show allosteric inhibition by tyrosine and phenylalanine, respectively. Anthranilate synthetase is not inhibited by tryptophan[2].

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German version: Angew. Chem. 79, 825 (1967)

[*] Prof. Dr. F. Lingens
Chemisches Institut der Universität
Wilhelmstr. 33
74 Tübingen (Germany)

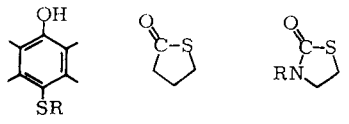
[1] *F. Lingens, W. Goebel,* and *H. Uesseler,* Biochem. Z. *346,* 357 (1966); Europ. J. Biochem. *1,* 363 (1967).

[2] *F. Lingens, W. Goebel,* and *H. Uesseler,* Naturwissenschaften *54,* 141 (1967); Europ. J. Biochem., in press.

Model Experiments on Oxidative Phosphorylation

By *Th. Wieland*[*]

Conversion of the free energy of chemical reactions, in the present case oxidation of bound hydrogen, into the "energy-rich" pyrophosphate linkage of adenosine triphosphate (ATP) by synthesis from adenosine diphosphate (ADP) and orthophosphate (P) is the fundamental process for the life of aerobic organisms. This conversion takes place, in some manner still unknown, in close connection with the "respiration chain" *i.e.* the organized enzyme system of the mitochondria, in which pyridinium nucleotide (NAD), flavine adenine dinucleotide (FAD), (presumably) ubiquinone, and cytochrome bring electrons of the fuel to oxygen. Since oxidative phosphorylation can be prevented by SH blocking agents, the system must contain essential thiol groups in its structural units. Model experiments on the oxidative conversion of an energy-poor phosphoric ester linkage into an energy-rich phosphate linkage have been performed in several laboratories. For instance, hydroquinone monophosphates, as well as *S*-alkyl thiophosphates, have been converted into phosphorylating agents, but oxidative activation of an inorganic phosphate has not previously been achieved in a model system. With *E. Bäuerlein* we have found two classes of compounds that produce oxidative linkage and activation of phosphate: monothiohydroquinone *S*-alkyl ethers *(1)* and thiolactones *(2)* lead to a 20 to 30 % yield of ATP on oxidation of a mixture of ADP and P by bromine



(1) (2) (3)

in an anhydrous medium, *e.g.* in pyridine. The process is prevented by presence of 2,4-dinitrophenol, particularly in the case of compound *(2)*. Thiazolidones *(3)*, in place of the thiolactone *(2)*, can also produce oxidative phosphorylation (*H. Aquila*).

Structures such as *(2)* and *(3)* (with larger rings) can be considered to be produced in the tertiary structures of proteins. The reaction with thiolactone, for which a plausible mechanism can be formulated, can be conceived as occurring at various places in the respiration chain, since the thiolactone could be oxidized, with simultaneous activation of phosphate, by all oxidizing members of the respiration chain (DPN, FAD, quinones, oxidized cytochromes).

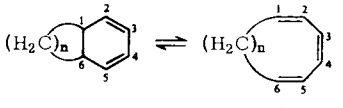
Lecture at Bonn (Germany) on May 23rd, 1967 [VB 83 IE]
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[*] Prof. Dr. Th. Wieland
Institut für Organische Chemie der Universität
Robert-Mayer-Str. 7–9
6 Frankfurt/Main (Germany)

Valence Tautomerism in Heterocyclic Systems

By *G. Maier* [*]

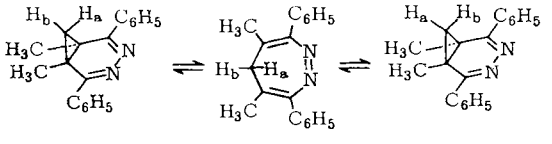
Valence tautomerism of the type *(1)* ⇄ *(2)*, where $n = 1$ or 2, has been described for carbocyclic compounds. We were interested in the question whether analogous changes could be realized if carbon atoms 3 and 4 were replaced by heteroatoms.



(1) (2)

Various *cis*-1,2-diacylcyclopropanes and *cis*-3,4-diacylcyclobutenes [oxidation of hexamethyl(Dewar benzene) by $KMnO_4$ gives 3,4-diacetyl-1,2,3,4-tetramethylcyclobutene] were therefore prepared and converted into cyclic azines by hydrazine.

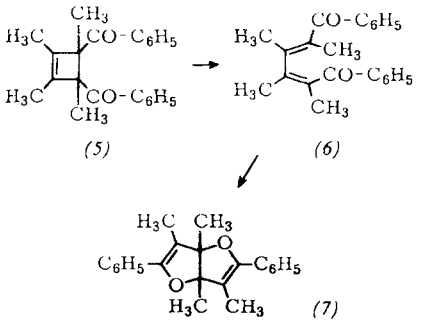
It transpired that valence-tautomeric relations persist after introduction of nitrogen atoms. This follows from, for instance, the temperature-dependence of the NMR spectrum of 1,6-dimethyl-2,5-diphenyl-3,4-diazanorcaradiene *(3)*. The two geminal cyclopropane protons H_a and H_b give two doublets at room temperature. The resolution is lost on warming to 70 °C, and at 130 °C a singlet arising from the two protons appears at a position midway between the



(3a) (4) (3b)

positions of the original signals. These changes are reversible and indicate the valence-tautomeric equilibrium *(3a)* ⇄ *(4)* ⇄ *(3b)*, which lies entirely on the bicyclic side.

Heating the diacylcyclobutenes also gives products that have been identified. If the reactions occurred in the manner of a Cope rearrangement with participation of two carbonyl groups, cyclic peroxides would be formed, but that is not the case. In the first step, stereospecific ring-opening in accordance with the Woodward-Hoffmann rules leads to *cis,trans*-diacylbutadienes. For instance, the dibenzoyl compound *(5)* is converted at 70 °C into the butadiene derivative *(6)*, and this in a subsequent reaction into the bicyclic compound *(7)*.



(5) (6) (7)

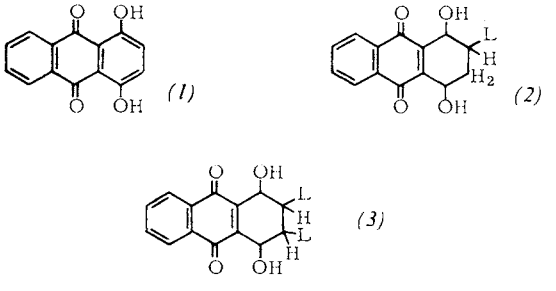
Lecture at Marburg (Germany) on May 5th, 1967 [VB 84 IE]
German version: Angew. Chem. 79, 827 (1967)

[*] Priv.-Doz. Dr. G. Maier
Institut für Organische Chemie der Technischen Hochschule
Richard-Willstätter-Allee
75 Karlsruhe (Germany)

Photochemical Studies of Quinizarin

By *H. Labhart* [*]

Photochemical reaction of quinizarin *(1)* (2×10^{-5} molar in degassed hexane) is often markedly accelerated by the presence of other substances (10^{-5} molar), benzophenone and some quinones being particularly effective. Measurements of the quantum yield as a function of the wavelength of the incident light have shown that with benzophenone as accompanying substance the primary step is excitation of that molecule. However, further reaction does not occur by sensitization of the triplet state of the quinizarin but, instead,



(1) (2) (3)

solvent radicals L·, which are first formed by hydrogen abstraction, react with quinizarin to give the photoproducts that are identified mass-spectrometrically. The UV spectrum of these products is very similar to that of 2,3-dihydroquinizarin. It is most probable that the compounds *(2)* and *(3)* are formed.

Lecture at Berlin (Germany) on May 8th, 1967 [VB 86 IE]
German version: Angew. Chem. 79, 826 (1967)

[*] Prof. Dr. H. Labhart
Physikalisch-Chemisches Institut der Universität
Rämistr. 76
CH-8001 Zürich (Switzerland)

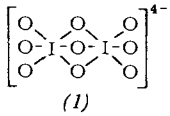
Periodates

By *H. Siebert* [*]

From the reactions of alkaline periodate solutions it can be concluded that they contain binuclear anions $[H_2I_2O_{10}]^{4-}$ Crystal structure analysis of the salt $K_4H_2I_2O_{10}\cdot8H_2O$ showed that the anion consists of two IO_6 octahedra with a

common edge. According to their IR spectra, many other periodates obtained from aqueous solution must contain an ion of the same structure. Salts containing the ions $[H_3I_2O_{10}]^{3-}$ and $[HI_2O_{10}]^{5-}$ have also been isolated.

Crystal structure analysis of $K_4I_2O_9$ established the structure *(1)*, with three oxygen bridges, for the anion.



(1)

The IO_6 group functions as a bidentate ligand in the periodate complexes of transition metals known hitherto, but it is probably tridentate in the recently prepared complexes containing the anions $[Pt(IO_6)_2]^{6-}$ and $[Pd(IO_6)_2]^{6-}$.

Lecture at Heidelberg (Germany) on June 13th, 1967 [VB 89 IE]
German version: Angew. Chem. 79, 827 (1967)

[*] Prof. H. Siebert
Anorganisch-Chemisches Institut der Universität
Tiergartenstr.
69 Heidelberg (Germany)

The Theory of Ring-opening Reactions

By *W. Kutzelnigg* [*]

The course of electrocyclic ring-closure and ring-opening reactions can often be elucidated from symmetry considerations alone. However, symmetry considerations alone lead only to the conclusion that ring-opening of the cyclopropyl cation, such as occurs after nucleofugal separation of a toluenesulfonate group from a cyclopropyl toluenesulfonate, should occur in a disrotatory manner. Semiquantitative consideration (by *Hoffmann*'s "extended Hückel method") of the course of reaction, starting from a cyclopropyl cation *in statu nascendi*, explains why, in agreement with experiment, one of the two possible disrotatory cleavages must be favored, namely, that in which the groups originally *trans* to the toluenesulfonate group turn outwards.

It follows that the cyclopropyl cation should be unstable (not even short-lived) and should rearrange to the allyl cation without involving any activation energy. Attempts are now in progress to support this concept by *ab initio* calculations. In agreement with this concept the toluenesulfonate group separates appreciably more easily if separation is accompanied by simultaneous ring opening. As soon as reaction is half complete the cation possesses almost all the π-electron energy of the allyl cation. In bicyclic systems such as were recently studied by *U. Schöllkopf, P. v. R. Schleyer, et al.* [1], complete ring-opening by the most favored route may be sterically hindered; in such cases a species representing an intermediate stage between the cyclopropyl and the allyl cation should be an intermediate of sufficiently long life and should show the reactions that are associated with approximately equal distribution of the positive charge over the three C atoms and with non-planar arrangement of the substituents on the central C atom.

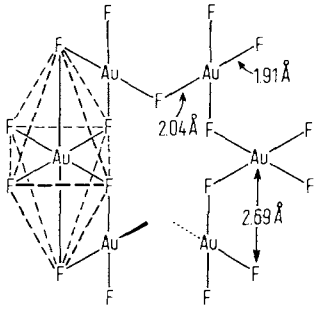
Lecture at Tübingen (Germany) on June 13th, 1967 [VB 91 IE]
German version: Angew. Chem. 79, 826 (1967)

[*] Dr. W. Kutzelnigg
Lehrstuhl für Theoretische Chemie der Universität
Bürgerstr. 50a
34 Göttingen (Germany)

[1] *U. Schöllkopf, K. Fellenberger, M. Patsch, P. v. R. Schleyer, H. W. van Dine*, and *T. Su*, Tetrahedron Letters *1967*, in press.

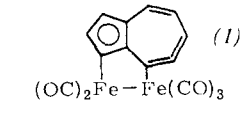
SELECTED ABSTRACTS

The crystal structure of gold trifluoride was determined by *F. W. B. Einstein, P. R. Rao, J. Trotter*, and *N. Bartlett* from a single-crystal diagram. AuF_3 is the least closely packed of the noble metal fluorides. The diamagnetic crystals are hexagonal (space group $P6_122-D_6$). AuF_3 is polymeric: four fluorine atoms surround the gold atom in an almost square arrangement and each "square" shares two *cis* fluorine atoms



with the neighboring squares. The non-bridging fluorine atoms at the same time represent the apexes of octahedrons around neighboring gold atoms, so that a hexagonal helix of AuF_6 octahedrons arises. / J. chem. Soc. (London) A *1967*, 478 / –Bu. [Rd 677 IE]

The crystal and molecular structures of azulenediiron pentacarbonyl *(1)* have been determined by *M. R. Churchill*. *(1)* crystallizes in the triclinic system (space group $C\bar{1}$) with $a = 7.32 \pm 0.01$ Å; $b = 14.48 \pm 0.02$ Å; $c = 14.76 \pm 0.02$ Å; $\alpha = 116.2 \pm 0.2°$; $\beta = 92.3 \pm 0.2°$; $\gamma = 93.0 \pm 0.2°$; $Z = 4$. The carbon atoms of the five-membered ring form a π-cyclopentadienyl system, which is bonded to an $Fe(CO)_2$ group, while three atoms of the seven-membered ring participate in a π-allyl bond to an $Fe(CO)_3$ group. Unequal Fe-C(allyl) bond

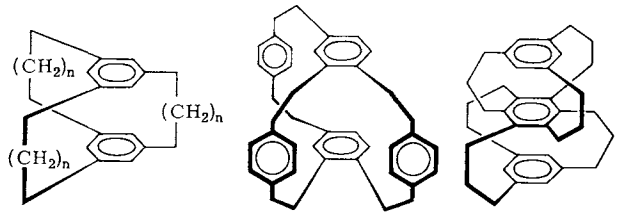


(1)

lengths, distortion of the azulene ligand from planarity, and a relatively long iron-iron bond (2.782 Å) indicate that the molecule *(1)* may be strained. / Inorg. Chem. *6*, 190 (1967) / –Sch. [Rd 659 IE]

Novel cage compounds such as *(1)*, *(2)*, and *(3)* have been prepared by *A. J. Hubert*. The principle of the synthesis is based on a cyclotrimerization of acetylenes with Ziegler catalysts $[TiCl_4/Al(iso\text{-}C_4H_9)_3]$. *(1)* can be obtained either from α,ω-alkadiynes (<1% yield) or from 1,3,5-tri-ω-alkynylbenzene (yields 16–32%). The starting material for *(2)* is *p*-di-ω-alkynylbenzene (0.4% yield of *(2)*, together with the 1,3,5-isomer and other (mixed) isomers). *(3)* is obtained from hexa(pent-4-ynyl)benzene.

(2) may include 1 molecule of solvent, *e.g.* cyclohexane. *(1)* with $n = 5$ (m.p. 265 °C, b.p. 200–250 °C/0.1 mm) can be obtained in 53% yield, since the bond strain and the π-elec-



(1) (2) (3)

tron repulsion reaches a minimum in this compound. Compounds with even *n* have lower melting points than those with odd *n*. The UV absorptions also alternate with *n*. / J. chem. Soc. (London) *C 1967*, 6, 11, 13 (1967) / –Bu.

[Rd 668 IE]

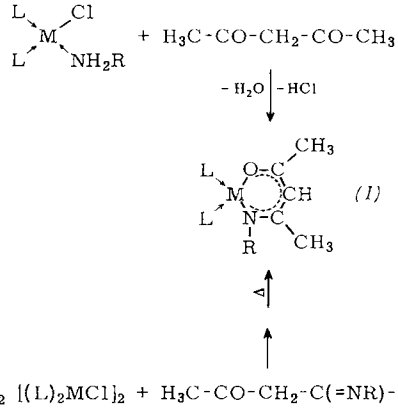
A versatile new enamine synthesis is reported by *W. A. White* and *H. Weingarten*. Stoichiometric quantities of $TiCl_4$, a secondary amine, and a ketone or aldehyde react within a few hours or days to give the desired enamine.

$$2\ R{-}CH_2{-}CO{-}R' + 6\ HNR''_2 + TiCl_4 \rightarrow 2\ RCH{=}C(NR''_2)R' + 4\ R''_2NH_2Cl + TiO_2$$

The yields are between 55 and 94%, *e.g.* 72% in the case of dimethyl(1-isopropyl-2-methylpropenyl)amine. / J. org. Chemistry *32*, 213 (1967) / –WG.

[Rd 669 IE]

Schiff bases of acetylacetone form chelates with Ir(I) and Rh(I). *F. Bonati* and *R. Ugo* were able to prepare dicarbonyl-(2-iminopent-3-en-4-olato)iridium(I) and -rhodium(I) complexes by two routes:



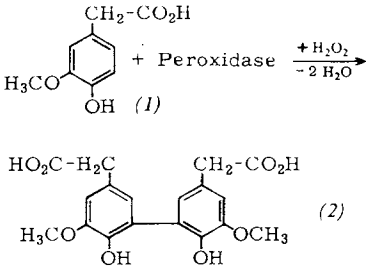
$$\tfrac{1}{2}\ [(L)_2MCl]_2 + H_3C{-}CO{-}CH_2{-}C(=NR){-}CH_3$$

These chelates *(1)* are crystalline, stable in air, sublimable, monomeric, diamagnetic, and soluble in nonpolar organic solvents. It is interesting to note that the Schiff bases are more readily hydrolysed in the form of the complexes than in the free state. A number of chelates and ligand-exchange products are given in the table.

M	L^1	L^2	R	M.p. (°C)	Color
Ir	CO	CO	p-CH_3–C_6H_4	153	yellow
Ir	CO	$P(C_6H_5)_3$	p-CH_3–C_6H_4	184	yellow
Ir	CO	CO	C_6H_5	139	red
Ir	CO	CO	C_3H_7	109	green
Rh	CO	CO	C_6H_5	124	yellow
Rh	CO	$P(C_6H_5)_3$	p-CH_3–C_6H_4	170	yellow
Rh	1,5-Cyclooctadiene		p-CH_3–C_6H_4	206	yellow

/ J. organometallic Chem. *7*, 167 (1967) / –Jg. [Rd 694 IE]

The fluorimetric determination of oxidases. *G. G. Guilbault*, *D. N. Kramer*, and *E. Hackley* have introduced (4-hydroxy-3-methoxyphenyl)acetic acid *(1)* (homovanillic acid) as a new reagent for the fluorimetric determination of oxidases. For example, when about 0.1 ml of the peroxidase solution under examination is added to 2.7 ml of 0.1 M Tris buffer (pH 8.5), 0.1 ml of 0.3% peroxide solution, and 0.1 ml of a solution of homovanillic acid (2.5 mg/ml), the fluorescent dimer *(2)* is formed (λ_{max}^{abs} = 315, λ_{max}^{em} = 425 mμ). With peroxide concentrations of 3×10^{-3} to 1×10^{-7} mole/l, it was possible to determine peroxidase concentrations of 0.006 to 2.3 units per ml from the time-dependence of the fluorescence



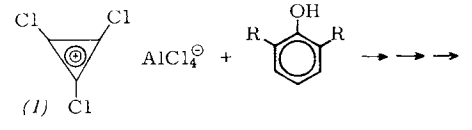
(1)

(2)

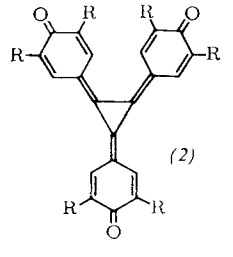
intensity. Since the reagent solution is stable, this method is superior to the diacetylfluorescein and scopoletin methods. / Analytic. Chem. *39*, 271 (1967) / –Jg. [Rd 693 IE]

Monomeric diphenylberyllium complexes $(C_6H_5)_2BeL_2$ have been described by *G. E. Coates* and *M. Tanah*. All complexes stabilized by chelating ligands, such as *N,N,N',N'*-tetramethylethylenediamine, glycol dimethyl ether, or glycol dimethyl dithioether, are monomeric and are relatively slowly hydrolysed. For example, the complex $(C_6H_5)_2Be{\cdot}CH_3SC_2H_4SCH_3$ (m.p. 127–128 °C), which is formed from beryllium powder and diphenylmercury in xylene on addition of the dithioether, is not completely decomposed in dilute H_2SO_4 at temperatures below 60 °C. Complexes with monodentate ligands, such as ether, dimethyl sulfide, trimethylamine, or triphenylphosphine, were shown tensimetrically to undergo partial dehydrogenation at low pressures. If one of the complexing heteroatoms carries a hydrogen atom (as in the case of secondary amines or alcohols), benzene is split off with formation of the dimeric, trimeric, and tetrameric complexes $(C_6H_5BeXR)_n$ (X = O, NR; n = 2,3,4). / J. chem. Soc. (London) A *1967*, 236 / –Bu. [Rd 672 IE]

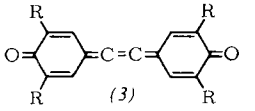
The synthesis of a triquinocyclopropane *(2)*, a diquinocyclopropanone, and a diquinoethylene *(3)* has been described by *R. West* and *D. C. Zecher*. The reaction of $C_3Cl_3^{\oplus}AlCl_4^{\ominus}$ *(1)* with 2,6-di-t-butylphenol in $CHCl_3$ followed by hydrolysis and treatment with triethylamine yields a quinocyclopropene (70%) containing two 3,5-di-t-butyl-4-hydroxyphenyl residues. Oxidation of this compound leads to *(2)*, a dark blue



(1)



(2)

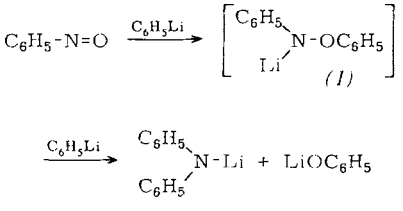


(3)

powder that decomposes at about 280 °C. If the reaction with *(1)* is carried out at 0 °C instead of at room temperature, the product obtained is bis(3,5-di-t-butyl-4-hydroxyphenyl)-cyclopropenone. On oxidation, this gives the violet ketone, whose solutions decompose within a few hours to form the red-purple compound *(3)*. / J. Amer. chem. Soc. *89*, 152, 153 (1967) / –Ma. [Rd 654 IE]

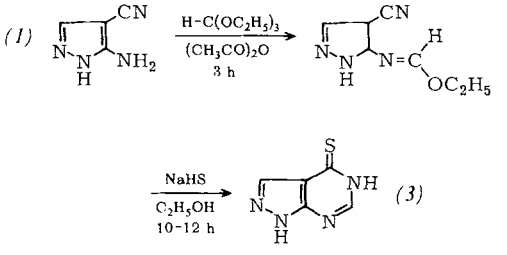
A new berkelium isotope, $^{251}_{97}$Bk, has been isolated by *H. Diamond, R. K. Sjoblom, R. F. Barnes, J. L. Lerner, D. J. Henderson*, and *P. R. Fields*. $^{251}_{97}$Bk is formed by α-decay of $^{255}_{99}$Es. ^{255}Es is present to the extent of 0.01 to 0.001 % in ^{253}Es, which is obtained by reactor irradiation of curium or californium. ^{251}Bk is a β emitter with a half-life of 57.0 ± 1.7 min; 34 and 140 keV γ radiation is also observed (94 and 184 keV γ radiation is probably also emitted). The absence of measurable γ intensities at 58.5 and 81 keV suggests that the ground state of $^{251}_{97}$Bk is not 7/2 + [633], as might be expected by analogy with ^{249}Bk. / J. inorg. nuclear Chem. *29*, 601 (1967) / –WG. [Rd 703 IE]

The inverse addition of phenyl-lithium to nitrosobenzene to give *O,N*-diphenyl-*N*-lithiohydroxylamine *(1)* has been described by *P. Buck* and *G. Köbrich*. *(1)* could not be isolated, since it undergoes rapid nucleophilic substitution by phenyl-lithium, with formation of lithium diphenylamide and lithium phenoxide.

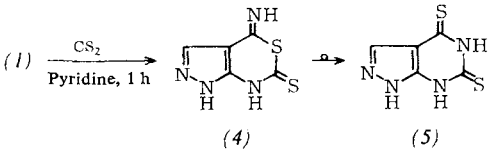


The course of the reaction is shown by the fact that, apart from deprotonation, *N,N*-diphenylhydroxylamine (which is obtainable from nitrosobenzene and C_6H_5MgBr) is inert to phenyl-lithium under the conditions of the reaction. The attack of aryl-lithium compounds on nitrobenzene (against the polarization of the nitro group) also takes place exclusively at the oxygen, as was shown by experiments with phenyl-lithium or *p*-tolyl-lithium and *p*-nitrotoluene or nitrobenzene. The course of this reaction has not yet been elucidated. / Tetrahedron Letters *1967*, 1563 / –Bu. [Rd 665 IE]

One-step syntheses of pyrimidinethiones and pyrimidinedithiones have been described by *E. C. Taylor, A. McKillop, S. Komen*, and *R. Warrener*. These compounds are of pharmaceutical interest. The synthesis can be illustrated for the case of *(3)*, which was formerly obtained in an impure state and in low yields from the same starting material *(1)* by a four-step



synthesis. *(3)* is obtained in a thin-layer chromatographically pure state and in 97% yield without isolation of the intermediate *(2)*. Pyrimidinedithiones such as *(5)* are also obtained from *(1)*. The rearrangement of the thiazine *(4)* into *(5)* (87% yield) is a well-known base-catalysed reaction. / Tetrahedron *23*, 885, 891 (1967) / –Bu. [Rd 666 IE]



BOOK REVIEWS

UV-Atlas organischer Verbindungen, Band 1 – UV-Atlas of Organic Compounds, Vol. 1. Compiled by the Documentation of Molecular Spectroscopy (DMS). Verlag Chemie GmbH., Weinheim/Bergstr. and Butterworths, London 1966. 1st Edit., iv, 32 pages of text, 23 tables, 208 spectra, ring book $ 20.00.

The present volume is the first of a planned five-volume UV atlas, and provides some idea of the care that has been taken in the planning of this work, which is ultimately to include about 1000 spectra. The selection of the substances dealt with is reflected in the following classification:

A. Compounds with C–C multiple bonds.
B. Compounds with C=O and C=S groups.
C. Compounds with C–N multiple bonds
D. Mononuclear aromatic compounds.
E. Polynuclear aromatic compounds.
F. Aromatic compounds containing non-benzoid rings.
G. Mononuclear heterocycles.
H. Condensed heterocycles.
I. Saturated organic compounds.
J. Compounds of biological interest.
K. Inorganic systems.
L. Spectrochemical substances.
M. Solvents.

For ease of comparison, all the spectra are printed on transparent paper and marked with a reference point. They can be superimposed on one another as desired, owing to the loose-leaf form of the Atlas. The plots are always linear in wave numbers and logarithmic in the extinction coefficient. All the spectra are provided with a wavelength scale, which saves calculation. The graphical representations are supplemented in many cases by tables containing further data on the wave numbers and extinction coefficients of the absorption maxima of homologous compounds, derivatives, or ions. After completion, the spectra of the principal groups (A)–(M) will be discussed and interpreted by the editors of the sections in question.

The first volume contains 57 spectra and 13 tables for Group D (editor: *H. H. Perkampus*), 132 spectra and 10 tables for Group H (editor: *S. F. Mason*), and 19 spectra for Group M, which is accompanied by a six-page introduction by the section editor *B. Hampel*, with valuable advice on the purification of various solvents.

The first volume does justice to the promises of the prospectus. We look forward with interest to the early publication of the later volumes[*]. *H. Labhart* [NB 617 IE]

[*] Editorial note: Volume 2 has now appeared. Volume 3 is due to appear in September 1967 and Volumes 4 and 5 should be available in January 1968.

Trivialnamenkartei-1. Ergänzungslieferung (Card Index of Trivial Names – 1st Supplementary Issue). Verlag Chemie GmbH., Weinheim/Bergstr. 1966. 1088 cards, DM 60.–.

In 1964, Verlag Chemie began to compile a card index of trivial names[1]. The first issue contained 8000 cards. Each card bears a number giving its position in the alphabet, the trivial name in question (in German on the left, in English on the right), the structural formula of the compound with stereochemical details (where known), the empirical formula, and a reference to a handbook or journal. It is explained that the aim of this card index is not to foster trivial names, but to provide information wherever none is supplied by the trivial name. For example, it should be of assistance to anyone who does not know what palustrinic acid Centaur X_4, or munetone is. However, he should also possess the first supplementary issue, which contains 1088 cards and which has just been published. It also contains a list of addenda to the cards of the first issue.

Further supplementary issues are planned, and it is really unnecessary to emphasize the value of this card index. Those who already have it at their disposal will have learnt to treasure it, and those who do not yet know it should acquire it as soon as possible for the sake of easy reading in chemical literature. *H. Grünewald* [NB 581 IE]

[1] Cf. Angew. Chem. *78*, 344 (1966); Angew. Chem. internat. Edit. *5*, 326 (1967).

Reactiones Organicae. Organische Reaktionen und Methoden. (Organic Reactions and Methods.) By *H. J. Ziegler*. Georg Thieme Verlag, Stuttgart 1967. Basic stock (12 batches): about 3000 cards; about 250 cards per batch. Price per batch: DM 220.-; 20% reduction when the complete work is ordered.

A greet deal has been done to classify chemical literature in such a way that any desired information can be found quickly and as fully as possible, but without padding. A new attempt to make the knowledge of preparative organic chemistry readily accessible is the card index entitled "Reactiones Organicae" that has been compiled by *H. J. Ziegler*. This index contains all the procedures from "Organic Syntheses", all the reaction types from "Organic Reactions" and (with the exception of the ring-closure reactions) from "Cahiers de Synthèse Organique", and all the reactions from "Namenreaktionen der Organischen Chemie". The basic stock contains 3000 cards. (Eight batches containing a total of 2000 cards have been issued so far.) It will be continuously supplemented and updated by further batches.

The card index consists of punched cards, each of which describes a reaction or a synthesis (sequence of reactions). In the heading on the front of each card, the reaction type is given on the left, the reaction conditions and reagents on the right, and references to Houben-Weyl and to "Cahiers" in the center. In the field below the heading, the reaction described is characterized by a complete formula, data on yields, and a literature reference. On the back of each card is the name of the reaction product, a short account of the procedure in German and in English, and a list of compounds (with yields) that can be prepared in the same way.

The "knack" of "Reactiones Organicae" is that any desired reaction is first reduced to a reaction type. For example, suppose that one wishes to find the possible methods for the oxidation of secondary amines to azomethines. This reaction can be represented in its simplest form by the equation

$$\text{CH–NH–} \rightarrow \text{C=N–}.$$

Code numbers for the partial formula on the left (starting group) and for that on the right (product group) are then found from two formula indexes supplied with the cards in the form of loose-leaf books. These numbers then enable a selector instrument to extract all the cards that describe such reactions. For more specialized problems, code numbers characterizing the reaction conditions and the overall constitution of the product are available.

The entire system is both cleverly conceived and easy to use. Aids (program blocks, color code) are provided to facilitate further the use of the card index and to make it foolproof even for assistants. The greatest advantage of "Reactiones Organicae", however, is the fact that no notation that is not familiar to the chemist, no hypotheses on reaction courses, and no classification of reactions are included, and that neither nomenclature problems nor language problems arise. Thus "Reactiones Organicae" is the ideal literature card index for the organic chemist engaged in preparative work.

H. Grünewald [NB 579 IE]

D-Glucose und verwandte Verbindungen in Medizin und Biologie (D-Glucose and Related Compounds in Medicine and Biology). Edited by *H. Bartelheimer*, *W. Heyde*, and *W. Thorn*. Ferdinand Enke Verlag, Stuttgart 1966. 1st Edit., xv, 1126 pp., 173 figures, 124 tables, cloth DM 228.–.

Contrary to what one might expect from its title and size, this book cannot be summed up in the words "all about glucose". It is not a sort of monograph in which one can quickly find out all about a certain chemical or biochemical property of this sugar or of one of its derivatives, but is rather a eulogy on this compound and its direct and indirect biosynthetic transformation products and precursors. The subject matter covered in the book is by no means narrow. For example, it contains long chapters on "The oxidative final stage of metabolism", *i.e.* on the transformation of the transformation products of the products of transformation of D-glucose, on "The quantum chemistry of photosynthesis, automatically written", where only a few of the compounds described are ultimately converted into or formed from glucose or glucose derivatives. One could, if one were so inclined, say that any carbon compound found in plant or animal cells or in microorganisms is a potential precursor or transformation product of D-glucose, provided that the organism in question can use glucose as a source of carbon. The editors are therefore forced to make a selection, unless they wish to compile a "Beilstein" of natural products. The question that arises now is whether the selection made was a good one. Closer examination shows that is it impossible to give any general answer; in the 45 chapters by 54 authors, the problem of relatedness of the subject under discussion to glucose is solved in various ways.

Almost half of the work is devoted to pharmacological, pathophysiological, and clinical aspects. Several articles in this part deal with the role of glucose in particular and/or of hydrocarbons in general in disease and in the function of various organs (endocrine disorders, diabetes mellitus, kidneys, liver, heart, lungs, joints, brain, skin, eyes, throat, nose, ears, tumors), in surgery, pediatrics, and psychiatry, and in sport. These chapters offer a great deal of valuable information to those with no medical training.

The general chemical and biochemical principles of these special chapters are, unavoidably, not always in agreement with the latest fundamental developments, which always penetrate into the more specialized sectors of a science only after a certain time lapse. Unfortunately, the same is also true of many of the fundamental articles in Section D, "Biochemistry and Physiology" (283 pages).

The length of this time lapse will not be discussed for the various articles. An average minimum value can be estimated from the fact that almost the entire molecular biology vocabulary (*e.g.* induction, repression, operon, messenger, allo-

sterism, end-product inhibition, isozyme, multienzyme complex) is missing from the index. "Enzyme induction" is mentioned in the index, but the passage referred to is simply the unsupported statement that "The adrenocortical hormones increase glyconeogenesis by true enzyme induction".

Section C, which deals with "Formation, occurrence, and importance in plants and microorganisms" (3 articles, 67 pages), concentrates on the discussion of photosynthesis (47 pages). The only article on microorganisms, "Constituent hydrocarbons of the bacterial cell" (20 pages), shows relatively little relation to glucose, but presents a well-rounded account of this field, which is complex from the point of view of structural chemistry. There is no general article on microorganisms, such as might be expected from the title of the book. The 113 pages of Section B, "Methods of determination" (2 articles) will probably be the first pages of the library copy to become grease-spotted and dog-eared; the material in this section appears to be full and carefully written, with a good understanding of the subject. We finally come to an introductory chapter, "Chemistry and pharmaceutical chemistry". This chapter presents a brief outline of carbohydrate chemistry, in which the problems of conformation, which are particularly important in connection with the enzymatic reactions of sugars, are dealt with in detail. The concept of instability factors and Hassel-Ottar and $\Delta 2$ effects are explained with the aid of molecular models.

The air oxidation of D-glucose to D-gluconolactone is discussed as an "Inference from the conformational behavior", and is compared with the enzymatic oxidation of glucose phosphate. The example is ill-chosen. Contrary to the statement that the enzymatic dehydrogenation "evidently depends on the axial position of the hydroxyl group on C-1 of the α-glucopyranose" in the same way as the chemical hydrogenation, glucose 6-phosphate (like all aldoses) is in fact enzymatically oxidized only in the β form. The correct chemical parallel to this should therefore be oxidation with bromine, in which oxidation takes place at the equatorial hydroxyl group of the β form.

There is no doubt that this book contains a great deal of valuable information that may be useful to anyone who is concerned with the biochemical, physiological, and medical aspects of sugars. However, just as a good memory depends on storage capacity and ability to recall, so the value of such a large handbook depends on whether the desired information, which is assumed to be present, can be found quickly and reliably. The index is not the best for ease of recall. This may be the type of index that must be expected in the future when indexes are compiled by machines. It is otherwise difficult to understand *e.g.* why methylglucoside (pp. 24 and 25), α-D-methylglucoside (pp. 22 and 58), β-D-methylglucoside (p. 22), α-methyl-D-glucopyranoside and β-methyl-D-glucopyranoside (p. 106) are listed separately in the index, though the substances are simply anomers of the same compound. The last two are given in English, since they occur in an article written in English. The German keyword "Gluconeogenese" is given in 15 different contexts and with 26 page numbers. However, none of these pages gives a clear definition mentioning the main enzyme reactions on which the phenomenon depends. Nevertheless, this definition is given clearly and precisely in a short section of an article written in English. To find this in the index, one must look under "glyconeogenesis", which comes seven pages after "Gluconeogenese".

What is "maltotriosyl"? It is an orthographic radical that owes its existence to the English terminology (without covalent or coordinate bond?) in the phrase "which transfers maltotriosyl residues".

Nevertheless, the enthusiasm that filled the editor and the authors and that led to the creation of this work is justified. D-glucose and related compounds form a family of imposing might, which plays an important part in all branches of animate nature, and which must fascinate the specialists in every phase of the development of our science.

K. Wallenfels [NB 585 IE]

Laboratory Handbook of Toxic Agents. Edited by *C. H. Gray*. The Royal Institute of Chemistry, London 1966. 2nd Edit., ix, 190 pp. Paperback 24s; 18s to Royal Institute of Chemistry members.

The book comprises five sections: I. General hazards involved in the handling of chemicals (12 pages). II. General precautions and accident prevention, including safe disposal of chemicals (pp. 15–23). III. First aid in cases of skin-contact and internal poisoning, including the different techniques of applying artificial respiration (pp. 27–35).

IV. The main section (pp. 39–166): 250 toxic gases, reagents, and solvents are listed in alphabetical oder (Acetaldehyde to Xylidine). The acute and chronic sings of poisoning are listed in a few key phrases for each substance, as are first aid measures, the TLV(MAC) value, and the necessary warning labeling. Each substance has about half a page devoted to it. Synonyms are referred back to the appropiate passages under their 'approved' names. Occasionally the nomenclature (in the absence of formulae) is difficult to understand for German readers, *e.g.* 'methyl chloroformate'; 'ethyl chloroformate' at least has 'ethyl chlorocarbonate' appended in parenthsis. Chapter V (pp. 169–188) deals with the precautions to be taken during handling of radioactive materials, and contains 14 literature references.

The book attempts to show how careful handling of chemicals can prevent accidents and when these occur, how further chanage can be avoided. A page prefaced to the text is to be filled in by the user with the name of the deputy safety officer, the nearest hospital for casualties, ambulance, doctors, and persons trained to give artificial respiration, as well as telephone numbers of poison information centers. The glossary on the two concluding pages is evidently intended for chemical laboratory workers, in that it explains simple medical terms such as anemia, leukemia, bronchitis, urticaria, *etc.* Unfortunately the book has no index.

The toxicological data contain mistakes – despite the collaboration of *Ethel Browning*. Thus fluorinated hydrocarbons are described as liver poisons but not so chloroform. No warning of the increase in the potency of alcohol intoxication following exposure to aniline and nitrobenzene is given, though this is an important matter for the layman. The book is suitable for obtaining rapid information about potential risks by all those who understand English nomenclature.

H. Oettel [NB 634 IE]

Ylid Chemistry. By *A. W. Johnson*. Organic Chemistry, Vol. 7. Academic Press, Inc., New York London 1966. 1st Edit., x, 388 pages, numerous figures, bound $ 12.50.

The Tower of Pisa leans because the ground subsided while it was being built. Similarly, the structure of organic chemistry, which is built on the three pillars of carbonium-ion chemistry, free-radical chemistry, and carbanion chemistry, cannot be regarded as safe so long as the last of the three pillars is weaker than the other two. This weakness is obvious from textbooks of organic chemistry.

To learn about the theoretical and practical importance of carbanion chemistry, one must turn to special books. A new addition to the ranks of such books is the present work on ylid chemistry by *A. W. Johnson*, who is himself a successful investigator in this field, and has presented a comprehensive picture of its development and its present state.

The author concentrates on the phosphorus ylids, which have been, and still are, intensively studied because of their preparative importance. The bonding in these compounds, which are formed by removal of an α proton atom the phosphonium cation (onium complex), is critically examined on the basis of their physical properties and reactivities. Further chapters are devoted to the olefination of carbonyl compounds and to the iminophosphoranes. This is followed by a discuss-

ion of the nitrogen ylids including the pyridinium betaines and diazo compounds; their rearrangements and their role in the Hofmann degradation are interpreted. The book unfortunately does not contain a chapter on the synthetic importance of this class of compounds, which opens up a new route to phenanthrenes, cyclopolyenes, and isoindoles. The As and Sb ylids, on which relatively little experimental work has been done, are then discussed. The book closes with a long chapter on sulfur ylids, which have attracted special interest as valuable preparative aids. No mention is made of the boron ylids, the study of which is still in its early stages; these are formed by the removal of an α-hydride from ate complexes, and their charge is opposite to that of the types mentioned above.

The reader gains the impression that the ylids and cryptoylids have opened up a field of carbanion chemistry that still conceals a wealth of theoretical and preparative problems inviting further study. The book is strongly recommended to organic and inorganic chemists involved in fundamental research, particularly in the organometallic field.

G. Wittig [NB 614 IE]

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Electron-Pair Repulsions and Molecular Shape

BY R. J. GILLESPIE [*]

The theory described in this article emphasizes the importance of interactions between the electron pairs in the valence shell of a central atom in determining stereochemistry and it assumes that interactions between the ligands are generally of lesser importance although sufficiently bulky groups, or chelate ligands, may play an important role in determining the stereochemistry. If lone-pair electrons are present in the valence shell of the central atom then the two theories (the theory of interaction of electron pairs and the theory of interaction between ligands) predict different structures. In the great majority of cases the determined structures are those expected if it is assumed that lone pairs are stereochemically active, i.e. if repulsions between electron pairs in the valence shell determine stereochemistry.

1. Introduction

It has not proved possible up to the present time to give a complete and exact quantum mechanical treatment for even a triatomic molecule, because the Schrödinger equation cannot be solved exactly for polyelectronic systems. In the treatment of such systems it is almost invariably assumed that the *n*-electron wave-function of a system can be written as a product, or sum of products, of *n* one-electron hydrogen-like atomic orbitals. In the familiar valence-bond theory directed valency is explained in terms of the directional character of p and d atomic orbitals.

However these hydrogen-like atomic orbitals are often rather unsatisfactory for describing the bonding orbitals in molecules and the concept of hybridization was introduced to obtain more satisfactory orbitals. It is well known that this type of treatment shows that two sp bonds are collinear, three sp^2 bonds lie in a plane at 120 °, and four sp^3 bonds are directed towards the corners of a tetrahedron; but this theory can make no other very useful predictions concerning the stereochemistry of molecules. Even these conclusions are, in fact, largely independent of the form chosen for the original one-electron orbitals and they arise essentially from the operation of the Pauli Exclusion Principle.

[*] Prof. R. J. Gillespie
Department of Chemistry, McMaster University
Hamilton, Ontario (Canada)

The purpose of this article is to outline an approach to stereochemistry which makes direct use of the Pauli Exclusion Principle without attempting to write down any explicit form for the wave functions of the individual orbitals or for the system as a whole.

2. The Pauli Exclusion Principle

The most general statement of the Pauli Exclusion Principle is that the wave function for any system must be antisymmetric to electron interchange. Thus for the coordinates (spatial and spin) of electrons 1 and 2 the Pauli Principle states that

$$\psi(x_1, x_2, x_3 \ldots) = -\psi(x_2, x_1, x_3 \ldots)$$

Now, if two electrons have the same coordinates (spatial and spin) *i.e.* if $x_1 = x_2 = x$, then

$$\psi(x, x, x_3 \ldots) = -\psi(x, x, x_4 \ldots)$$

and hence

$$\psi(x, x, x_3 \ldots) = 0.$$

Thus if two electrons have the same spin and space coordinates the wave function vanishes, or in other words it is not possible for two electrons having the same spin to be at the same point in space. In general there is a

low probability of two electrons of parallel spin being close together in space and a high probability of their being far apart [1,2].

Hence if a nucleus has associated with it two electrons of parallel spin their most probable relative location is at 180° to each other, for three electrons it is in a plane at 120° to each other and the most probable relative location for four electrons of parallel spin is at the corners of a regular tetrahedron. We can imagine that the electrons share the spherical space around the nucleus. Thus when there are two electrons they each occupy a hemisphere and when there are three electrons they each occupy a 120° segment of a sphere (Fig. 1), *i.e.*, the electrons are regarded as occupying

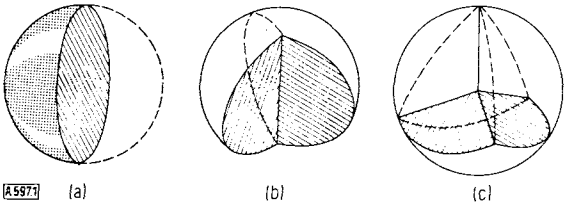


Fig. 1. Segments of a sphere representing orbitals for two, three, and four electron-pairs.

non-overlapping orbitals of these shapes. These electron distributions arise from spin-correlation between the electrons and are therefore a consequence of the Pauli Exclusion Principle. In molecules such as CH_4, NH_3, and H_2O the central atom has a set of four electrons of the same spin which tend to have a tetrahedral arrangement and another set of elctrons of the opposite spin which also tend to have a tetrahedral arrangement. Electrostatic repulsion between the electrons tends to reinforce the tetrahedral arrangements and also to keep the two tetrahedra apart. However the attraction of the other nuclei (the hydrogen nuclei in the above examples) causes pairs of electrons of opposite spin to be drawn into the same region of space, *i.e.* into the same orbital, so that the two tetrahedra come into approximate coincidence and we are led to the picture of pairs of electrons of opposite spin occupying four localized tetrahedrally directed orbitals (Fig. 1). If there are three such electron pairs, as in EF_3, then they occupy three localized orbitals directed at angles of 120° to one another.

3. Electron-Pair Arrangements

A useful model for understanding the most probable arrangements of different numbers of electron pairs around a central nucleus is that in which each electron pair is regarded as a point on the surface of a sphere surrounding the central nucleus [3]. We then ask how these points will arrange themselves, if, in accordance with the Pauli Exclusion Principle, they tend to keep as far apart as possible, or to state it more exactly, if the least distance between any two particles is maximized.

This problem has been treated by several mathematicians [4,5] and the results are shown in Fig. 2. The arrangement of five points is indeterminate in that it may be the trigonal bipyramid or the square pyramid, or any intermediate arrangement. The best arrangement for ten particles has not been determined.

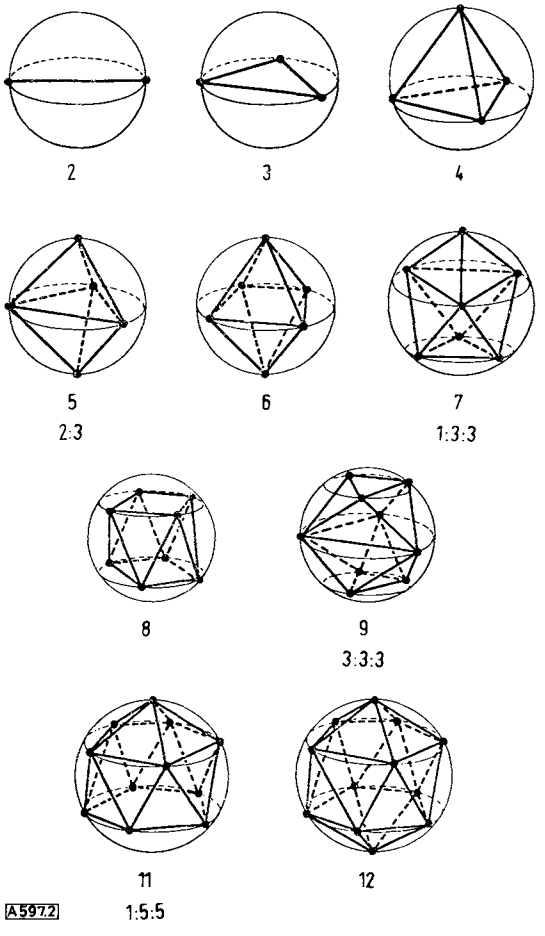


Fig. 2. Arrangements of particles on the surface of a sphere for which the least distance between any pair of particles is maximized.

Alternatively, we may consider the packing of spheres around a central nucleus, each sphere representing the orbital of a pair of electrons. Thus three spheres adopt an equilateral triangular arrangement, four spheres a tetrahedral arrangement, six spheres an octahedral arrangement *etc.* This is the tangent sphere model first proposed by *Kimball* [6] and extensively applied in recent years by *Bent* [7]. The sphere is only a rough approximation to the orbital shape and it can be somewhat improved by adding a conical cap with its apex at the nucleus.

If we describe a polyelectronic system in terms of hydrogen-like one-electron orbitals and combine them to obtain an antisymmetrized molecular orbital (thereby taking account of the Pauli Exclusion Principle), our original simple picture of the individual one-elec-

[1] *P. G. Dickens* and *J. W. Linnett*, Quart. Rev. (chem. Soc., London) *9*, 339 (1957).

[2] *J. W. Linnett*, The Electronic Structure of Molecules, Methuen, London 1964.

[3] *R. J. Gillespie*, Canad. J. Chem. *38*, 818 (1960).

[4] *K. Schutte* and *B. L. van de Waerden*, Math. Ann. *123*, 96 (1951); *L. Jeech*, Math Gazette *41*, 81 (1957).

[5] *H. S. M. Coxeter*, Trans. New York Acad. Sci. *24*, 320 (1962).

[6] For references to *G. E. Kimball*'s unpublished work cf. [7].

[7] *H. A. Bent*, J. chem. Educat. *40*, 446 (1963).

Table 1. Shapes of molecules of the non-transition elements and of d^0, d^5(spin-free), and d^{10} transition elements.

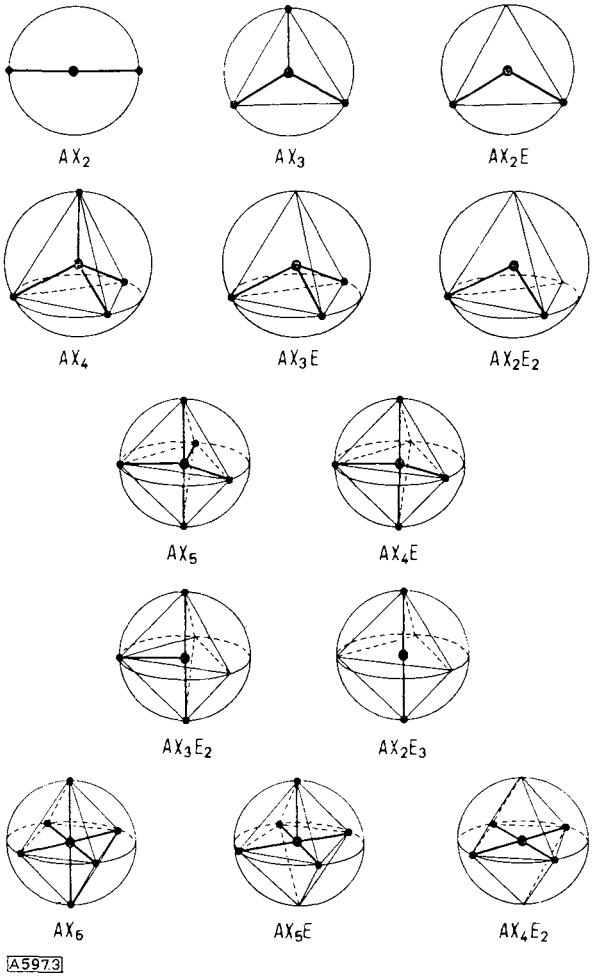
No. of electron pairs	Arrangement	Type of molecule	Shape	Examples
2	Linear	AX_2	Linear	Hg_2Cl_2, HgX_2, CdX_2, ZnX_2, $Ag(CN)_2^{\ominus}$, $Au(CN)_2^{\ominus}$, $(AuCN)_n$
3	Triangular	AX_3	Triangular	BX_3, GaI_3, $In(CH_3)_3$, $(Cu(CN)_2^{\ominus})_n$
		AX_2E	V-shaped	SnX_2, PbX_2
4	Tetrahedral	AX_4	Tetrahedral	$(BeCl_2)_n$, $(Be(CH_3)_2)_n$, $BeX_4^{2\ominus}$, $BX_4^{\ominus}$, CX_4, $NX_4^{\ominus}$, $OBe_4(CH_3CO_2)_6$, BeO, ZnO, AgO, Al_2Cl_6, SiX_4, GeX_4, PbX_4, AsX_4, CuX, $ZnX_4^{2\ominus}$, $HgX_4^{2\ominus}$, TiX_4, ZrX_4, ThX_4
		AX_3E	Trigonal-pyramidal	NX_3, $OH_3^{\oplus}$, PX_3, AsX_3, SbX_3, P_4O_6, As_2O_3, Sb_2O_3, $(AsO_2^{\ominus})_n$
		AX_2E_2	V-shaped	OX_2, SX_2, SeX_2, TeX_2
5	Trigonal-bipyramidal	AX_5	Trigonal-bipyramidal	PCl_5, PF_5, PF_3Cl_2, $SbCl_5$, $Sb(CH_3)_3Cl_2$, $NbCl_5$, $NbBr_5$, $TaCl_5$, $TaBr_5$, V_2O_5, $(VO_3^{\ominus})_n$
		AX_4E	C_2V	SF_4, SeF_4, R_2SeCl_2, R_2SeBr_2, R_2TeCl_2, R_2TeBr_2
		AX_3E_2	T-shaped	ClF_3, BrF_3, $C_6H_5ICl_2$
		AX_2E_3	Linear	$ICl_2^{\ominus}$, $I_3^{\ominus}$, XeF_2
6	Octahedral	AX_6	Octahedral	SF_6, SeF_6, TeF_6, MoF_6, WF_6, WCl_6, S_2F_{10}, $Te(OH)_6$, $(NbCl_5)_2$, $PCl_6^{\ominus}$, $PF_6^{\ominus}$, $Sb(OH)_6^{\ominus}$, $SbF_6^{\ominus}$, $(SbF_5)_n$, $SiF_6^{2\ominus}$, $SnCl_6^{2\ominus}$, $PbCl_6^{2\ominus}$, $TaF_6^{\ominus}$, $NbF_6^{\ominus}$, $VF_6^{\ominus}$, $TiCl_6^{2\ominus}$, $FeF_6^{3\ominus}$
		AX_5E	Square pyramidal	BrF_5, IF_5
		AX_4E_2	Square	$ICl_4^{\ominus}$, I_2Cl_6, $BrF_4^{\ominus}$, $ICl_2 \cdot SbCl_6$, XeF_4

tron distributions is largely destroyed. If we wish to retain the idea of describing the electron distribution in terms of one-electron orbitals, the best picture is obtained by constructing hybrid orbitals from the original atomic orbital. These hybrid orbitals have the property that they are more concentrated in separate regions of space than the original atomic orbitals and they overlap less. The explicit forms of these hybrid orbitals do not necessarily give a more accurate description of the electron density in a molecule than our crude picture of non-overlapping orbitals.

It seems more logical[*] therefore to start the description of a molecule with localized non-overlapping orbitals rather than with hydrogen-like atomic orbitals which are then transformed into new orbitals by the process of hybridization.

4. Molecular Shapes

The arrangements of electron pairs shown in Fig. 2 may be used to predict the stereochemistry of molecules with coordination numbers up to twelve. Each of the preferred arrangements of a given number of electron pairs can give rise to several molecular shapes depending on the relative numbers of bonding pairs and lone pairs. If A is a central atom, X a ligand, and E a non-bonding pair then the shape of a singly bonded molecule AX_mE_n is determined by the preferred arrangement of the $m + n$ electron-pairs. The various possible molecular shapes that can be obtained in this way are given in Table 1 and Fig. 3 for up to six electron-pairs[8,9]. These are indeed the shapes of the known molecules of the type AX_mE_n.



A5973

Fig. 3. Shapes of singly bonded molecules containing up to six electron-pairs in the valence shell of the central atom.

[*] As the process of hybridizing atomic orbitals has been widely misunderstood and often incorrectly regarded as a phenomenon rather than as a simple mathematical operation there is a certain advantage in any theory that avoids the use of this concept.

[8] *R. J. Gillespie* and *R. S. Nyholm*, Quart. Rev. (Chem. Soc., London) *11*, 339 (1957).

[9] *R. J. Gillespie*, J. chem. Educat. *40*, 295 (1963).

The shapes of molecules containing multiple bonds are also readily understood on the basis of the same arrangements of electron pairs. For example, in ethylene each carbon atom is surrounded by four tetrahedrally arranged electron pairs, two pairs being shared between the two carbon atoms to give the double bond, *i.e.* two bent bonds. It is generally more convenient, however, to consider the two electron-pairs of a double bond or the three electron-pairs of a triple bond as occupying a large double- or triple-bond orbital. The general shape of a molecule AX_mE_n where one or more of the ligands is bonded by a multiple bond is then given by the value of $m + n$ where m is now the number of ligands or bonding orbitals, counting only one four-electron orbital, and one six-electron orbital for each double and triple bond respectively [8,9]. Thus the shape of ethylene is based on 120° arrangement of three bonding-orbitals and no lone pairs while the pyramidal shape of the $SOCl_2$ and XeO_3 molecules is based on the tetrahedral arrangement of three bonding orbitals and a lone pair. Various possible molecular shapes for molecules containing multiple bonds are shown in Fig. 4.

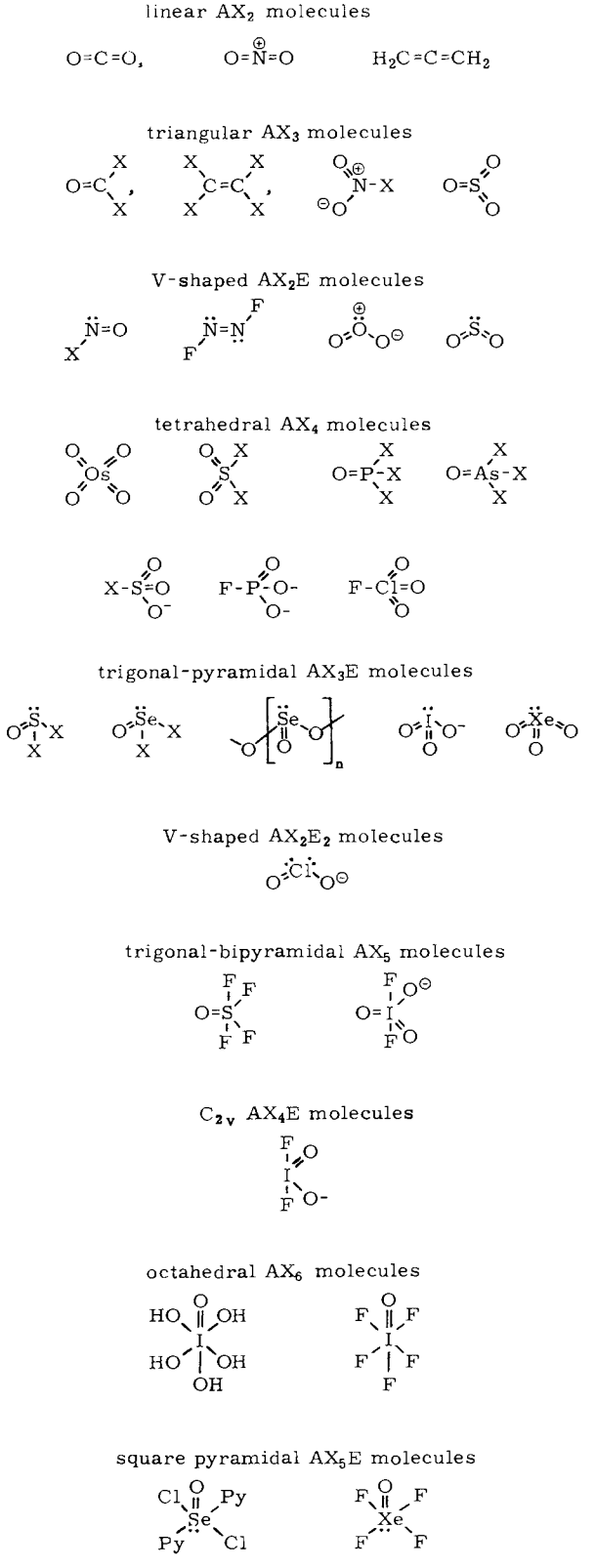


Fig. 4. Shapes of molecules containing multiple bonds.

5. Interpenetrating or "Soft" Orbitals

So far we have considered only the gross shapes of molecules. However our theory can be refined to provide an understanding of many of the finer details of molecular shape. First, it might be argued that electron clouds are not hard objects as we have assumed, but can penetrate each other to some extent. The concept of maximizing the least distance between points on the surface of a sphere is equivalent to assuming that the points exert a repulsive force on each other of $F = 1/r^n$, where $n = \infty$.

If some penetration, or overlap of the orbitals can occur, *i.e.* if the orbitals are regarded as "soft", rather than "hard", then this is equivalent to a force law with $n < \infty$ and probably equal to a value between 6 and 12 [9]. If the interaction between the points were purely electrostatic the force law would be Coulombs law, *i.e.* $n = 2$. The preferred arrangements of particles on the surface of a sphere under the action of an inverse-square force law have been deduced previously [10]. They are the same as those for $n = \infty$ except for the case of seven particles. We conclude then that, except for this case, the arrangements shown in Fig. 2 are independent of the value of n, if $n \geqslant 2$, and that they are, therefore, valid for soft as well as for hard orbitals.

For five electron-pairs the best arrangement for $n = 2$, and indeed for any value of $n < \infty$, is the trigonal bipyramid and not the square pyramid. The special case of seven electron-pairs is discussed in Section 11.

6. Bond Angles in Molecules Containing Lone Pairs

As lone pairs are under the attractive influence of only one nucleus while bonding pairs are attracted by two nuclei, it is reasonable to suppose that the charge clouds of lone-pair electrons are larger and occupy more of the "surface" of the central atom than the bonding electrons (see Fig. 5). This has several important consequences.

[10] *L. Foppl*, J. reine angew. Math. *141*, 251 (1912).

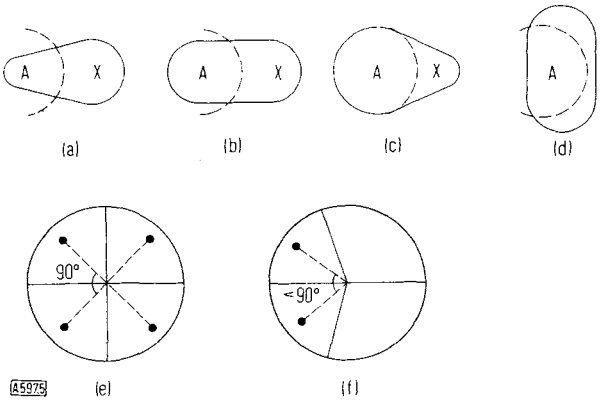


Fig. 5. Shapes of bonding and non-bonding orbitals.

(a), (b), and (c) illustrate the effect of decreasing the electronegativity of the ligand X; the electron pair occupies an increasingly large area of the "surface" of the central atom A. (d) illustrates a lone pair that occupies a still larger area on the surface of the central atom A. (e) represents a two-dimensional arrangement of four equivalent bonding orbitals giving a bond angle of 90° (109.5° in three dimensions). (f) shows the effect of replacing two of the bonding pairs by lone pairs, thereby reducing the bond angle to less than 90° (< 109.5° in three dimensions).

As bonding pairs are replaced by lone pairs the angles between the bonding pairs, *i.e.* between the bonds, will decrease. For example, in the series CH_4, NH_3, H_2O the bond angle decreases from the tetrahedral angle of 109.5° in CH_4 to 107.3° in NH_3 and to 104.5° in H_2O as one and two bonding pairs are successively replaced by lone pairs. Alternatively, one can say that lone pairs of electrons repel other electron pairs more strongly than bonding pairs. If, in an octahedral arrangement of six electron pairs, one is a lone pair, as in molecules such as IF_5 and BrF_5, the bond angle is less than the ideal octahedral value of 90°.

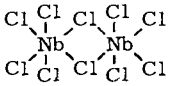
If alternative positions are available for one or more lone pairs in a molecule then, because of their greater size and stronger interaction with other electron pairs, they tend to occupy those positions which give them the most space, which keep two or more as far apart as possible, and which minimize their interactions with other electron pairs. Thus in an AX_4E_2 molecule the lone pairs occupy *trans* positions so that the molecule has a square-planar shape.

7. Variation of Bond Angles with Ligand Electronegativity

An increase in the electronegativity, or effective nuclear charge, of a ligand will cause a decrease in the size of the orbital of the bonding electron-pair [1,8]. This orbital will, therefore, occupy less of the surface of the central atom, leaving more room for the other orbitals. (Fig. 5). Thus, bond angles decrease with increasing electronegativity of the ligands as in the following examples:

F_2O (103.2°) < H_2O (104.5°), NF_3 (102°) < NH_3 (107.3°),
PCl_3 (100°), < PBr_3 (101.5°) < PI_3 (102°),
$AsCl_3$ (98.4°) < $AsBr_3$ (100.5°) < AsI_3 (101°).

An interesting example of a different type is provided by the dimeric molecule of niobium pentachloride which has the structure *(1)* [11]. The bridging chlorine



(1)

atoms carry a formal positive charge and must, therefore, have a higher effective electronegativity than the other chlorine atoms. This distorts the regular octahedral arrangement of chlorine atoms around the niobium so that the two bridging chlorine atoms, which have the smaller orbitals, have a bond angle at niobium of less than 90°, while the other chlorine atoms have bond angles of greater than 90°.

8. Bond Angles in Molecules Containing Multiple Bonds

Since double- and triple-bond orbitals are larger than single-bond orbitals, angles involving multiple bonds will be larger than those involving single bonds [9]. Thus, each carbon atom in ethylene would, to a first approximation, have a 120° arrangement of one double- and two single-bond orbitals, but since the double-bond orbital is larger than the single-bond orbitals, the angle between the double and single bonds is greater than 120°, and the angle between the single bonds is less than 120°. In all other AX_3 molecules we find similar bond angles (cf. Table 2).

Similarly in AX_4 and AX_3E molecules where one of the bonds is a double bond, the angles involving this bond are always greater than the tetrahedral angle

Table 2. Bond angles (°) in some molecules containing double bonds.

AX_3 Molecules

	$\widehat{XCX}$	$\widehat{XCO}$		$\widehat{XCX}$	$\widehat{XCC}$
F_2CO	112.5	123.2	$(CH_3)_2C{=}C(CH_3)_2$	109	125
Cl_2CO	111.3	124.3	$(CH_3)_2C{=}CH_2$	109	125
H_2CO	118	121			
$(NH_2)_2CO$	118	121			

AX_4 Molecules

	$\widehat{XPX}$		$\widehat{XPX}$
POF_3	102.5	PSF_3	100.3
$POCl_3$	103.6	$PSCl_3$	100.5
$POBr_3$	108	$PSBr_3$	106

	$\widehat{XSX}$	$\widehat{OSO}$		$\widehat{XSX}$	$\widehat{OSO}$
F_2SO_2	96.1	124	$(NH_2)_2SO_2$	112.1	119.4
Cl_2SO_2	112.2	119.8	$(CH_3)_2SO_2$	115	125

AX_3E Molecules

	$\widehat{XSX}$	$\widehat{XSO}$	$\widehat{XSX}$	$\widehat{XSX}$	$\widehat{OSO}$
F_2SO	92.8	106.8	$(C_6H_5)_2SO$	97.3	106.2
Br_2SO	96	108	$SeOCl_2$	106	114
$(CH_3)_2SO$	100	107			

[11] *A. Zalkin* and *D. E. Sands*, Acta crystallogr. *11*, 615 (1958).

while the others are smaller. When two double bonds are present the angle between the double bonds is always the largest angle (cf. Table 2). No octahedral AX_6 molecules containing double bonds have had their structures determined accurately, but it may be predicted that in molecules such as $O{=}I(OH)_5$ and $O{=}IF_5$ the angles involving the double bond will be slightly greater than 90 °.

9. Bond Angles at a Central Atom Having an Incompletely Filled Valence Shell [12]

The orbitals in a filled shell effectively occupy all the available space. Any influence tending to reduce the angle between the orbitals will cause appreciable orbital overlap and hence will be strongly resisted. The valence shells of the elements of the first short period, in particular B, C, N, O, and F, are completely filled by four electron-pairs. Thus for AX_4 molecules where A is a first-row atom and for AX_3E and AX_2E_2 molecules, where X is also a first-row atom, the bond angles are always within a few degrees of 109.5 °.

The orbitals in an incompletely filled shell do not occupy all the available space and the angles between them are therefore more easily changed. If the 3d subshell can be filled, the elements of the second short period can, in principle, have up to nine electron-pairs in their valence shells. In fact, for reasons that are not well understood, the valence shells of these elements are effectively completed by only six electron-pairs, as in $PF_6^{\ominus}$ and SF_6.

For these elements, therefore, it is reasonable to assume that bonding electron-pairs do not interact with each other very strongly until the angle between them is the same as in the octahedron, namely 90 °. Thus, on replacing a bonding pair with a lone pair – *e.g.* in the transition from SiH_4 to PH_3 – the lone pair is able to spread out around the "surface" of the phosphorus atom until the bonding pairs are at an angle of approximately 90 ° to each other. Hence the bond angle in PH_3 is only 93.3 °. Replacing another bonding pair by a lone pair – in the transition from PH_3 to H_2S – causes a further small decrease in the bond angle to 92.2 °.

The same idea would also apply to electron pairs constrained to move in a plane and this is much easier to illustrate diagrammatically. Figure 6 shows an atom that is large enough to accommodate four electron-pairs in its (two-dimensional) valence shell. If the same atom has only three electron-pairs in its valence shell and if they are all equivalent bonding pairs, they will be arranged at 120 ° to each other, but they will not occupy all the space in the valence shell. However, if one of the three pairs is a non-bonding pair, it can expand and push the bonding pairs together until they make an angle of approximately 90 ° to each other. Thus we see that the bond angle is easily distorted from 120 ° towards the limiting value of 90 °.

When an atom with a filled valence-shell and one or more non-bonded electron pairs is bonded to an atom with an incomplete valence-shell, there is a tendency

[12] *R. J. Gillespie*, J. Amer. chem. Soc. *82*, 5978 (1960).

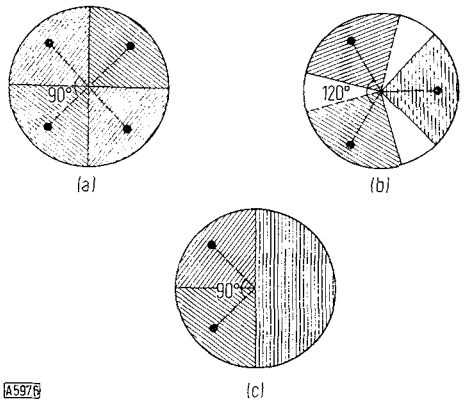


Fig. 6. A two-dimensional representation of the effect of a lone pair in an incomplete valence shell.

(a) shows a valence shell filled with four electron-pairs. (b) shows an incompletely filled valence shell containing only three electron-pairs. (c) shows the effect of replacing one bonding pair by a lone pair, thereby reducing the bond angle to approximately the same value as in (a).

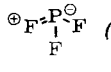
for the unshared pairs to be transferred from the filled shell to the unfilled shell, because in this way electron-pair repulsions are minimized, or in other words, the lone-pair electrons are able to expand into the vacant space on the adjacent atom rather than crowding together the bonding pairs in the filled shell of the same atom.

In the series of molecules PF_3, PCl_3, PBr_3, and PI_3, and AsF_3, $AsCl_3$, $AsBr_3$, and AsI_3 it might be expected, because of the decreasing electronegativity of the halogen atom and the consequent increasing size of the bonding orbitals, that the bond angle would increase steadily from the fluoride to the iodide. The expected increase in bond angle is observed from the chloride to the iodide, but in both cases the fluoride is anomalous, having the largest rather than the smallest bond angle (see Table 3). This may be attributed to the unshared

Table 3. Bond angles for Group V halides.

NF_3	PF_3	AsF_3	–
102.1	104	102	–
–	PCl_3	$AsCl_3$	$SbCl_3$
–	100.1	98.4	95.2
–	PBr_3	$AsBr_3$	$SbBr_3$
–	101.5	100.5	97
–	PI_3	AsI_3	SbI_3
–	102	101	99

pairs of fluorine having a strong tendency to delocalize into the incomplete shell of the central atom, thereby giving the bonds some double-bond character and, therefore, increasing the size of the bonding orbitals and hence the bond angle. In the other halides the halogen atoms have incomplete shells, so there is little tendency for their electron pairs to delocalize onto the central atom and there is little or no double-bond character in these bonds, *i.e.* the strong interactions between the electron pairs in the valence shell of the fluorine atom compared with the other halogen atoms result in structures such as *(2)*,



(2)

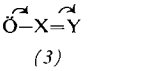
being considerably more important in the fluorides than in the other halides.

In OX_2 and NX_3 molecules where X is a ligand having an incomplete valence shell, delocalization of the lone-pair electrons on O or N occurs giving partial double-bond character to the OX or NX bonds, which, together with the partial removal of the lone-pair electrons from the central atom, causes a considerable increase in the bond angles in these molecules. Thus the SiOSi bond angle generally falls in the range 130–140 ° (see Table 4) while the $N(SiH_3)_3$ molecule is planar with bond angles of 120 °. In SX_2 molecules, however, there is little tendency for the lone pairs of sulfur to be transferred to the ligand and hence the bond angles are less than, rather than greater than, 109.5 ° (see Table 4). When the ligand X in an OX_2 molecule is a very strong acceptor, the transfer of the lone-pair electrons into the OX bonds may be essentially complete, in which case a linear molecule results. Collinear XOX bonds have been found, for example, in the molecules $(Cl_5RuORuCl_5)^{4\ominus}$ and $(TiCl_2(C_5H_5))_2O$.

Table 4. Bond angles (°) in XOX and XSX groups.

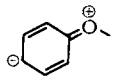
	$\widehat{SiOSi}$		$\widehat{SiSSi}$
α-Quartz	142	$(SiS_2)_n$	80
α-Cristobalite	150	$[(CH_3)_2SiS]_2$	75
$(SiO_3^{2\ominus})_n$	137.5	$[(CH_3)_2SiS]_3$	110
$(H_3Si)_2O$	144	$(SiH_3)_2S$	100
$[(CH_3)_2SiO]_3$	136		
$[(CH_3)_2SiO]_4$	142		
	$\widehat{POP}$		$\widehat{PSP}$
P_4O_6	127.5	P_4S_{10}	109.5
P_4O_{10}	123.5	P_4S_3	103
$P_4O_{12}^{4\ominus}$	132	P_4S_7	106
$(PO_3)_n^{n\ominus}$	129	$P_4S_3I_2$	104
$P_2O_7^{4\ominus}$	134		
$P_3O_{10}^{5\ominus}$	121.5		
	$\widehat{SOS}$		$\widehat{SSS}$
$(SO_3)_3$	114	S_8	105
$(SO_3)_n$	121	S_n	100
$HS_2O_7^{\ominus}$	114	$S_4^{2\ominus}$	104.5
$S_3O_{10}^{2\ominus}$	122	$(C_6H_4SO_2)_2S$	106.5
$S_2O_7^{2\ominus}$	124	$(CH_3SO_2S)_2$	104
		$S_4O_6^{2\ominus}$	103
	$\widehat{COC}$		$\widehat{COC}$
$(C_2H_5)_2O$	108	$(p\text{-}IC_6H_4)_2O$	123
$(CH_3)_2O$	111	$(p\text{-}BrC_6H_4)_2O$	123
1,4-Dioxane	108	$(C_6H_5)_2O$	124
Paraldehyde	109.5	$p\text{-}C_6H_4(OCH_3)_2$	121

Similar effects are observed when the ligand, although having a filled valence shell, is part of an unsaturated group *e.g.* as in *(3)*, *i.e.* is forming one or more multiple bonds to other atoms.



(3)

In such a case X behaves as if it had an incomplete shell since one of the electron pairs of the X=Y double bond may be partially transferred to Y leaving X electron-deficient and thus facilitating the transfer of lone pairs on O into the O–X bond. Hence for aliphatic compounds the COC bond angle is always very close to, and generally a few degrees smaller than, 109.5 °, but for aromatic molecules the bond angle is generally in the range 120–125 ° (see Table 4). This may be attributed to the partial double-bond character of the O–C bonds, *i.e.* the importance of contributing structures such as *(4)*.



(4)

The planar 120 ° arrangement of the bonds around nitrogen in urea and formamide can be similarly explained.

10. AX_5, AX_4E, and AX_3E_2 Molecules

Molecules in which the central atom has five electron-pairs in its valence shell present a number of features of interest. In the trigonal-bipyramid arrangement of five points on the surface of a sphere, the axial and equatorial positions are not equivalent. The axial positions have three nearest neighbors at 90 °, while the equatorial positions have only two such nearest neighbors at 90 ° and two at 120 °. For $n \geqslant 4$ the total force on the axial positions is greater than that on the equatorial positions, hence this is not an equilibrium arrangement and equilibrium can only be reached if the axial electron pairs are at a greater distance from the inner core of the central atom than the equatorial pairs.

If we use the hard sphere model and allow each sphere to touch the central atom, then the equatorial spheres do not touch each other and, as mentioned before, the exact arrangement is indeterminate. If, on the other hand, we insist that the spheres touch each other, then

Table 5. Equatorial and axial radii of ten-electron valence-shell central atoms in AX_5, AX_4E, and AX_3E_2 molecules.

AX_5	r_{eq} (Å)	r_{ax} (Å)
PCl_5	1.05	1.20
PF_5	0.89	0.94
$P(C_6H_5)_5$	1.08	1.22
CH_3PF_4	0.90	0.97
$(CH_3)_2PF_3$	0.91	1.00
PCl_2F_3	0.95	1.06
$SbCl_5$	1.32	1.44
$(C_2H_2Cl)_3SbCl_2$	1.46	1.38
AX_4E		
SF_4	0.91	1.01
SOF_4	0.90	0.96
$(C_6H_5)_2SeBr_2$	1.14	1.36
$(C_6H_5)_2SeCl_2$	1.14	1.31
$(CH_3C_6H_4)_2SeCl_2$	1.17	1.40
$(CH_3C_6H_4)_2SeBr_2$	1.17	1.40
$(CH_3)_2TeCl_2$	1.33	1.52
$(C_6H_5)_2TeBr_2$	1.37	1.54
$IO_2F_2^{\ominus}$	1.27	1.36
AX_3E_2		
ClF_3	0.94	1.04
$C_6H_5ICl_2$	1.23	1.46
BrF_3	1.08	1.18

the axial pairs cannot be in contact with the central atom and the bipyramid consists, in fact, of two tetrahedra, the distance of the axial pairs from the central atom being $\sqrt{2}$ times that of the equatorial pairs. Several consequences follow:

(a) As the total interactions on the equatorial pairs are less than those on the axial pairs, or in other words, as there is more space in the equatorial positions than in the axial positions, the lone-pair electrons always occupy the equatorial positions and we obtain the molecular shapes shown in Fig. 3.

(b) The covalent radius of the central atom in the axial direction must be greater than in the equatorial direction. In all molecules of this type that have been studied, this has proved to be the case. The ratio $r_{ax}/r_{eq} = 1.1 - 1.2$ which is, as expected, less than the value of $\sqrt{2}$ predicted by the hard sphere model [13–15] (Table 5).

(c) As the lone pairs take up more space than the bonding pairs, the bond angles in AX_4E and AX_3E_2 are in general less than the ideal values of 180 °, 120 °, and 90 ° (see Table 6).

Table 6. Bond angles (°) in AX_4E and AX_3E_2 molecules.

	equatorial-equatorial AX_4E	axial-axial
SF_4	101	173
$(CH_3)_2TeCl_2$	98.2	172.3
$IO_2F_2^{\ominus}$	100	180
$(C_6H_5)_2SeBr_2$	110	180
$(p\text{-}CH_3\text{—}C_6H_4)_2SeBr_2$	108	183 [*]
$(p\text{-}CH_3\text{—}C_6H_4)_2SeCl_2$	106.5	182 [*]
$(C_6H_5)_2TeBr_2$	94.2	182 [*]
	AX_3E_2	
ClF_3	87.5	
BrF_3	86.2	
$C_6H_5ICl_2$	86	

[*] These exceptions are discussed in Section 14.

(d) If there is more than one type of ligand, the least electronegative ligands, *i.e.* those with the largest bonding orbitals, will occupy the equatorial positions and the most electronegative will occupy the axial positions. This is always found to be the case [15]. For example in PCl_3F_2 and PCl_2F_3 the chlorine atoms are in equatorial positions and in CH_3PF_4 and $(CH_3)_2PF_3$, the methyl groups occupy equatorial positions [16, 17].

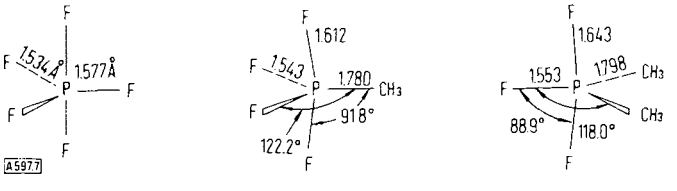


Fig. 7. Molecular parameters for PF_5, CH_3PF_4, and $(CH_3)_2PF_3$.

The molecular parameters [17] of CH_3PF_4 and $(CH_3)_2PF_3$ (Fig. 7) are of considerable interest as they illustrate very well how interaction between electron pairs determines stereochemistry. The methyl groups are less electronegative than the fluorines and therefore the electron pairs forming the bonds to the methyl groups take up more room on the "surface" of the phosphorus atom than do the electron pairs binding the F atoms. Therefore, it follows that: (*i*) the methyl groups occupy the equatorial positions; (*ii*) in the equatorial plane bond angles decrease in the order CPC > FPC > FPF; (*iii*) the FPF angles are all less than 90 ° or 180 °; and (*iv*) successively replacing fluorine by methyl groups in PF_5, CH_3PF_4, and $(CH_3)_2PF_3$ causes an increase in all the bond lengths, as the effective electronegativity of the central atom is decreased, but as the repulsions exerted on the axial bonding electrons are greater than on the equatorial bonding electrons the axial bonds increase in length proportionately more than the equatorial bonds.

Double bonds would always be expected to occupy equatorial positions, as has indeed been found in the case of SOF_4.

Intramolecular exchange of the ligands (pseudo-rotation) occurs very readily in trigonal bipyramidal molecules [14, 15, 17, 18] (Fig. 8). Consider the model of five

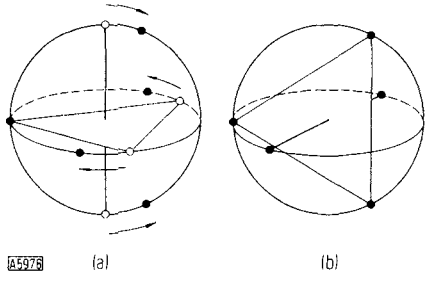


Fig. 8. Pseudo-rotation in a trigonal bipyramid molecule.
(a) o original position of ligands; • final position of ligands. (b) rotated form of trigonal bipyramid.

hard orbitals. The best arrangement is indeterminate and no energy is required to transform the trigonal bipyramid into the square pyramid. The trigonal bipyramid can then be reformed in such a way as to exchange the axial and equatorial positions. For soft orbitals the square pyramid structure has a slightly higher energy than the trigonal bipyramid and the activation energy for the intramolecular exchange of ligands, *via* the square pyramidal configuration as a transition state, is therefore small and exchange occurs rapidly. Thus the ^{19}F spectrum of PF_5 consists of a single doublet due to P–F spin-spin coupling, indicating that all five fluorine atoms are equivalent, whereas two doublets of relative area 2:3 would be expected. This has been attributed to the rapid intramolecular fluorine exchange described above [18]. In this internal motion of the molecule at no time do the electron pairs come closer than the critical angle of 90 °.

In contrast, it may be noted that in a similar internal exchange in an octahedral molecule, for example, the con-

[13] *R. J. Gillespie*, Canad. J. Chem. *39*, 318 (1961).

[14] *R. J. Gillespie*, J. chem. Soc. (London) 4672 (1963).

[15] *E. L. Muetterties* and *R. A. Schurn*, Chem. Reviews in press.

[16] *E. L. Muetterties, W. Mahler, K. J. Packer*, and *R. Schmutzler*, Inorg. Chem. *3*, 1298 (1964).

[17] *L. S. Bartell* and *K. W. Hansen*, Inorg. Chem. *4*, 1775 (1965).

[18] *S. Berry*, J. chem. Physics *32*, 933 (1960).

version of a *cis* isomer to a *trans* isomer, would involve a transition state with angles between electron pairs considerably smaller than 90°. Strong orbital repulsions prevent such an internal motion in this case.

11. Coordination Numbers Greater than Six

For seven, eight, nine, eleven, and twelve electron-pairs the hard sphere model predicts the 1:3:3, square antiprism, 3:3:3, 1:5:5, and icosahedral structures, respectively. For eight, nine, and twelve electron-pairs replacing hard orbitals ($n = \infty$) by soft orbitals ($n < \infty$) does not lead to any change in the general shape.

For seven electron-pairs, it has been found that as n decreases the most stable arrangement changes from the 1:3:3 to the 1:4:2, and finally the 1:5:1, or pentagonal bipyriamid (Fig. 9)[3,19,20]. Calculation shows

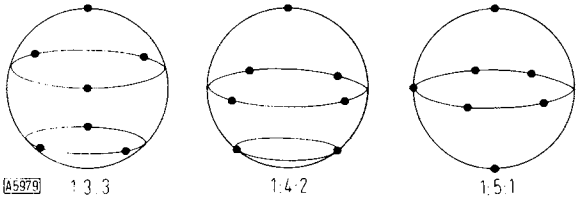


Fig. 9. Arrangements of seven particles on the surface of a sphere.

that the energies of all three arrangements are very similar[19,20] and it does not seem to be possible to predict with any certainty which structure will be adopted in any given case, particularly if the ligands are not equivalent; as for example, if they have different electronegativities, if one or more are multiply bonded, or if they are chelating ligands.

With non-equivalent ligands $NbOF_6^{3\ominus}$ has the 1:3:3 and $UO_2F_5^{3\ominus}$ the pentagonal bipyramid structure. For seven equivalent ligands the 1:3:3 structure has been observed for $ZrF_7^{3\ominus}$, the 1:4:2 structure for $NbF_7^{2\ominus}$, and $TaF_7^{2\ominus}$, and the 1:5:1 structure for $UF_7^{3\ominus}$. Although IF_7 has been reported to have the pentagonal bipyramid 1:5:1 structure[21], this has been disputed[22]. The ^{19}F-NMR spectrum of IF_7 in the liquid state can only be accounted for if all seven fluorines undergo a rapid intramolecular exchange, and thus become magnetically equivalent[23]. This easy intramolecular exchange presumably occurs because of the existence of several forms of seven coordination which differ very little in energy as in the similar case of five coordination[24].

If one of the seven electron-pairs is a lone pair, then because this occupies more space than the other bonding pairs, the molecule is likely to adopt that structure in which the lone pair has the minimum number of nearest neighbors, *i.e.* the 1:3:3 structure in which the lone pair is in the unique axial position. It seems probable that this is the structure of XeF_6[25] and we can also predict that this will be the structure of $IF_6^{\ominus}$.

We expect eight- and nine-coordinated molecules with equivalent ligands and no lone pairs on the central atom to have the square antiprism and 3:3:3 structures, respectively. Unfortunately, there are very few examples of such molecules whose structures have been determined, but, as predicted, $TaF_8^{3\ominus}$ is a square antiprism and $ReH_9^{2\ominus}$ and $Nd(H_2O)_9$ have the 3:3:3 structure. For high coordination numbers in general, several structures will have very similar energies and although for eight coordination and nine coordination one structure appears to be the most stable, for any value of n, other structures may be of very similar energy and a variety of factors, such as the presence of non-equivalent ligands, chelating ligands, or lone-pair electrons, might cause one of these structures to be more stable for a particular molecule than the square antiprism and 3:3:3 structures. The most likely alternative arrangements for any given number of electron pairs can be obtained by using some simple empirical rules relating to the most probable arrangement of particles on a sphere:

(*i*) There may be particles at one or both of the poles.

(*ii*) There will be particles located on circles lying between the poles and perpendicular to the vertical axis joining the poles.

(*iii*) The numbers of particles on successive circles in passing from the pole to the equator must either stay constant or increase by two.

(*iv*) The arrangements of particles on neighboring circles are staggered with respect to each other, two particles by 90°, three by 60°, four by 45° *etc.*

Using these rules we find the following arrangements for six electron-pairs; 1:4:1, 2:2:2, and 3:3, all of which are identical with the octahedron. For seven coordination, we have the 1:3:3, 1:4:2, and 1:5:1 arrangements (see Fig. 9). The apparently possible 1:2:2:2 arrangement is identical with the pentagonal bipyramid. For eight electron-pairs we obtain the 4:4 (square antiprism), 2:2:2:2 (dodecahedron), 2:4:2, 2:2:4, 1:3:3:1, and 1:6:1 (hexagonal bipyramid) arrangements. The cube is a special case of the 1:3:3:1 structure, but considering it as a 4:4 structure shows that it is expected to be less stable than the square antiprism. The apparently possible 2:4:2 structure may be seen to have the same stability as the cube and is, therefore, also less stable than the square antiprism. The 1:6:1 structure is also clearly less stable than the 1:3:3:1 structure. Hence the most probable structures for eight coordination are the 4:4 (square antiprism), 2:2:2:2 (dodecahedron), 2:2:4, and 1:3:3:1 structures (see Fig. 10).

[19] *D. Britton*, Canad. J. Chem. *41*, 1632 (1963).

[20] *T. A. Claxton* and *G. C. Benson*, Canad. J. Chem. *44*, 157 (1966).

[21] *R. D. Burbank*, Acta crystallogr. *15*, 1207 (1962); *16*, 700 (1963).

[22] *J. Donohue*, Acta crystallogr. *18*, 1018 (1965).

[23] *R. J. Gillespie* and *J. W. Quail*, Canad. J. Chem. *42*, 2671 (1964).

[24] *E. L. Muetterties*, Inorg. Chem. *4*, 169 (1965).

[25] *L. S. Bartell, R. M. Gavin, H. B. Thompson*, and *G. L. Cherniak*, J. chem. Physics *43*, 2546 (1965); *K. Hedberg, S. H. Peterson, R. R. Ryan*, and *B. Weinstock*, J. chem. Physics *44*, 1726 (1966).

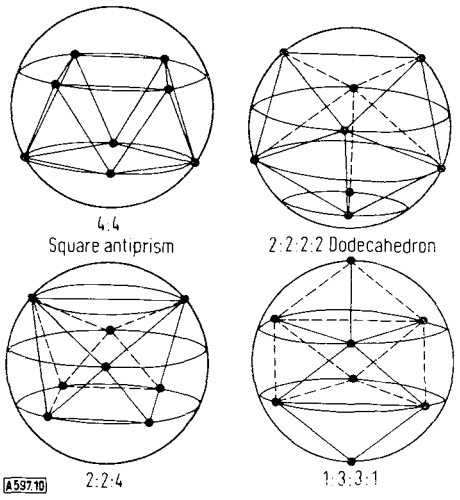


Fig. 10. Most probable structures for eight coordination.

For eight equivalent non-chelating ligands the square antiprism is expected to be the most stable structure and it has been observed in the case of $TaF_8^{2\ominus}$. The dodecahedron has been observed for $Mo(CN)_8^{4\ominus}$ which has non-bonding d electrons and also for a number of chelate complexes such as $Zr(C_2O_4)_4^{4\ominus}$. Several uranyl complexes, *e.g.* $UO_2(OAc)_2$, have the 1:3:3:1 structure and the nitrate $UO_2(NO_3)_2$ has the 1:6:1 structure. In these cases the doubly bonded oxygen atoms occupy the axial positions where they are as far apart as possible. *Hoard* and *Silverton* have discussed the square antiprism and dodecahedron forms of eight coordination in some detail [26].

According to the above rules, the 3:3:3, 1:2:2:2:2, 1:4:4, 1:2:4:2, 1:2:2:4, 1:6:2, and 1:7:1 arrangements are possible for nine electron-pairs. Of these the 3:3:3 arrangement is predicted to be the most stable for nine identical electron-pairs and is, in fact, the only structure that has been observed for nine-coordinated molecules.

12. Noble-Gas Compounds

The structures of all the noble-gas compounds that have been prepared in the last few years are in accord with the general rules for predicting structures that have been outlined in this review. As some apparently possible compounds have not yet been prepared we have the opportunity to make some predictions. Known and predicted structures are given in Fig. 11 [27].

The fluorides XeF_2, XeF_4, XeF_6, and XeF_8 have been prepared. XeF_2 is an AX_2E_3 molecule and has the expected linear structure. XeF_4 is an AX_4E_2 molecule and has the expected square planar structure. XeF_6 is an AX_6E molecule and will, therefore, not be octahedral [25]. Of the possible structures, a distorted octahedron with D_3 symmetry based on the 1:3:3 arrangement of seven electron-pairs seems the most likely be-

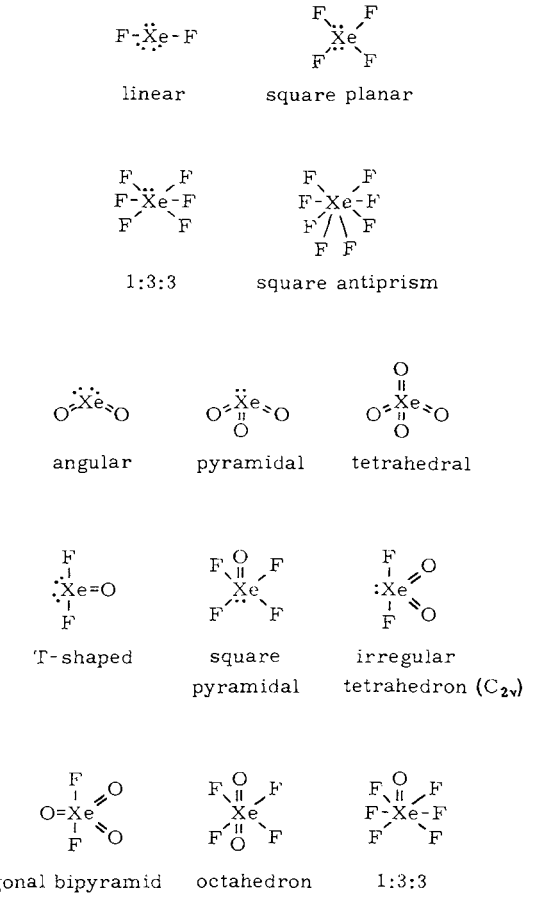


Fig. 11. Known or predicted structures for some noble gas compounds.

cause the lone pair, if it occupies the unique axial position, has only three near neighbors whereas all the other positions have four near neighbors, as does the unique axial position in the otherwise favorable 1:4:2 structure. The structure of XeF_8 has not been determined, but it is predicted to be a square antiprism.

The dioxide XeO_2 is not known but it would be an AX_2E_2 molecule and is, therefore, predicted to be angular in shape. The trioxide XeO_3 is an AX_3E molecule and is, therefore, predicted to be pyramidal as has indeed been observed. The tetroxide XeO_4 is an AX_4 molecule and it must, therefore, be tetrahedral.

The oxyfluorides $XeOF_2$, XeO_2F_2, XeO_3F, $XeOF_4$, XeO_2F_4, and $XeOF_6$ are all possible compounds. Of these only $XeOF_4$ is known with certainty and its structure has been determined; it has the square pyramidal structure predicted for an AX_5E molecule. Because of their greater size the lone pair and the double bond are expected to occupy *trans* positions, as is indeed observed. $XeOF_2$ is an AX_3E_2 molecule and is predicted to be T-shaped (like ClF_3) with the oxygen atom in an equatorial position. XeO_2F_2 is an AX_4E molecule and is predicted to have a shape similar to that of $IO_2F_2^{\ominus}$ with the oxygen atoms and the lone pair in the equatorial positions if a trigonal bipyramid. XeO_3F_2 is an AX_5 molecule and is expected to be a trigonal bipyramid with the three oxygen atoms in the equatorial positions. XeO_2F_4 is an AX_6 molecule and would be expected to be octahedral with the oxygen atoms in *trans* positions. $XeOF_6$ is an AX_7 molecule

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and is predicted, with somewhat less certainty, to have a 1:3:3 structure closely resembling that of XeF_6 with the oxygen atom replacing the lone pair.

Xenon hexafluoride forms the anions $XeF_8^{2\ominus}$ and $XeF_7^{\ominus}$ [28]. The possible structures of these two anions are of great interest as they are the only known examples of molecules containing a lone pair and seven or more ligands. The $XeF_8^{2\ominus}$ ion is an AX_8E molecule and, therefore, its shape will be based on an arrangement of nine electron-pairs. As all nine electron-pairs are not equivalent, this will not necessarily be the 3:3:3 arrangement. A probable alternative is the 1:4:4 arrangement in which the lone pair occupies the unique position. The shape of the molecule could then be described as a somewhat distorted square antiprism in which the face containing the lone pair would be somewhat enlarged and squashed down towards the central xenon atom. The structure of $XeF_7^{\ominus}$, provided that it does not have a higher effective coordination number as a consequence of fluorine bridging, will have a structure based on the arrangement of eight electron-pairs. Again this may not be the square antiprism arrangement and a probable alternative is the 1:3:3:1 arrangement with the lone pair in one of the axial positions.

13. Transition Elements

In the case of transition elements it is necessary to take into account any interactions between the non-bonding d-shell and the bonding pairs in the valence shell. If the d-shell of the central atom is spherically symmetric *i.e.* d^0, d^5 (spin free), or d^{10}, it will have no effect on the arrangement of the valence-shell electron-pairs and the structures of these molecules will be exactly the same as the corresponding molecules of non-transition elements.

In other cases we must consider how an incomplete and therefore unsymmetrical inner d-shell can affect the arrangement of the ligand electron-pairs. This is best discussed in terms of the ligand-field theory and the Jahn-Teller effect. Any molecule with a degenerate electronic state will distort in such a manner as to remove this degeneracy and to reduce the symmetry of the molecule. This can be visualized as resulting from the repulsion between the d-shell and the valence-shell electron-pairs. In ligand-field theory the repulsion is considered to be between the d-shell and the ligands, but we prefer to relate stereochemistry to the arrangement of the bonding electron-pairs rather than the ligands themselves; in any case the general conclusions are the same.

Consider AX_6 molecules. In the absence of any interaction with a d-shell, or if the d-shell is spherically symmetric these will be strictly regular octahedral molecules. Now ligand-field theory shows that an octahedral arrangement of ligands splits the d-shell into two levels, the d_{xy}, d_{xz}, and d_{yz} orbitals (or t_{2g} orbitals) and the $d_{x^2-y^2}$ and d_{z^2} orbitals (or e_g orbitals). Since the t_{2g} orbitals have a greater electron density between the bonding electron pairs while the e_g orbitals have a greater electron density in the direction of the bonding electron pairs, the former are of lower energy than the latter. If either of these two sub-levels is unsymmetrically occupied then some of the bond pairs suffer a greater repulsion than others and the octahedron is distorted, although the effects produced by the t_{2g} orbitals are expected to be very small and have not been observed. It is easily seen that an unsymmetrical occupation of the e_g orbitals will give rise to a tetragonal distortion so that the symmetry is reduced from O_h to D_{4h}, but it cannot be predicted whether this distortion will give rise to an elongated, or a compressed octahedron, both have been observed for d^7, d^8, and d^9 systems. In these cases it is a reasonable approximation to regard the d-shell as having an ellipsoidal (either prolate or oblate) shape. The arrangement of six electron-pairs around a prolate ellipsoid will give an elongated octahedron, while an oblate ellipsoid would give a compressed octahedron. Strong interaction with the d-shell may cause an octahedral complex to lose its axial ligands (and their electron pairs) thus giving rise to a planar AX_4 complex. Alternatively, such a structure can be regarded as arising from the interaction of an ellipsoidal d-shell with a tetrahedral AX_4 molecule. In some cases where the interaction with the d-shell does not completely dominate the interaction between the four bonding electron-pairs, a distorted tetrahedral structure might be expected, as has indeed been observed for $CuCl_4^{\ominus}$ and $CuBr_4^{\ominus}$. The predicted distortions of an AX_5 trigonal bipyramid molecule have been discussed in detail elsewhere [29].

14. Exceptions

There are only a few cases where the stereochemistry of a molecule appears to be dominated by interactions between ligands. For example, the ions $SeX_6^{2\ominus}$ and $TeX_6^{2\ominus}$, where X = Cl, Br, or I, are of the AX_6E type and, therefore, should have a distorted octahedral structure like XeF_6. In fact they have regular octahedral structures [30, 31]. Here the lone pair has no stereochemical effect and must be presumed to occupy a spherical orbital closer to the nucleus than the bonding orbitals, as was first suggested by *Pauling* many years ago [30]. It has been claimed that the ligands, when they are sufficiently large, can only be packed around the central atom in an octahedral arrangement [31], in other words, it is assumed that this is a case where interaction between ligands dominates over the interaction between valence-shell electron-pairs and the lone pair is forced into an inner orbital.

As the ions $XeF_7^{\ominus}$ and $XeF_8^{\ominus}$ are known it is clear that six fluorine atoms do not take up all the space around the central xenon atom and that there is, therefore, room for the lone pair which accordingly exerts its stereochemical effect, with the result that the structure of XeF_6 is non-octahedral. Since the molecule IF_7 is known, $IF_6^{\ominus}$ may similarly be predicted with confidence as having a non-octahedral structure.

The interesting point arises, however, that eight fluorine atoms might possibly take up all the space around the xenon, in which case the lone pair would be forced into an inner orbital and would thus exert a reduced, or even zero, stereochemical effect. In this latter case the structure would then be predicted to be a regular square antiprism. Similarly, it might be expected that some AX_4E molecules in which X is a large ligand would have a tetrahedral shape, but no examples are

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yet known. It is interesting to note, however, that some molecules of this type do have structures that are closer to the tetrahedral shape than is predicted by consideration of the repulsions between five electron-pairs. In the molecules

$(p\text{-}CH_3C_6H_4)_2SeBr_2$, $(p\text{-}CH_3C_6H_4)_2SeCl_2$, and $(C_6H_5)_2TeBr_2$

the angle between the axial ligands is greater than 180° instead of less than 180° as predicted (see Table 6). It seems that the lone pair is not exerting its full stereochemical effect.

These seem to be the only cases where the simple rules discussed in this article do not predict the correct structures. It is perhaps not unreasonable to claim that these rules give a better understanding of the structures of simple molecules than any other theory. For example, no other theory can successfully account for the changes in bond lengths and bond angles in the molecules PF_5, CH_3PF_4, and $(CH_3)_2PF_3$.

Because of the similar energies of different structures, predictions are less certain for high coordination numbers, but this must also be the case for alternative theories. It is to be hoped that in the future, the ideas presented here can be given a sounder theoretical basis and that they can be incorporated into a still more comprehensive and more successful theory of molecular structure.

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Chemical Gamma-Resonance Spectroscopy[**]

BY V. I. GOLDANSKII[*]

Two of the most important contributions that nuclear physics has made to modern science and technology have been in the fields of nuclear energy and isotope labeling. In recent years nuclear physics has stimulated the appearance and extremely rapid development of yet another new and equally important scientific discipline, namely gamma-resonance spectroscopy. This new branch of spectroscopy, which is based on the Mössbauer effect[1–3] is playing an increasingly important role in physics, chemistry, biology, geology, and in the elucidation of various technical problems. – This paper deals briefly with the basic physics of the Mössbauer effect and the characteristics of Mössbauer (gamma-resonance) spectra, and then considers various applications of this new type of spectroscopy. Particular attention is paid to the fundamentals and development of chemical gamma-resonance spectroscopy[4–9] as a technique for the resolution of problems in various fields of chemistry and biology and to the range of problems tackled in recent years in our laboratory of nuclear and radiation chemistry at the Institute of Chemical Physics of the Academy of Sciences of the USSR. A number of reviews and monographs dealing with the application of the Mössbauer effect in chemistry have already been written[4–12]. The following work is based mainly on experimental results obtained by research workers in the Soviet Union.

I. The Mössbauer Effect

Let us first consider the Mössbauer effect, the phenomenon of recoil-less resonance absorption and emission of gamma-quanta, which was discovered by *Rudolf Mössbauer* in Germany in 1958 and for which he was awarded the Nobel prize in physics in 1961.

The phenomenon of resonance is known in mechanics, acoustics, optics, and radio engineering. When tuning our radio to the transmitting station we adjust the frequency of the receiver's oscillatory circuit to the same frequency as that of the transmitters oscillatory circuit. Sometimes even considerable revolving of the tuning knob leaves the audibility

[*] Prof. Dr. V. I. Goldanskii
Institute of Chemical Physics
Vorobjevskoje Shaussee 2-B
Moscow, B-334 (USSR)

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almost unaltered, and at other times even the slightest touch may abruptly disturb reception. In the latter instance the resonance is sharper or, in other words, more sensitive to any interference.

Quantum systems, *i.e.* molecules, atoms, and atomic nuclei, represent resonant radiation receivers and transmitters. The radiation frequencies ω of such systems are determined by the energy difference E_r between the excited and the ground state:

$$E_r = \hbar\omega,$$

where $\hbar \approx 6.6 \times 10^{-16}$ sec-eV is Planck's constant (see Fig. 1). Another important characteristic of resonance is its width Γ, which is related to the average lifetime of the excited state τ:

$$\Gamma = \frac{\hbar}{\tau}$$

The ratio Γ/E_r characterizes the resonance sharpness; the lower its value, the better the selectivity of the resonance system.

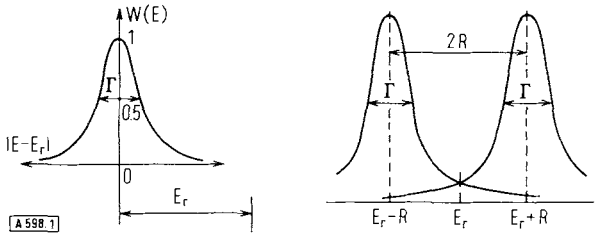


Fig. 1. Illustration of the resonance phenomenon.

Left: Probability of resonance excitation $W(E)$ depending on deviation of the transmitted energy E from resonance value E_r. Γ is the natural resonance width.

Right: Emission and absorption resonance lines displaced by the recoil energy $R = E_r/2mc^2$ towards energies lower than or higher than E_r.

Two characteristic cases of resonance – atomic (yellow D-line of sodium) and nuclear (transition from an excited 23.8 keV state of ^{119}Sn to the ground state) – are given for comparison in Table 1.

Table 1. Main criteria of characteristic atomic and nuclear resonance transitions.

Parameter	Atom (D-line of Na)	Nucleus (^{119}Sn)
Transition energy E_r (eV)	2.1	23800
Lifetime of excited state τ (sec)	1.5×10^{-8}	2.7×10^{-8}
Natural resonance width Γ (eV)	4.4×10^{-8}	2.4×10^{-8}
Resonance sharpness Γ/E_r	2.1×10^{-8}	10^{-12}
Recoil energy R (eV)	10^{-10}	2.5×10^{-3}
Ratio of recoil energy to transition energy R/E_r	$\approx 4.8\times10^{-11}$	$\approx 10^{-7}$
Ratio of recoil energy to resonance width R/Γ	$\approx 2.3\times10^{-3}$	$\approx 10^{5}$

It is obvious that the resonance width Γ of the atom and that of the atomic nucleus are approximately equal, whereas the energy of transition in the nucleus is higher than that in the atom by four powers of magnitude; therefore, the selectivity of nuclear resonance is thousands of times higher than that of atomic resonance. A change in the energy of an emitted or absorbed gamma-quantum by only one trillionth suffices either to destroy or reproduce resonant conditions. (If this degree of accuracy (10^{-12}) were to apply in the measurement of the radius of the entire solar system then figures would be obtained which would be accurate to within the height of a two-storey building.) It can be appreciated that the prospects of observing gamma-resonance seemed very attractive; however, because of the extreme selectivity of this resonance, combined with the great energy of gamma-quanta, the discovery of gamma-resonance was delayed for a number of years.

A gamma-quantum (or an optical quantum) departing from a nucleus (or an atom) imparts to that nucleus (or atom) a momentum in the opposite direction. The energy of the recoil is given by

$$R = E_r^2/2mc^2,$$

where m is the mass of the source of radiation and c is the velocity of light. In the case of an atom, the recoil energy is much less than the resonance width ($R \ll \Gamma$), and consequently recoil does not interfere with observation of the resonance phenomena. The situation is quite different in the case of nuclei; the recoil energy is hundreds of million times greater, and the emission line is displaced far away (by $2R$) from the position of the absorption line ($E_r + R$) towards lower energies ($E_r - R$). The position of the absorption line is accounted for by additional kinetic recoil energy R imparted to the absorbing nucleus excited by energy E_r. Resonance appears to be possible only at the expense of partial superposition of two lines separated by recoil; moreover the shapes of these lines are distorted owing to thermal motion of the nuclei and the resulting Doppler shift of the gamma-quantum frequency.

Recoil-less nuclear gamma-resonance (NGR) was discovered under conditions where the emitting and absorbing nuclei (^{191}Ir in *Mössbauer*'s first experiment) were in a crystal lattice, bound by chemical bonds to billions of nuclei of the same sort. The recoil on emission or absorption of a gamma-quantum is insufficient to break these bonds and therefore the recoil energy is dissipated in excitation of the quanta of atom vibrations in the lattice, *i.e.* of phonons. The case may be, especially at low temperatures, that no phonon excitation is effected, the transition energy is then divided between a quantum and the whole lattice and the denominator of the expression for recoil energy will represent not the mass of an individual nucleus but the mass of the lattice. As in the case of firing an infinitely heavy gun, the recoil energy tends to zero, *i.e.* it becomes much less than the resonance width ($R \ll \Gamma$) and does not interfere with observation of the latter. An intense resonance line, maintaining its position and width, appears on the background of shifted and broadened absorption and emission spectra whose peaks are separated by $2R$ from one another by recoil (see Fig. 2).

It is of interest to note that *Mössbauer* explained his experimental results on the basis of a theory proposed by *Lamb* for the explanation of the appearance of a similar line in experiments on neutron scattering. This

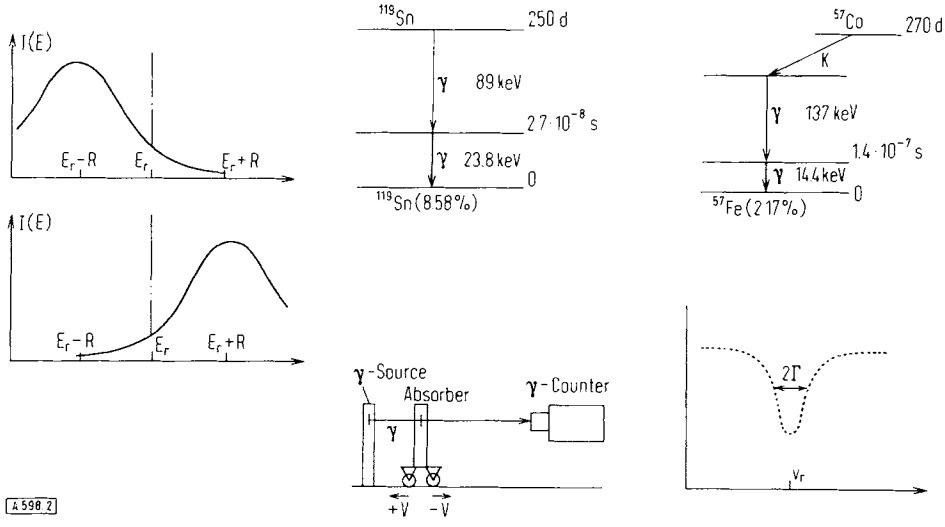


Fig. 2. Illustration of the Mössbauer effect.

Left: The spectra of gamma-quanta emission and absorption. A resonance line of natural width is observed against a background of displaced and broadened spectra (scale of 1:200 in case of ^{191}Ir at 88 °K). Formulae for the Mössbauer effect probability f' in the Debye approximation (Θ = Debye temperature):

$$f' = \exp\{-2W(T)\};\ T \ll \Theta:\ W = \frac{3}{4}\cdot\frac{R}{k\Theta};\ T \gg 0:\ W = \frac{3}{4}\cdot\frac{R}{k\Theta}\cdot 4\frac{T}{\Theta}$$

Top center and right: decay diagrams for ^{119}Sn and ^{57}Co → ^{57}Fe. Half-lives, transition energies, and natural abundances for tin and iron are shown. Bottom center and right: schematic representation of a gamma-resonance experiment (*i.e.* dependence of the gamma-quantum counting rate on the velocity of the absorber (or source) and the approximate shape of such a spectrum.

$$V \approx c\,\frac{\Gamma}{E_r} \approx (10^{-12}\ :\ 10^{-13})\,c \approx (10^{-2}\ :\ 10^{-3})\ \text{cm/sec}.$$

theory had been developed some 20 years before the discovery of recoil-less nuclear gamma-resonance. It is rather unfortunate that, due to excessive specialization, both by those conducting experiments with gamma-quanta and by those concerned with interactions of neutrons in solids, the discovery of the Mössbauer effect should be delayed for such a long time.

From the discussion so far it is clear that the nuclear-resonance line of natural width represents a kind of high-precision measuring instrument. How is the Mössbauer effect observed and quantitatively studied?

First of all, a transmitter and a receiver are needed; their parts are played, respectively, by the excited emitting nucleus and the stable nucleus of the same isotope, *i.e.* a resonance absorber for gamma-quanta. Figure 2 shows decay schemes for two nuclei most commonly utilized in gamma-resonance spectroscopy, namely ^{119}Sn and ^{57}Fe (formed in the radiation source from the ^{57}Co parent nucleus by K-electron capture). Secondly, a control of the gamma-quantum energy is necessary. The frequency and the tone of a sound signal are known to change with displacement of the sound source; such changes are due to the Doppler effect. The same effect was utilized by *Mössbauer* to change the gamma-quanta energy in GR spectroscopy, where, due to extremely sharp resonance, a low velocity movement of the absorber relative to the source is sufficient. This velocity $V = \Gamma \cdot c/E_r$ is estimated according to the value of Γ/E_r, *i.e.* on the properties of the nucleus selected for study, in fractions of mm/sec (^{119}Sn, ^{57}Fe) and occasionally in fractions of micron/sec (^{67}Zn).

Study of the dependence of the counting rate on the velocity of the absorber placed between the source (emitter) and the counter, is the most important experimental step in gamma-resonance spectroscopy. The approximate shape of this function, called the gamma-resonance or Mössbauer spectrum (GR spectrum), is given in Fig. 2. The peak or the resonance line corresponds to minimum counting, *i.e.* to maximum adsorption, when the absorber is moving at some certain velocity. Thus the essence of obtaining gamma-resonance spectra consists in compensation of all external factors affecting the resonance transition energy by appropriate displacement of the absorber or the quanta source, and thereby making a quantitative investigation of these factors.

Mössbauer's discovery provided research workers with a tool for the precise measurement of gamma-quanta energy. However, the potentiality of this new tool was not immediately appreciated. At first the new phenomenon seemed to be confined to the relatively limited scope of elucidating problems of nuclear physics. The development of GR spectroscopy, and its application in solid-state physics, chemistry, biology, geology, and engineering was the result of work carried out by many scientists of various countries.

II. Parameters of Gamma-Resonance Spectra

The motion of atoms within molecules and in crystal lattices, as well as the interaction of the charge and the electric and magnetic moments of the nucleus with surrounding electron shells all affect the gamma-quantum energy; consequently, each of these effects can be investigated by means of gamma-resonance spectroscopy.

A schematic list of Mössbauer spectrum parameters and of information contained therein is presented in Fig. 3.

Let us begin with the probability of the Mössbauer effect f' displayed in the resonance peak area (Fig. 3a). The f' value defines the range of thermal atomic vibrations within molecules and lattices, *i.e.* their mean square amplitude $\overline{r^2}$. A detailed theory connecting the f' value and its temperature dependence with the vibrational frequency spectrum of a composite crystal lat-

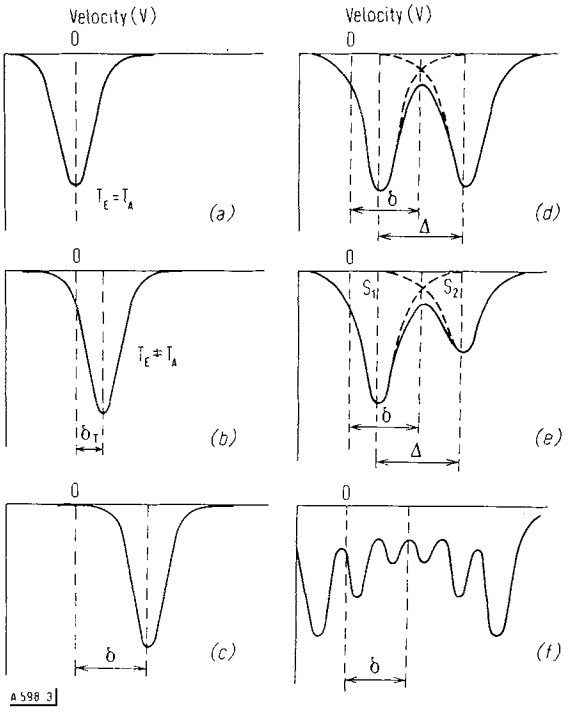


Fig. 3. Parameters of gamma-resonance spectra and information supplied by them (E = source, A = absorber):

a) Source ≡ absorber, the peak area is proportional to $f'(T) \sim \exp[-r^2/(\lambda/2\pi)^2]$ where r^2 is the mean square of the atomic displacement;

b) Source ≡ absorber, the temperature shift of the line $\delta_T = \frac{1}{2} E_\gamma \frac{\overline{V^2}}{c^2}$ gives the value of mean square velocity V^2 of the atom in vibrational motion;

c) Source ≠ absorber, the isomeric (chemical) shift of the line $\delta \sim \frac{\Delta R}{R}\left\{|\psi(0)|^2_A - |\psi(0)|^2_E\right\}$ supplies information on density (square of wave function) of s electrons at the nucleus;

d) Source ≠ absorber, quadrupole splitting $\Delta \sim Qq$ gives the value of the electric field gradient on the nucleus $q = \frac{\partial^2 V}{\partial z^2}$;

e) Source ≠ absorber, the asymmetry quadrupole splitting supplies information about the anisotropy of atomic motion in molecules and lattices: $x^2 \neq \overline{y^2} \neq z^2$ or on electron paramagnetic relaxation;

f) Source ≠ absorber, magnetic splitting ($1/2 \rightarrow \pm 1/2$; $3/2 \rightarrow \pm 3/2$, $\pm 1/2$): $\Delta M \quad \mu/IH$ (where I is the spin, μ the nuclear magnetic moment) characterizes an effective local magnetic field H on the nucleus.

tice and impurity atoms was developed by *Yu. M. Kagan* [13,14].

An important part of this theory deals with the role of the so-called optical branches of vibrational spectra in the probability of recoil-less gamma-resonance. The optical branches possess comparatively high energies (and consequently small amplitudes) and characterize, in the long-wave approximation, the motion of atoms relative to their nearest neighbors in contrast to simultaneous displacements of many atoms in acoustic vibration branches. The existence of optical branches is essential because they provide for the possibility of observing gamma-resonance spectra in systems containing light atoms (this is of particular importance for chemistry), as well as at rather high temperatures. The theory predicted also the possibility of anisotropy of the Mössbauer effect in single crystals [15], which is associated with different amplitudes of atomic vibrations along different crystal axes ($\overline{x^2} \neq \overline{y^2} \neq \overline{z^2}$). Indeed, such an anisotropy in single crystals was soon established [16–18].

It should be noted here that the width of a resonance line also gives a certain amount of information about the diffusion of atoms [19–20]. If the emitter and the absorber of our first example are chemically identical and their temperatures are the same, then maximum absorption occurs with the absorber at rest: $V = 0$. If the absorber temperature T_0 is now changed to T_1, the absorption maximum will shift by a certain value δ_T as shown in Fig. 3b. This temperature shift [21] defines the average kinetic energy of the atomic vibrations in the lattice, and hence their mean square velocity $\overline{V^2}$.

A parameter of paramount importance is the isomeric (chemical) shift of the resonance line (Fig. 3c) due to the difference of chemical state of atoms of the emitter and the absorber. This shift, which is caused by changes in the electrostatic interaction energy of electric charges of the nucleus and the electron shells, was first observed by *Kistner* and *Sunyar* [22] during experiments with various compounds of iron.

Isomeric shift is determined by a product of two magnitudes, one of nuclear origin (relative change of the nuclear charge radius due to nuclear excitation) and the other of extranuclear origin. It is the latter, *i.e.* the difference in squares of electron wave functions (in other words of electron densities) in the region of absorbing and emitting nuclei that is of special interest for chemists since it defines the structures of s-electron shells and the participation of s electrons in chemical bonds.

Interaction between the nuclear electric quadrupole moment (in the ground and/or excited states) with a non-uniform electric field results in quadrupole splitting of gamma-resonance spectrum lines (Fig. 3d) proportional to the product of the quadrupole moment Q and the electric field gradient q. Of these two values the first is nuclear; the second is a molecular value, which defines the properties of p- and d-electron shells. The possibility of describing separately the contribution from s, p, and d electrons to chemical bonds by means of correlating isomeric shifts and quadrupole splitting is an essential advantage of chemical gamma-resonance spectroscopy allowing, for instance, distinction to be made between the role of changes in ionicity and in the extent of hybridization of chemical bonds [22a].

Quadrupole splitting frequently turns out to be asymmetrical even for absolutely isotropic polycrystalline substances (as shown in Fig. 3e) [22b]. Such an integral asymmetry of two peaks with respect to their area was

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[22a] *V. I. Goldanskii, E. F. Makarov*, and *R. A. Stukan*, J. chem. Physics, in press.

[22b] The asymmetric quadrupole splitting observed in the Mössbauer spectra of polycrystalline substances is termed the Goldanskii effect.

observed for the first time in spectra of organotin compounds and thoroughly investigated and interpreted at the Institute of Chemical Physics in Moscow [23-25]. This asymmetry is a result of the Mössbauer effect anisotropy in respective crystallites ($\overline{x^2} \neq \overline{y^2} \neq \overline{z^2}$) and its observation opens up possibilities for investigating structural features of single crystals by experimenting with polycrystalline material (in a sense similar to plotting of X-ray debyegrams). Recently, the above mentioned cause of asymmetry of the quadrupole splitting was quantitatively studied and confirmed for single crystals and polycrystals of siderite ($FeCO_3$) [25a].

It is also worth mentioning that investigation of the "anisotropic" asymmetry of quadrupole splitting and its explanation has done away with confusing trivial hypotheses on the overlapping of spectra of various hypothetical admixtures or structural isomers.

A further variant of asymmetric quadrupole splitting is connected with interaction between the electric field and the magnetic field occurring at nuclei under the influence of unpaired electrons of the atomic shells [26]. This "paramagnetic" asymmetry is more intense the longer the time of paramagnetic relaxation, *i.e.* the slower the electron spin flipping. Therefore, unlike the "anisotropic" asymmetry of quadrupole splitting, the "paramagnetic" asymmetry weakens as the temperature increases.

The ordered or very slowly relaxing unpaired electrons of external shells cause polarization of the internal electrons thus cancelling full compensation of the magnetic effect of anti-parallel spins of two s electrons of the shell closest to the nucleus. As a result, enormous magnetic fields are set up inside the atom; these can be determined from magnetic (Zeeman) splitting of gamma-resonance spectrum lines (Fig. 3f).

A number of theoretical papers (cf., for example, [27]) are concerned with problems of the magnetic splitting of nuclear gamma-resonance lines, which can range from a single line to a well-resolved hyperfine structure. The spectrum is temperature dependent, the width of individual peaks being related to the time of paramagnetic relaxation and, of course, to the transition from paramagnetic to ferromagnetic or antiferromagnetic states.

The theory of coherent phenomena [28, 29], for example, of suppression of gamma-resonance absorption in an ordered nuclear setup, as compared to an individual nucleus or a random system, occupies a prominent place in papers on gamma resonance. As a result of this suppression, the lifetime of an excited nucleus in an ordered lattice may turn out to be longer than that in the free state, *i.e.* the width of the excited level will be less than the natural resonance width. Conversely, shorter lifetimes and more rapid disintegrations are also possible [28c]. The problems of coherent effects in emission and propagation of gamma-quanta, the wavelength of which is many thousand times less than that of visible light, are naturally of exceptional interest. There is little doubt that any future achievement in solving these problems will be closely connected with the Mössbauer effect.

A striking variety of experimental methods are currently in use in research on the structure of matter: optical spectroscopy, electron spin resonance, nuclear magnetic resonance, and quadrupole resonance, X-ray structural analysis, electron and neutron diffraction, and neutron scattering. Of course, none of these methods may be considered as a panacea for solution of all problems connected with crystalline or molecular structure. The nuclear gamma-resonance method presents no exception in this respect; despite its potentialities, a given problem can be solved only when it is used in conjunction with other methods.

The greatest limitation of gamma-resonance spectroscopy is that the Mössbauer effect can be observed only for a substance in the solid phase and not for all chemical elements (see Fig. 4). Because of the general increase in energies of the lower levels with decreasing nuclear mass, the recoil energy for light-element nuclei is so great that the Mössbauer effect becomes

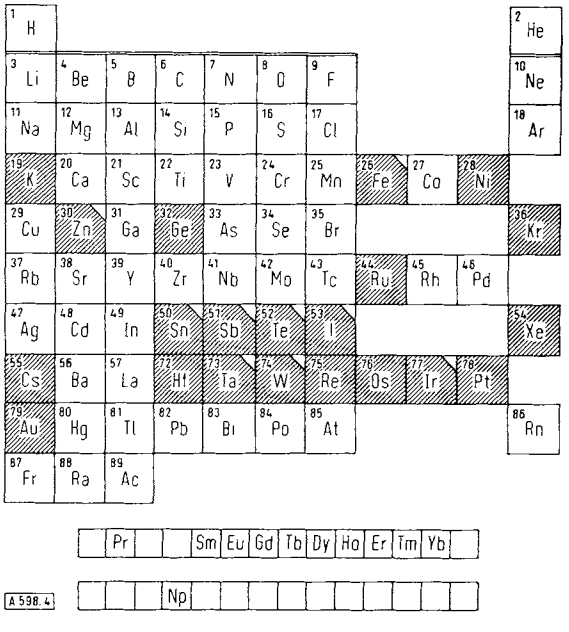


Fig. 4. Elements for which the Mössbauer effect has been observed (shaded squares).

A light top right-hand corner in a shaded square means that the effect has been detected even at room temperature. The effect is to be expected for almost all lanthanides and actinides; chemical symbols in respective squares show for which elements of these series the effect has already been observed. Silver is not shaded since its ratio Γ/E is very low ($\approx 10^{-22}$) and therefore the experiments with Doppler shift of gamma-quanta absorption have not been carried out.

[23] *V. I. Goldanskii, G. M. Gorodinskii, S. V. Karjagin, L. A. Korytko, E.F. Makarov, I.P. Suzdalev*, and *V.V. Chrapov*, Doklady Akad. Nauk SSSR *147*, 127 (1962).

[24] *V. I. Goldanskii, E. F. Makarov*, and *V. V. Chrapov*, Ž. eksper. teoret. Fiz. *44*, 752 (1963).

[25] *S. V. Karjagin*, Doklady Akad. Nauk SSSR *148*, 1102 (1963).

[25a] *I. A. Vinogradov, V. I. Goldanskii, E. F. Makarov*, and *I. P. Suzdalev*, Ž. eksper. teoret. Fiz., in press.

[26] *M. Blume*, Physic. Rev. Letters *14*, 96 (1963).

[27] *A. M. Afanas'ev* and *Yu. M. Kagan*, Ž. eksper. teoret. Fiz. *45*, 1660 (1963); *47*, 1108 (1964).

[28] *Yu. M. Kagan* and *A. M. Afanas'ev*, a) Ž. eksper. teoret. Fiz. *48*, 327 (1965); b) *50*, 271 (1966); c) Z. eksper. teoret. Fiz., Pis'ma v Redakciju *2*, 130 (1965).

[29] *M. I. Podgoretzkii* and *I. I. Rojzen*, Ž. eksper. teoret. Fiz. *39*, 1473 (1960).

vanishingly small. At present potassium is the lightest of the elements observed to give the Mössbauer effect.

Despite the absence of such common elements as carbon, nitrogen, oxygen, and silicon in the "Mössbauer list", the field of application of gamma-resonance is extremely wide since gamma-resonance nuclei are frequently introduced as observers to elucidate the properties of other systems. In the following sections, a selection of important and impressive examples illustrate the successful application of gamma-resonance spectroscopy in various fields of chemistry and biology.

III. Some Applications of Nuclear Gamma Resonance (NGR) in Solid-State Physics

Brjuchanov, *Deljagin*, and *Kagan*[30] introduced tin into vanadium and compared the temperature dependence of the gamma-resonance probability (Fig. 5a) with that estimated by means of the theory of impurity nucleus vibrations in the cubic lattice[13]. The spectrum of the host-lattice vibrations required for such a theory had been found independently in experiments with sub-thermal neutrons[30a,30b]. The perfect

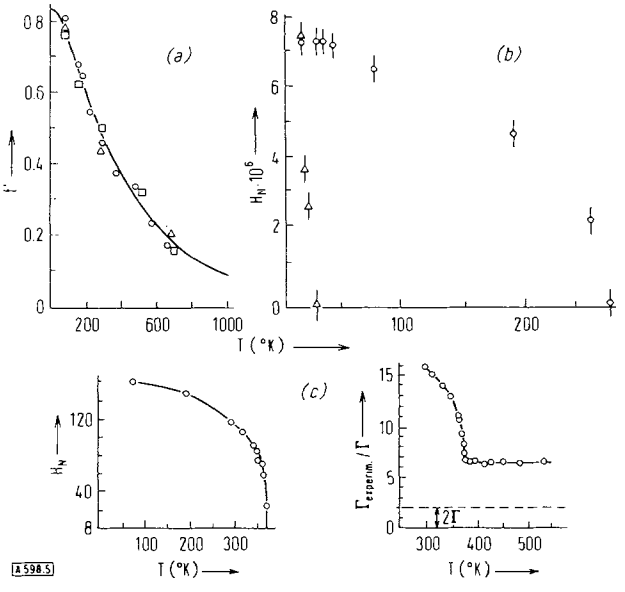


Fig. 5. Application of the Mössbauer effect in solid-state physics.
a) Temperature dependence of the effect probability $f'(T)$ for ^{119}Sn nuclei in vanadium;
b) temperature dependence of the magnitude of the local magnetic field on ^{161}Dy nuclei in gadolinium: $H_N(0) = 7.3$ MOe;
c) temperature dependence of the local magnetic field on ^{57}Fe nuclei (in kOe) and the width of the gamma-resonance spectrum line of ^{119}Sn in $FeSn_2$.

agreement between theory and experiment shows the broad potentialities of quantitative gamma-resonance spectroscopy of simple and complex crystal lattices.

Interaction of unpaired electrons of external shells with internal s electrons of the atom may lead, under certain conditions, to very strong local magnetic fields in the vicinity of the atomic nucleus. The magnitude of these fields is determined directly from the hyperfine structure of NGR spectra, since the magnetic moment of the absorbing nucleus (*i.e.* the nucleus in the ground state) is generally known from other experiments. Fig. 5b shows the temperature dependence of the field (recently obtained[31] at the Kurchatov Institute of atomic energy) for impurity nuclei of dysprosium (^{161}Dy) formed in the metallic gadolinium lattice by neutron capture and two subsequent beta-decay events. At a temperature of 5 °K the local magnetic field attains a value of 7.3 MOe. The nature of the diminution of the field with decreasing temperature indicates that two states of dysprosium occur (for the first the local field disappeared at about 20 °K, for the second – simultaneously with the disappearance of the ferromagnetism of gadolinium – at a Curie temperature of about +290 °K).

A clear correlation between a macroscopic magnetic property, such as the spontaneous magnetization of the sublattices of anti-ferromagnetic $FeSn_2$, and the local magnetic fields at nuclear sites was demonstrated at the same Institute[32]. In this work, the magnitudes of magnetic fields were determined both for iron and for tin (Fig. 5c); for iron directly from the line splitting, for tin from the width of the line with the unresolved hyperfine structure (this width decreases with diminishing local field at the nuclear sites).

Randomization of electron spins through their continuous fast flipping certainly leads to disappearance of the magnetic hyperfine structure of NGR spectra, since in this case the local field on the nucleus averaged over time becomes zero. The general theory of gamma resonance in systems with unpaired electrons, which allows for all these circumstances, has been verified for numerous examples. Only two obvious cases of alteration of the nature of NGR spectra in such systems will be given here.

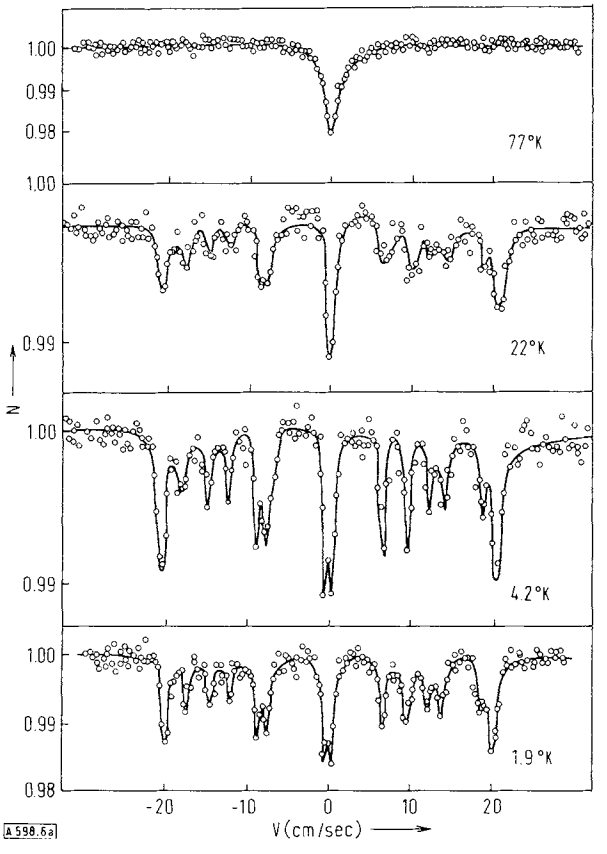


Fig. 6. Application of the Mössbauer effect in solid-state physics.
a) Gamma-resonance of ^{161}Dy in a Dy-Al garnet at different temperatures;

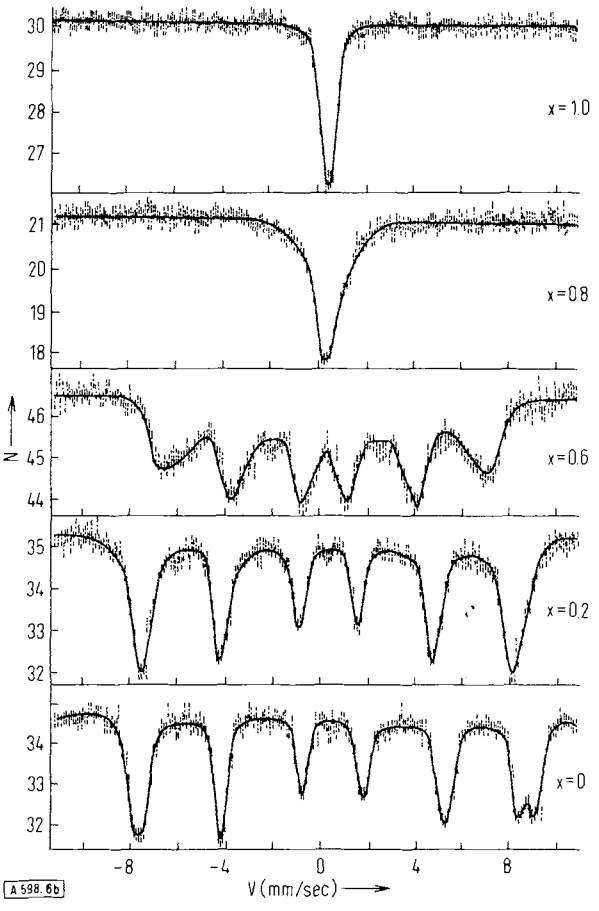
[30] *W. A. Brjuchanov*, *N. N. Deljagin*, and *Yu. M. Kagan*, Ž. eksper. teoret. Fiz. *45*, 1372 (1963).

[30a] *A.T. Stewart* and *B. N. Brockhouse*, Rev. mod. Physics *30*, 250 (1958).

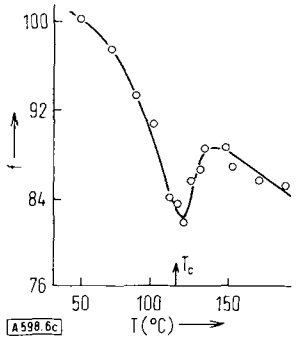
[30b] *N. A. Cernopljokov*, *M. G. Zemljanov*, and *A. G. Čičerin*, Ž. eksper. teoret. Fiz. *43*, 2080 (1962).

[31] *I. I. Lukaševič*, *V.V. Skljarevskii*, *B. N. Samojlov*, *E. P. Stepanov*, *K. P. Alesin*, and *N. I. Filippov*, Ž. eksper. teoret. Fiz., Pis'ma v Redakciju *3*, 81 (1966).

[32] *V. I. Nikolaev*, *Yu. I. Ščerbina*, and *S.S. Yakimov*, Ž. eksper. teoret. Fiz. *45*, 1372 (1963).



b) Gamma-resonance spectra of ^{57}Fe in a nickel-zinc-ferrite spinel for different degrees (x) of replacement of iron by zinc in the tetrahedral lattice (Zn_xFe_{1-x}) $[Ni_{1-x}Fe_{1+x}]O_4$. (Ordinate: number of counts in arbitrary units.);



c) Mössbauer effect probability diminishing as a result of increasing mobility of atoms in the ferrielectric lattice of $Pb_2[FeNb]O_2$ near the Curie temperature (114 °C).

Fig. 6a shows dysprosium (^{161}Dy) spectra [33] for a dysprosium-aluminum garnet, which is anti-ferromagnetic at a temperature below 2.49 °K, and becomes paramagnetic at a temperature above this point (the Néel point), Here, the transition to the paramagnetic state does not cause abrupt disappearance of the hyperfine structure. The latter disappears only gradually with diminishing electron-relaxation time, *i.e.* with more frequent flipping of spin with increasing temperature. Such an increase in flipping entails broadening of the hyperfine structure lines in accordance with the theory.

Fig. 6b shows spectra [34] of the ferrite spinels (Zn_xFe_{1-x}) $[Ni_{1-x}Fe_{1+x}]O_4$. Here, iron is incorporated in the tetrahedral sublattice (together with zinc) and in the octahedral sublattice (together with nickel). The interaction between these sublattices induces the occurrence of uncompensated antiferromagnetism (so-called ferrimagnctism). As iron is dislodged in the tetrahedral sublattice by the zinc ions, interaction between the sublattices weakens, and the ferromagnetic material is converted into a paramagnetic material with a very short spin-lattice relaxation time; the magnetic splitting of the spectrum line disappears.

It should be mentioned that the properties of ferrites are not only of theoretical interest but are also of practical interest since their magnetization is not accompanied by substantial loss of energy by eddy currents, even at ultra-high frequencies. Of similar dual interest is the application of the Mössbauer effect to the study of ferroelectrics, which display dielectric polarization even in the absence of an external electric field. The electrical properties of ferroelectrics are in many respects similar to ferromagnetic magnetization. In both cases there is a certain critical temperature (Curie temperature) above which thermal motion destroys the ordering of electrical and magnetic moments, and thus eliminates ferroelectric and ferromagnetic properties.

V. V. Skljarevskii et al. [35] observed a sharp increase in the mobility of atoms in a ferroelectric lattice at a temperature close to the temperature of transition from the ferroelectric state to the paraelectric state *i.e.* phase transition of the second kind. Indeed, Fig. 6c shows that an abrupt decrease in the probability of the Mössbauer effect on iron in the ferroelectric $Pb_2[FeNb]O_6$ was observed close to the Curie temperature (114 °C).

Observations of the Mössbauer effect led also to the discovery of new magnetic phenomena. For example, *Borg et al.* [36] as well as *Craig et al.* [37] found a magnetic ordering of electron spins in highly diluted solid solutions of iron (5 %) in gold (95 %). The conservation of the same magnetic hyperfine structures – the number of lines, their width and splitting values (Fig. 7a) – at an imposed external axial magnetic field of about 30 kOe, indicates that the variant of spin ordering effected in this alloy is antiferromagnetic. Thus, the so-called indirect or super-exchange interaction of unpaired electrons takes place here through the conduction electrons rather than through homopolar valence bonds as, for example in various magnetic oxides or ferrites.

Quantitative analysis of indirect interaction between 3d electrons of iron *via* 4s conduction electrons was carried out by another research group [38, 38a] in experiments with iron containing small amounts of aluminum. Fig. 7b shows the variations in the field strength at the iron nuclei according to the distance between the iron atoms and the closest admixed aluminum atoms.

The magnetic field is proportional to the electron-spin density at a ^{57}Fe nucleus. The electron spin density is made up of contributions of core s electrons and conduction s electrons. It was shown experimentally that in Fe–Al alloys the core contribution remains constant over a wide range of solute concentrations. It was concluded that the change in the field, as obtained with the help of a computer from the GR spectra of Fe at different concentrations of Al (see Fig. 7b), is caused by the changes in the spin densities of conduction electrons. Thus it was shown that the nearest-neighbor and second-neighbor Al atoms decrease the field on iron, *i.e.* the indirect exchange reaction between the localized 3d spins *via* the 4s conduction band is antiferromagnetic in these cases.

[33] *I. Nowik* and *H. H. Wickman*, Physic.Rev. *140*, A 869 (1965).

[34] *V. I. Goldanskii, V. F. Belov, M. N. Deviševa*, and *V.A.Truchtanov*, Ž. eksper. teoret. Fiz. *49*, 1681 (1965).

[35] *V. V. Skljarevskii, I. I. Lukaševič, V. N. Romanov, N. I. Filippov, Yu. N. Venevtzkev*, and *A. S. Viskov*, Ž. eksper. teoret. Fiz., Pis'ma v Redakciju *3*, 212 (1966).

[36] *R. J. Borg, R. Booth*, and *C. E. Violet*, Physic. Rev. Letters *11*, 463 (1963).

[37] *P. P. Craig* and *W. A. Steyer*, Physic. Rev. Letters *13*, 802 (1964).

[38] *M. B. Stearns* and *S. S. Wilson*, Physic. Rev. Letters *13*, 313 (1964).

[38a] *A. W. Overhauser* and *M. B. Stearns*, Physic. Rev. Letters *13*, 316 (1964).

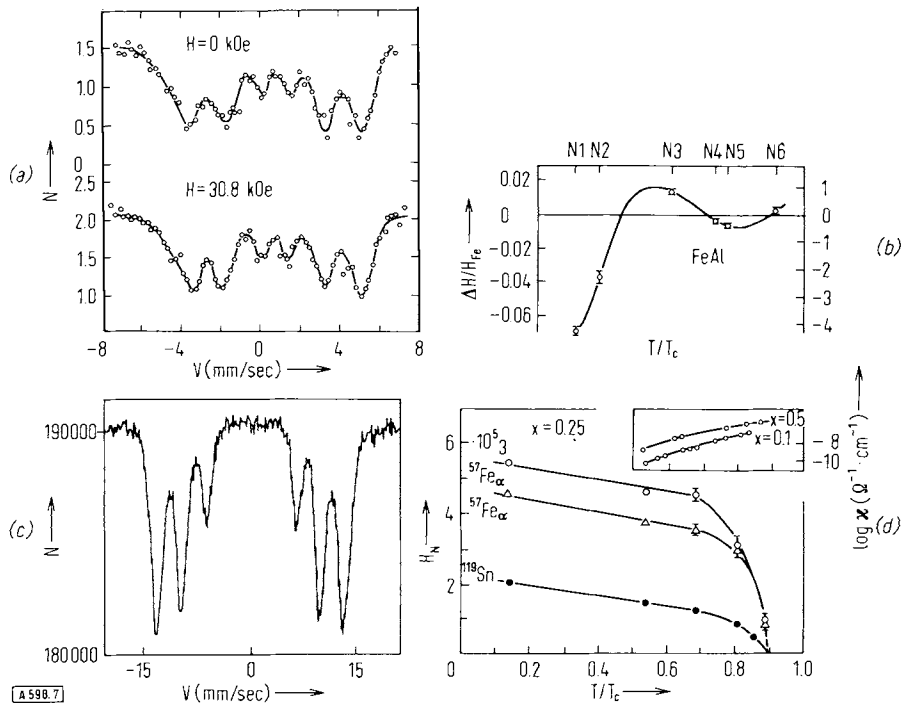


Fig. 7. Application of the Mössbauer effect in solid-state physics.

a) GR spectra of ^{57}Fe in iron-gold alloys ($Fe_{0.05}Au_{0.95}$) in the absence of and in the presence of an external axial magnetic field;

b) the local magnetic field at ^{57}Fe nuclei as a function of the average distance between iron atoms and their nearest-neighbor aluminum atoms (role of the indirect effect *via* conduction electrons);

c) the GR spectrum of ^{119}Sn in the yttric ferrite garnet $\{Y_{3-x}Ca_x\}$ $[Sn_xFe_{2-x}](Fe_3)O_{12}$;

d) temperature dependence of local magnetic field on iron nuclei in two sublattices and on tin nuclei, and of electroconductivity of the ferrite garnet (top right).

A still more peculiar example of indirect magnetic interaction is the super-exchange induction of the magnetic fields on nuclei of diamagnetic tin atoms introduced into yttric ferrite garnets $\{Y_{3-x}Ca_x\}$ $[Sn_xFe_{2-x}]$ $(Fe_3)O_{12}$, This effect was observed independently by *Goldanskii et al.*[39] and by *Belov et al.*[40] about three years ago. Fig. 7c shows the Mössbauer spectrum of the tin in this garnet. The spectrum parameters, the chemical shift (equal to the shift for SnO_2), quadrupole splitting (absent in this case, which means that all Sn bonds are equal), the effect probability and its temperature dependence (characteristic of tin with a coordination number of 6), warranted the conclusion that, in this yttric ferrite, tin is not directly bound with iron, but is connected with it through oxygen: Sn—O—Fe. Nevertheless, a considerable magnetic field – over 200 kOe at 77 °K – was observed at the nucleus of a diamagnetic tin atom as indicated by Zeeman splitting of the spectrum line into six components; at the Curie point it disappeared, as did the field on the iron nuclei (see Fig. 7c). Later measurements[39a] showed that the sign of the local magnetic field at the tin nucleus (similarly to that at the iron nuclei in the same octahedral sublattice) coincides with the sign of the imposed external magnetic field. Rather low values are obtained for the electrical conductivity of ferrite: 10^{-10} to 10^{-8} ohm^{-1} cm^{-1} (upper right-hand corner of Fig. 7d). The conductivity increases with decreasing field.

Thus, it was ascertained that the unpaired electron of iron polarizes the internal s electrons of tin at the expense of super-exchange interaction through two chemical bonds Fe—O and O—Sn. In other words, delocalization of the unpaired electron of iron was observed in an inorganic system having only σ bonds and it was found that this delocalization manifests itself by the polarizing exchange interaction between the unpaired electron and internal s shells.

IV. Examples of the Application of Gamma-Resonance Spectroscopy in Chemistry

Work on the development and the application of gamma-resonance spectroscopy in chemistry began in our laboratory some seven years ago. The results obtained in our first experiments, which were carried out mainly with organotin compounds, provided general substantiation of the applicability of gamma-resonance spectroscopy to the elucidation of chemical problems. For instance, the Mössbauer effect was observed in polymers and amorphous materials. It appeared that, due to optical branches of vibrational spectra, recoilless gamma-resonance was best displayed in systems consisting mostly of light atoms, *e.g.* H, C, N, O. Further, it was shown that it is possible to investigate the influence of chemical bonds in the immediate neighborhood of, and more distant from, the "Mössbauer atom". Finally, the asymmetric doublet structure in a quadrupole splitting for a polycrystalline specimen was investigated and interpreted.

Some applications of gamma-resonance spectroscopy in structural chemistry are illustrated by Fig. 8 and 9. The marked difference of the SnF_4 spectrum from the spectra of other tin halides (Fig. 8) and the study of data on chemical shift, quadrupole splitting, and the Mössbauer effect probability led to the conclusion that the SnF_4 structure is octahedral, that here the coordination number of tin is 6, and that the coplanar bonds

[39] *V. I. Goldanskii, V. A. Truchtanov, M. N. Deviševa,* and *V. F. Belov,* Ž. eksper. teoret. Fiz., Pis'ma v Redakciju *1,* 31 (1965); Physics Letters *15,* 317 (1965).

[39a] *V. I. Goldanskii, M. N. Devisheva, E. F. Makarov, G. V. Novikov,* and *V. A. Truchtanov,* Ž. eksper. teoret. Fiz., Pis'ma v Redakciju *4,* 63 (1966).

[40] *K. P. Belov* and *I. S. Lyubutin,* Ž. eksper. teoret. Fiz., Pis'ma v Redakciju *1,* 26 (1965).

between the tin and the four fluorine bridge atoms, which are responsible for formation of the inorganic polymer, are different from the bonds with the other two fluorine atoms. It is of interest that all six Sn–F bonds in salts of the K_2SnF_6 type become equivalent, and quadrupole splitting of the lines vanishes [41]. Tin coordination numbers of 5 and 6 were found from Mössbauer spectra for many organotin compounds.

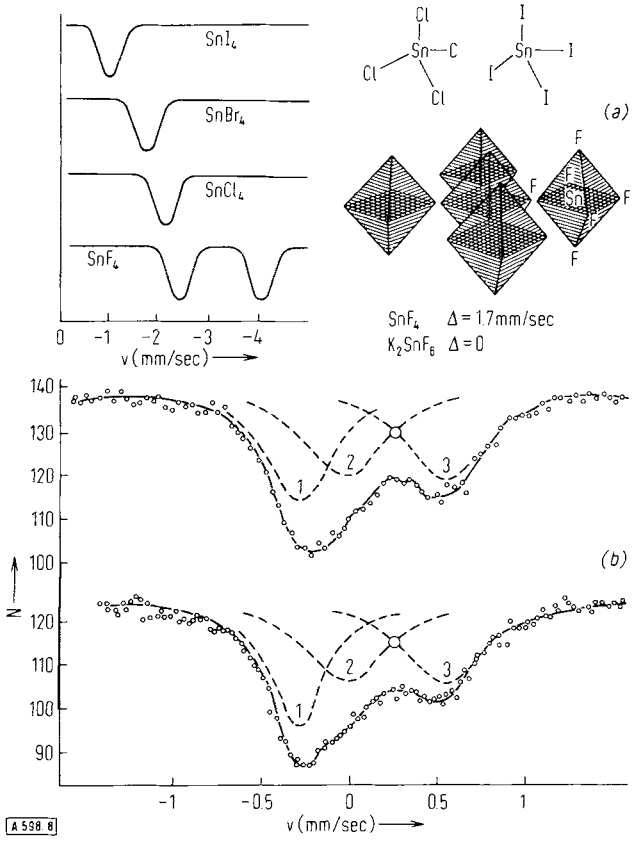


Fig. 8. Chemical gamma-resonance spectroscopy.

a) GR spectra of tin halides and their structures;

b) GR spectra of Prussian blue Fe(III) + $[Fe(CN)_6]^{4\ominus}$ (above) and Turnbull's blue Fe(II) + $[Fe(CN)_6]^{3\ominus}$ (below);
1: singlet $[Fe(CN)_6]^{3\ominus}$; 2,3: doublet Fe(III).

The structure of both Prussian blue and Turnbull blue is $[Fe(III)]_x\ [Fe(II)\ (CN)_6]_y$.

The spectra of two well-known iron complexes, *i.e.* Prussian blue and Turnbull blue, are shown in Fig. 8. It has been shown in a number of laboratories [5, 42–45] that the spectra of these two compounds are identical. As a rule (for an exception, see [45]) these spectra were regarded as superpositions of the $Fe^{3\oplus}$-doublet and the single line of the complex hexacyanoferrate(II) anion $[Fe(CN)_6]^{4\ominus}$. Thus, both Prussian blue and Turnbull blue turned out to be the same compound, and it is now considered that in these compounds the iron inside the complex occurs in the form of Fe(II), and in the external coordination sphere in the form of Fe(III).

The nuclear gamma-resonance spectra of xenon (^{129}Xe and ^{131}Xe) made it possible to ascertain the electronic structures of XeF_2 and XeF_4 [46–48] (see Fig. 9a). Quadrupole splittings that are identical in magnitude (but with opposite signs) must correspond to these two structures. Moreover, by using the radioactive iodine compound $K^{129}ICl_4$ as emitter of resonance gamma-quanta it was shown that a chlorine xenon compound $XeCl_4$, which was previously unknown, is formed in the process of β-decay of iodine (to ^{129}Xe); it was identified by its gamma-resonance spectrum (see Fig. 9b). In a similar way, β-decay of $K^{129}IO_3$ and $K^{129}IO_4$ gives rise to the formation of xenon oxides, XeO_3 and XeO_4.

The elucidation of the structure of iron dodecacarbonyl $Fe_3(CO)_{12}$ also serves as characteristic example

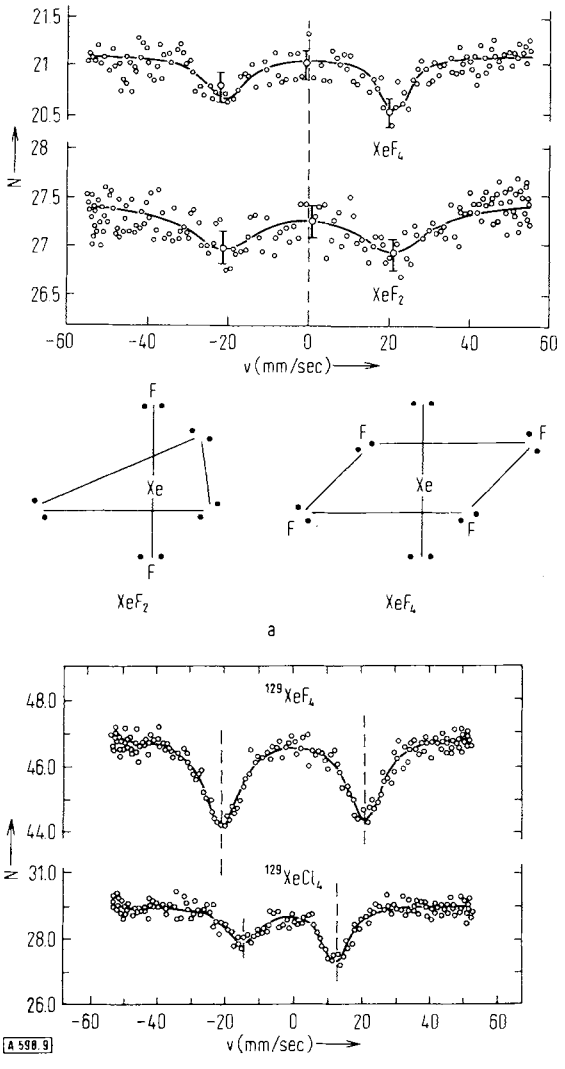


Fig. 9. Chemical gamma-resonance spectroscopy.

a) GR spectra of XeF_2 and XeF_4 and their structures:

b) GR spectra of XeF_4 and $XeCl_4$ obtained on beta-decay of $K^{129}ICl_4$.

[41] *V. I. Goldanskii, E. F. Makarov, R. A. Stukan, T. N. Sumarokova, V. A. Truchtanov,* and *V. V. Chrapov,* Doklady Akad. Nauk SSSR *156,* 400 (1964).

[42] *L. M. Epstein,* J. chem. Physics *36,* 2731 (1962).

[43] *J. F. Duncan* and *P. W. R. Wigley,* J. chem. Soc. (London) *1963,* 1120.

[44] *W. Kerler, W. Neuwirth, E. Fluck, P. Kuhn,* and *B. Zimmermann,* Z. Physik *173,* 321 (1963).

[45] *K. Otto* and *A. Ito,* Rev. mod. Physics *36,* 459 (1964).

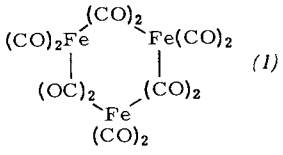
[46] *C. L. Chernick, C. E. Johnson, Y. G. Malon, G. Y. Perlow,* and *M. R. Perlow,* Physics Letters *5,* 103 (1963).

[47] *G. J. Perlow* and *M. R. Perlow,* Rev. mod. Physics *36,* 353 (1964).

[48] *G. J. Perlow* and *M. R. Perlow,* J. chem. Physics *41,* 1157 (1964).

of the fruitful application of nuclear gamma-resonance in structural chemistry.

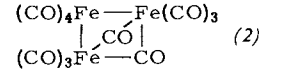
Three variants of the structure of iron dodecacarbonyl have been discussed previously in various papers (see, *e.g.*, the references [8, 9, 11]): the linear structures $(CO)_4Fe(CO)_2Fe(CO)_2Fe(CO)_4$ and $(CO)_3Fe(CO)_3Fe(CO)_3Fe(CO)_3$ designated as 4.2.2.4 and 3.3.3.3, and the cyclic one



(1)

all three having bridge bonds between the iron atoms *via* carbonyl groups.

X-ray structural analysis [49] resulted in selection of the cyclic structure *(1)*. However, all three iron atoms would be equivalent in this structure, whereas observations of the Mössbauer effect had shown a complex gamma-resonance spectrum of iron, shaped as a trident formed by superposition of the singlet and the quadrupole-split doublet. This spectrum rules out the above cyclic structure, and of the two linear variants it is more consistent with that of 3.3.3.3. However, this structure could not be allotted since it contradicted X-ray analysis indications. On the basis of a repeated X-ray analysis [50] the cyclic structure *(1)* was corrected – the structure of iron dodecacarbonyl is now assumed to be *(2)*.



(2)

Naturally, there are many cases in which a full interpretation of results requires complicated calculations, as for example in the use of the molecular orbital method. In this connection one might mention the various explanations of differences in ferrocene and ferricinium spectra [4, 51].

The application of gamma-resonance spectroscopy in chemical kinetics and physical chemistry of surface phenomena is illustrated by a number of examples in Figures 10 and 11. Curves describing the kinetics of oxidation of solid dibutyltin in air with formation of dibutyltin oxide [52] are shown in Fig. 10a; these curves were obtained by observation of variations in the intensity of nuclear gamma-resonance (NGR) spectra of initial compounds and reaction products as a function of time. The example that is of more common interest is that in which the tin atoms serve as observers in the characterization of the properties of dipolar aprotic solvents [53]. Dimethyl formamide and tetrahydrofuran are widely used as solvents in organic chemistry, and strongly affect the kinetics of nucleophilic heterolytic reactions. It appears that the quantitative aspect of the solvent properties may be defined from the increase in quadrupole splitting of the NGR spectra of solutions of polar compounds, such as dibutyltin dichloride (cf. Fig. 10b).

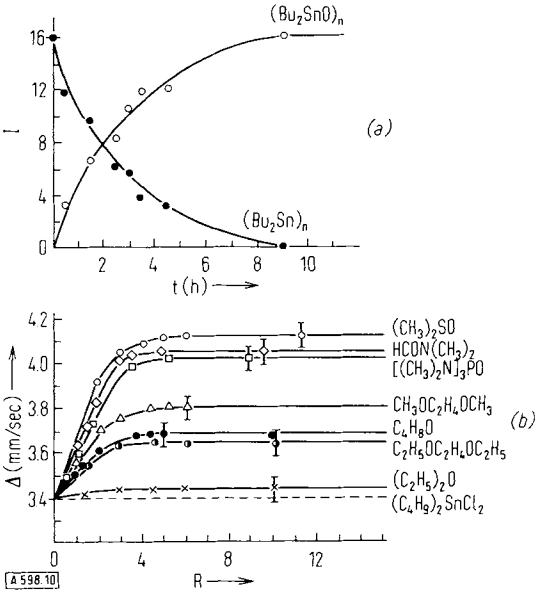


Fig. 10. Chemical gamma-resonance spectroscopy.

(a) Curves depicting kinetics of the decrease in the dibutyltin $(Bu_2Sn)_n$ content and increase in its oxidation product $(Bu_2SnO)_n$: obtained by analysis of GR spectra of tin (ordinate: intensity of Mössbauer effect in arbitrary units).

(b) Increasing quadrupole splitting of the GR-spectrum line of tin in dibutyltin dichloride, the latter dissolved in various dipolar aprotic solvents (abscissa: molar ratio of solvent to $(C_4H_9)_2SnCl_2$).

Indeed, both the increase in quadrupole splitting and the kinetic effects [53a, 53b] are of the same origin; they are caused by strong reactions of the solvents with the cationoid, but not with the anionoid parts of molecules. In contrast to the strongly solvated cations, the weakly solvated anions appear to be extremely reactive [53c, 53d].

Gamma-resonance spectra supply information both on the chemical state (chemical shifts, quadrupole splitting) and on the dynamics of surface atoms (asymmetry of quadrupole splitting). For example, the spectra of tin on a silicagel [54] surface shows two oxide forms – SnO and SnO_2. (The silica gel surface was prepared in the following way: (i) Ion exchange between $CaCl_2$ and the $H^{\oplus}$ ions of the silica gel OH groups, (ii) ion exchange between $SnCl_2$ and $Ca^{2\oplus}$.) On the basis of the stronger temperature dependence of the Mössbauer effect probability f' for the adsorbate SnO_2 (Fig. 11a), it may be inferred that the oxide SnO is chemisorbed while the dioxide SnO_2 is attached to the surface by van der Waals forces only. Root mean

[49] *L. Dahl* and *P. Rundle*, J. chem. Physics *26*, 1751 (1957).

[50] *L. Dahl* and *J. Blount*, Inorg. Chem. *4*, 1373 (1965).

[51] *U. Zahn, P. Kienle*, and *H. Eicher*, Z. Physik *166*, 220 (1962).

[52] *V. I. Goldanskii, V.Ya. Ročev*, and *V.V. Chrapov*, Doklady Akad. Nauk SSSR *156*, 909 (1964).

[53] *V. I. Goldanskii, O.Yu. Ochlobystin, V.Ya. Rochev*, and *V.V. Chrapov*, J. organometallic Chem. *4*, 160 (1965).

[53a] *L. I. Zacharkin, O.Yu. Ochlobystin*, and *K. A. Toilevic*, Izvest. Akad. Nauk SSSR, Ser. Chim. *7*, 1347 (1964).

[53b] *L. I. Zacharkin*, and *O.Yu. Ochlobystin*, J. organometallic Chem. *3*, 257 (1965).

[53c] *A. J. Parker*, Quart. Rev. *16*, 163 (1962).

[53d] *O.Yu. Ochlobystin*, Uspechi Chim. *36*, 34 (1967).

[54] *I. P. Suzdalev, V. I. Goldanskii, E. F. Makarov, A. S. Plačinda*, and *L. A. Korytko*, Ž. eksper. teoret. Fiz. *49*, 1424 (1965).

square amplitudes of thermal vibrations along the surface (0.07 Å) and normal to it (0.13 Å) were established from the quadrupole splitting asymmetry of SnO. In the case of SnO_2 it is possible to distinguish two factors of the Mössbauer effect probability, namely the role of atomic vibrations inside the molecule and that of molecular vibrations on the surface of the silica gel.

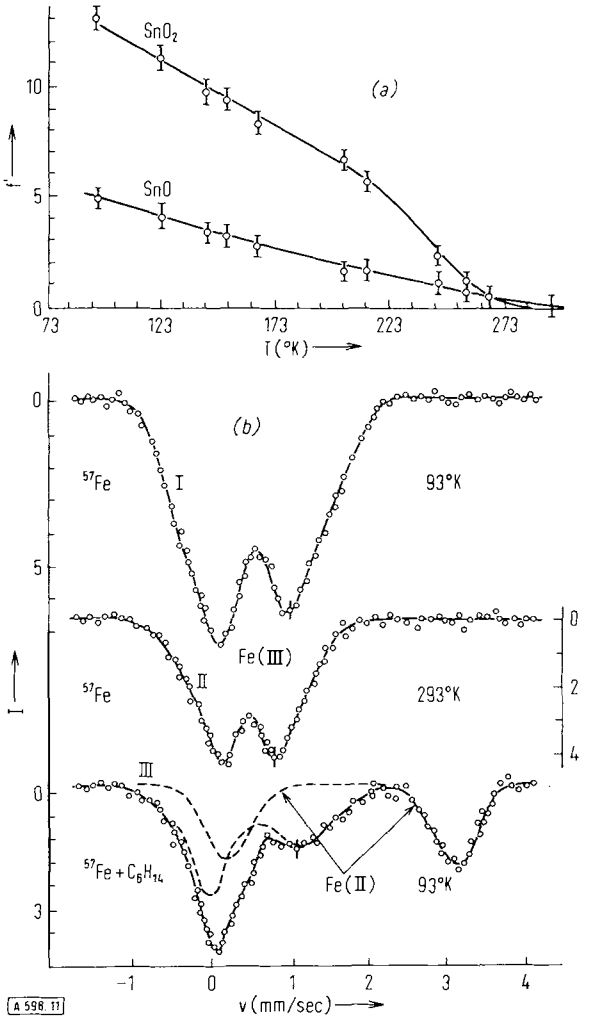


Fig. 11. Chemical gamma-resonance spectroscopy.

(a): Temperature dependence of the Mössbauer effect probability f' for two oxidized forms of tin (SnO and SnO_2) on the surface of silicagel;

(b): GR spectra of iron in mordenite before adsorption (I and II; at 93 °K and 293 °K) and after adsorption of hexane (III; 93 °K).

The gamma-resonance spectra of synthetic zeolites have also been obtained[55]. At present, zeolites attract general attention as efficient separating and drying agents for mixtures. For the investigation of the structures and the adsorption properties of faujasite (Y) and mordenite (M), the sodium in these compounds was replaced by iron, which was highly enriched in ^{57}Fe. The basic structural unit of these zeolites is an octahedron consisting of silicon-oxygen and aluminum-oxygen tetrahedrons. The octahedrons are connected with one another *via* oxygen bridges forming the channels which form the internal surface of zeolites. The spectra given in Fig. 11b confirmed the suggestion[56] that two types of adsorption centers exist, localized and non-localized. It was found that only Fe(III) ions had been localized before adsorption, while localization of Fe(II) was induced only by filling of zeolite channels with various adsorbed compounds (for example, hexane). Accordingly, a doublet in the gamma-resonance spectrum of trivalent iron was observed before adsorption whilst after adsorption another doublet arising from Fe(II) with much larger quadrupole splitting appeared.

Spectroscopy has proved to be of immense value in the elucidation of problems in polymer science.

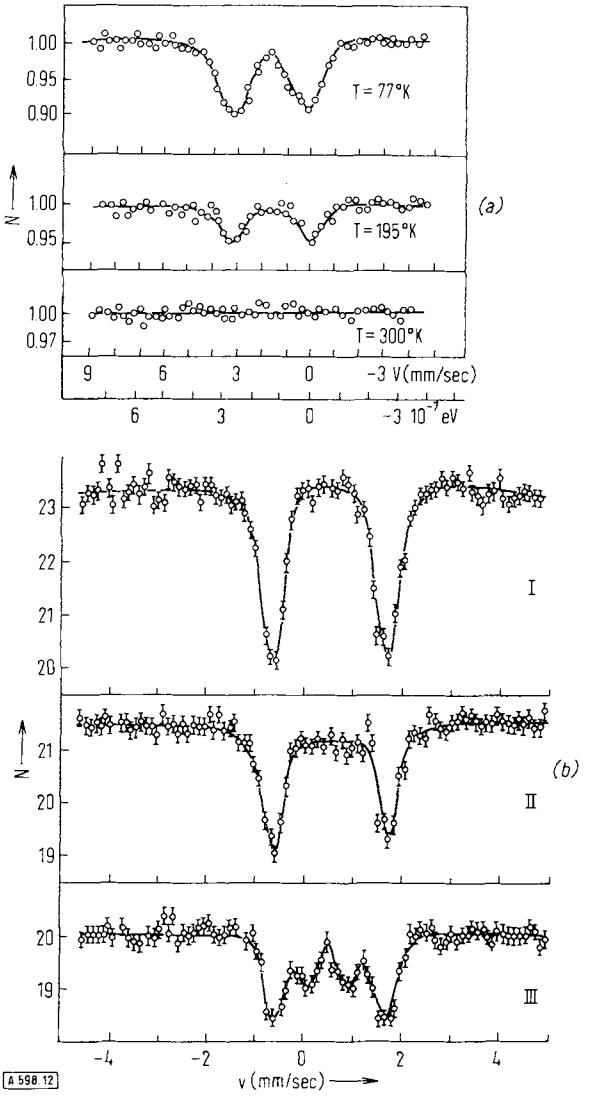


Fig. 12. Chemical gamma-resonance spectroscopy.

(a): The first NGR-spectrum of a polymer (polymethylmethacrylate with triethyl tin introduced into side groups).

(b): The GR spectrum of ferrocene (I), of soluble (II), and of insoluble (III) polyferrocenes.

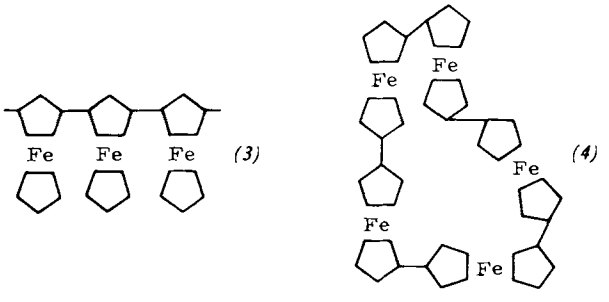
Fig. 12a shows the spectrum of tin in polymethyl methacrylate, in which a number of methyl groups are replaced by triethyltin. This represents an example of one of the first Mössbauer spectra of polymers to be obtained[57]. A comparison was made of the spec-

[55] *V. I. Goldanskii, I. P. Suzdalev, A, S. Plačinda,* and *L. G. Štyrkov,* Doklady Akad. Nauk SSSR *169,* 827 (1966).

[56] *M. M. Dubinin,* Doklady Akad. Nauk SSSR *159,* 166 (1964).

[57] *V. A. Bryuchanov, V. I. Goldanskii, N. N. Delyagin, E. F. Makarov,* and *V. S. Špinel,* Ž. eksper. teoret. Fiz. *42,* 637 (1962).

tra[58] of soluble polyferrocenes and insoluble polyferrocenes, *i.e.* of linear polymers *(3)* whose chains involve only one of the two cyclopentadienyl rings bonded to each iron atom, and polymers in which both cyclopentadienyl rings are involved in a continuous three-dimensional network. The spectrum of such an insoluble polymer *(4)* (Fig. 12b) consists of two doublets; the cross-linked regions exhibit a weaker quadrupole splitting and a relatively high Mössbauer effect probability. At room temperature, gamma-resonance is observed only for these cross-linked regions. The spectra may therefore be used to determine directly the extent of cross-linking in polyferrocene, and moreover provide information about the removal of electrons to the conduction levels of the cross-linked regions – such knowledge is important in the description of the properties of organic semiconductors.



Very curious results were obtained in the study of radiation damage in polyethylene, to which stabilizers, such as dibutyltin dimaleate, had been added. The strong, Co-γ-radiation-induced change of the chemical shift in the NGR spectra of tin in this compound (Fig. 13a) shows the detachment of two butyl radicals, tetravalent tin being converted to the divalent species. Obviously it is this reaction that is responsible for the effect of organotin stabilizers as inhibitors of oxidative aging of polymers[59].

A number of papers on kinetics of chemical conversions (*e.g.* solid-phase polymerization[60]) contain reports of sudden accelerations of reactions in the vicinity of a melting point or other phase transitions in the solid state. Such accelerations are assumed to be connected with an increase in the mobility of atoms in a solid under these conditions. In this connection, great interest attaches to the temperature dependence of the Mössbauer effect probability for different iron salts in ice[61]. It may be seen from Fig. 13, that within a certain temperature range close to −90 °C, the recoil-less nuclear-gamma resonance of iron atoms in $Fe(ClO_4)_2$ and $FeCl_2$ simply disappears, which is a direct indication of the sharp increase in mobility of the iron atoms in ice near the point of its phase transition.

This result is similar to that obtained later in the study of ferroelectrics for a second-order phase transition (cf. Section III).

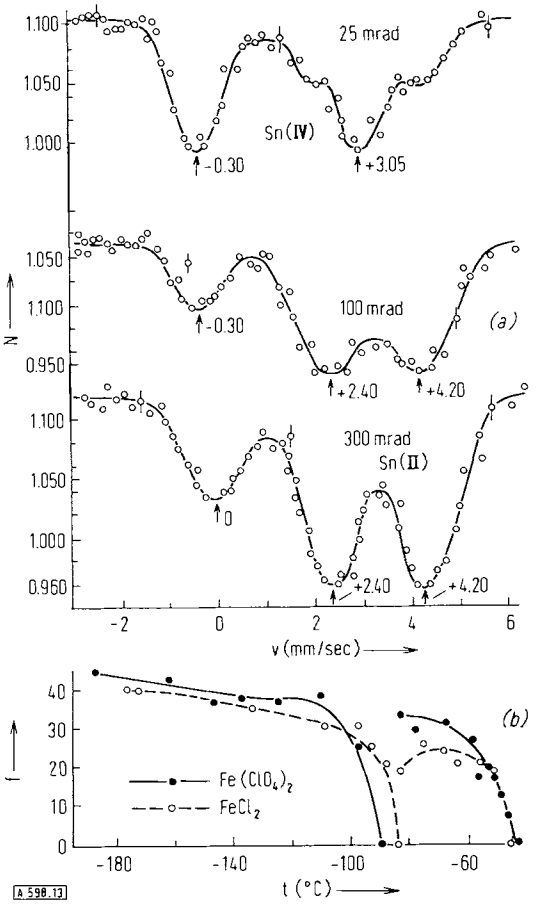


Fig. 13. Chemical gamma-resonance spectroscopy.

(a): GR spectra of dibutyltin dimaleate in polyethylene before and after irradiation by a ^{60}Co gamma source. Decomposition follows the scheme: $(C_4H_9)_2Sn(CO_2CH)_2 \rightarrow 2\ C_4H_9 + Sn(CO_2CH)_2$.

(b): Temperature dependence of the Mössbauer effect probability f' for iron in frozen aqueous solutions of $Fe(ClO_4)_2$ and $FeCl_2$ within the range of −196 °C to −40 °C (the phase transition point for ice is close to −90 °C).

V. Nuclear Gamma-Resonance as a Method of Chemical Analysis

First of all let us consider a specialized but highly promising application of the Mössbauer effect in trace analysis[62,63]. Since gamma resonance is observed only for certain isotopes of certain elements (for example, ^{57}Fe), a new technique suggests itself for the study of the kinetics and mechanism of complicated reactions, and the structures of many chemical compounds. To this end it is necessary to study the dependence of the nuclear gamma-resonance spectrum upon the chemical state of the Mössbauer isotope in the system.

Even the first attempts to combine the Mössbauer effect with the tracer technique disclosed electron exchange between Fe(II) and Fe(III) ions in solid salts at

[58] *V. F. Belov, T. P. Višnyakova, V. I. Goldanskii, E. F. Makarov, Ya. M. Pauskin, T. A. Sokolinskaya, R. A. Stukan*, and *V. A. Truchtanov*, Doklady Akad. Nauk SSSR *159*, 831 (1964).

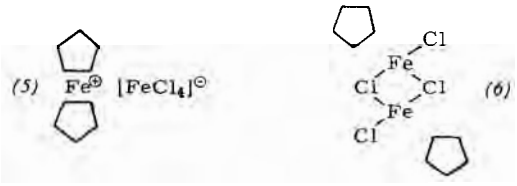
[59] *A. Yu. Aleksandrov, S. M. Berlyant, V. L. Karpov, S. S. Leščenko, O. Yu. Ochlobystin, E. E. Finkel*, and *V. S. Špinel*, Vysokomolekuljarnye Soedineniya *6*, 2105 (1964).

[60] *V. A. Kargin* and *V. A. Kabanov*, Ž. vses. chim. Obšč. im. D. I. Mendeleeva *9*, 602 (1964).

[61] *I. Dezci, L. Keszthelyi, B. Molnar*, and *L. Poes*, Physics Letters *18*, 28 (1965).

[62] *R. A. Stukan, V. I. Goldanskii*, and *E. F. Makarov*, Doklady Akad. Nauk SSSR *165*, 1347 (1965).

[63] *R. A. Stukan* and *L. P. Yur'eva*, Doklady Akad. Nauk SSSR *167*, 1311 (1966).



78 °K [62]. Assignment of the first of the two possible structures *(5)* and *(6)* to ferricinium ferrichloride thus became possible [63].

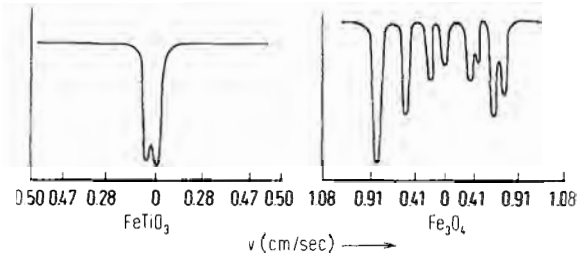


Fig. 14. Analytic applications of gamma-resonance spectroscopy. GR spectra of two iron minerals – ilmenite $FeTiO_3$ and magnetite Fe_3O_4.

Figure 14 shows the Mössbauer spectra of two minerals – ilmenite ($FeTiO_3$) and magnetite – at room temperature [64]. Magnetic splitting of the resonance line is observed for magnetite but not for ilmenite. Thus, it is possible to distinguish between the two minerals solely on the basis of the scattering of gamma-quanta by their surfaces. A given ore can be rapidly classified as iron (Fe:Ti > 10) or titanium (Fe:Ti < 10) ore, by determining the ilmenite-magnetite ratio in this way.

There are indications in scientific literature [65,65a] that the Mössbauer effect has been proposed for use in distant analysis (from a spacecraft) of the mineral composition of the surfaces of the moon and of Mars.

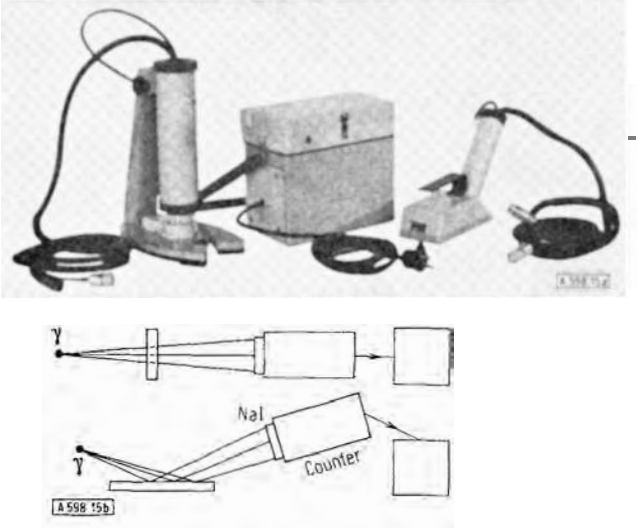


Fig. 15. (a): MAK-1 gamma-resonance tin detectors operating for absorption (left) and scattering (right).

(b): Arrangement of detector for absorption (top) and for scattering (bottom).

[64] *V. I. Goldanskii, B. G. Egiazarov, V. M. Zaporožetz, Yu. M. Ostanevič*, and *I. D. Čuprova*, Priklad. Geofizika *44*, 202 (1965).

[65] *P. J. Klass*, Aviation Week and Space Technology *9*, 89 (1963).

[65a] Angew. Chem. *77*, 263, 265 (1965); Angew. Chem. internat. Edit. *4*, 248 (1965).

Since 1962 Soviet scientists have been working on various designs of gamma-resonance devices for determining the tin content (in the form of cassiterite (SnO_2)) of ores and minerals. From 1963 to 1965 these devices were tested under field conditions for different tin deposits, and in the summer of 1965 our device (MAK-1) was accepted for serial manufacturing. Figure 15 shows the principles of its operation both for absorption and for scattering of gamma-quanta by the objects tested. A picture of the MAK-1 portable gamma-resonance tin detector weighing about 3.5 kg is also shown in Figure 15.

Instead of delivering the ore to the laboratory for chemical investigation, it is sufficient to determine whether or not the counting rate for gamma-quanta changes with a slight movement of the resonance source. In a few minutes the tin content is known as accurately as can be determined by chemical analysis. Geologists and economists claim that every such instrument saves over 7000 roubles a year.

VI. Some Applications of Gamma-Resonance Spectroscopy in Biology

Application of the Mössbauer effect in biology [66, 66a] is favored at present mainly because iron – one of the principal elements showing this effect – is a component of hemoglobin and a number of ferments (see *e.g.* [71]). Moreover, it is present in all native nucleic acids, in which it evidently plays an essential, though not yet established, biological role.

The tobacco mosaic virus contains merely 0.01 wt.-% iron. However, removal of this very small amount of iron deprives the virus of its infectious properties and causes decomposition of the RNA molecule into smaller subunits, as has been shown by sedimentation measurements. Reintroduction of iron regenerates the RNA and the infectious nature of the virus is reestablished [67]. Before elucidating the role of iron in this system, it was necessary to ascertain the nature of its bonding in nucleic acids. By comparison of the spectrum of $FeCl_3$ and those of its complexes with nitrogeneous bases such as guanine and guanosine, with sugars such as ribose and deoxyribose and finally, with nucleic acids such as RNA and DNA, (Fig. 16a) it was demonstrated [68, 69] that incorporation of iron into RNA and DNA takes place *via* formation of coordinate bonds between Fe(III) ions and sugars. The latter act as electron donors in RNA and reduce the iron to Fe(II); in DNA they do not display donor properties. It is quite possible that these data might help to explain the essential difference in the biological roles of DNA and RNA.

[66] *U. Gonser* and *R. W. Grant*: Mössbauer Effect Methodology. Plenum Press, New York 1965, p. 21.

[66a] *A. J. Bearden, T. H. Moss, W. S. Caughey*, and *C. A. Beaudreau*, Proc. nat. Acad. Sci. USA *53*, 1246 (1965).

[67] *H. S. Loring, Y. Fujimoto*, and *L. F. Eng*, Proc. nat. Acad. Sci. USA *45*, 287 (1959).

[68] *R. A. Stukan, A. N. Il'ina, Yu. Š. Moškovskii*, and *V. I. Goldanskii*, Biofizika *10*, 343 (1965).

[69] *Yu. S. Moškovskii, A. N. Il'ina, R. A. Stukan*, and *V. I. Goldanskii*, Biofizika *11*, 524 (1966).

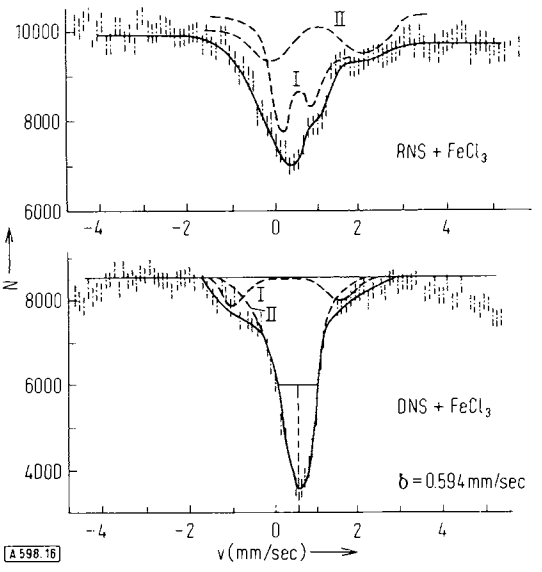


Fig. 16. Gamma-resonance spectroscopy in biology.

GR spectra of iron bound to RNA and to DNA. In case of RNA the complexity of the spectrum is caused by the two valence states of iron: (I) $Fe^{3\oplus}$ coordinated with ribose and (II) $Fe^{2\oplus}$ coordinated with ribose; in the case of DNA the spectrum represents superposition of the singlet due to $Fe^{3\oplus}$ coordinated with deoxyribose and that due to $Fe^{3\oplus}$ coordinated with bases.

A gamma-resonance spectrum[70] has recently been obtained of a living object, the hydrogeneous bacteria *Hydrogenomonas Z-1* grown in a ferric chloride medium that had been enriched in ^{57}Fe. This spectrum exhibits components due to both major iron valence states, *i.e.* Fe(II) and Fe(III) are apparently present in the cytochrome system of these bacteria. A change in the valence state of iron during the fixation of nitrogen by azobacteria has recently been observed and investigated[71].

Interesting research in biomechanics has been conducted by *Hillman et al.*[72]: A miniature ^{57}Co source (^{57}Fe served as absorber) was attached to the ear tympanum and the latter made to vibrated under the influence of acoustic oscillations. Since the oscillation frequency (10^3–10^4 sec^{-1}) was preset, and the tympanum velocity (of the order of 10^{-4} cm/sec) could be determined by the Doppler shift of the absorption maximum in the gamma-resonance spectrum, it was possible to ascertain the amplitude of oscillation of several Ångström at an accuracy of 1–2 Å. There are a number of analogous applications of the Mössbauer effect in engineering where one wishes to measure and control *e.g.* speeds, shifts, and accelerations. Pressure measurements can be based on the dependence of both chemical shifts and of Mössbauer effect probability on compression of matter; changes in component population of the hyperfine structures of gamma-resonance spectra, namely when the magnitude of kT becomes commensurable with the difference in energies of individual HFS lines ($kT \lesssim 10^{-5}$ eV, *i.e.* $T \lesssim 0.1\,^{\circ}K$), allow precise measurement of very low temperatures.

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German version: Angew. Chem. 79, 844 (1967)

[70] *Yu. Š. Moškovskii, E. F. Makarov, G. A. Zavarzin, I.Ya. Vedenina, S. S. Mardanyan,* and *V. I. Goldanskii,* Biofizika *11*, 357 (1966).

[71] *Yu. S. Moškovskii, I. D. Ivanov, R. A. Stukan, G. I. Matchanov, S. S. Mardanyan, Yu. M. Belov,* and *V. I. Goldanskii,* Doklady Akad. Nauk SSSR *174*, 215 (1967).

[72] *P. Hillman, H. Schechter,* and *M. Rubinstein,* Rev. mod. Physics *36*, 360 (1964).

Physical Causes of Aging in Plastics

BY H. A. STUART [*]

A number of physical changes that take place in a polymer below the glass transition temperature without the action of a medium are first described, and are then explained on the basis of changes in supramolecular order. Pure stress crazing with the characteristic self-limitation of craze growth is then considered. Models are developed to explain stress crazing under the influence of a wetting medium. Attempts to reduce stress crazing are then treated and the article closes with a discussion of the influence of morphological structure on crazing and cracking.

I. Introduction

A large amount of experimental data on the chemical causes of aging, *i.e.* corrosion, of plastics has been published [1] and a systematic account has been given by *Kern* [2]. The physicochemical causes of aging, *e.g.* loss of plasticizer by diffusion, evaporation, or extraction have also been discussed recently in a review by *Voigt* [3].

In the examination of the physical causes of aging, it is convenient to distinguish between processes that take place with no outside agency, *i.e.* purely thermodynamic processes, and those that are due to external agents. The most common sign of aging is the occurrence of internal stresses, and hence the tendency toward crazing, cracking, and embrittlement, which may be due *e.g.* to crystallization or to changes in the supramolecular or morphological order also in a noncrystalline material. Other possible causes are plasticizer migration and the evaporation of small molecules such as monomer or water.

Both external and internal stresses, particularly in the presence of swelling wetting media, also leads to surface cracking and fissuring of the material (crazing). Naturally, any cracking also assists chemical attack, *e.g.* by oxygen, and so accelerates aging of the material. The present report will be deliberately confined to physical causes of aging, to which very little study has so far been devoted, although in practice combinations of the various aging effects are encountered.

Aging in metals is mainly due to electrochemical or purely chemical processes, though physical factors (*e.g.* mechanical stresses in stress-crack corrosion) may also be involved. In high polymers, physical factors and particularly the supramolecular order (see below) and the mobility of the molecules have a much greater influence, not only on the properties of the material, but also on the physical and chemical processes responsible for aging. This is due to the long-chain, anisotropic structure of the macromolecules. The van der Waals' forces between the chains of a polymer are much weaker than the valence forces acting in the chain direction. Consequently, mechanical stresses can lead to slipping of the chains relative to one another, plastic flow, and crazing without the need for rupture of the main polymer chain.

In a noncrystalline material or in the noncrystalline regions of a semicrystalline material, the packing of the macromolecules is rather disordered and loose. Consequently, transport and rate processes, particularly diffusion processes, and hence also any chemical reactions, take place mainly in the noncrystalline regions. If the substance is cooled below its glass transition temperature, the movement of the chain segments, *i.e.* the microbrownian motion, is frozen in and the substance becomes vitreous and hard, or even brittle. Once the microbrownian motion has stopped, the substance becomes progressively less able to reach its thermodynamic equilibrium state.

Insofar as polymers crystallize, the coiling and entanglement of the chains kinetically inhibit the formation of states of supramolecular order, *e.g.* crystallization, and are thus partly responsible for the many morphological structures of high polymers. Thus we know of very finely crystalline substances, such as the crystalline-amorphous system described by *Abbitz* and *Gerngross* [4], spherulites of widely varying structures and degrees of order, lamellar single crystals, and regions in which the chains are parallel (for further details see [4] and [5]). Owing to kinetic inhibition, a bulk polymer material never achieves complete crystallization either on cooling from the melt or on precipitation from solution, or even on subsequent

[*] Prof. Dr. H. A. Stuart
Laboratorium für Physik der Hochpolymeren am
Institut für physikalische Chemie der Universität
Jakob-Welder-Weg 15
65 Mainz (Germany)

[1] See, *e.g.*, *B. Doležel*: Chemische und physikalische Einwirkungen auf Kunststoffe und Kautschuk. Kohl's Technischer Verlag, Oberursel/Ts., 1963; also: Aging of Plastics. IUPAC-Symposium, Düsseldorf, Oct. 19, 1959. The lectures have appeared in Kunststoffe *49*, (1959).

[2] *W. Kern*, lecture delivered at the conference: Alterung und Korrosion von Kunststoffen, October 1966, Frankfurt/Main; published in Korrosion, Vol. 20, Verlag Chemie, Weinheim 1967.

[3] *J. Voigt*, lecture delivered at the conference: Alterung und Korrosion von Kunststoffen, October 1966, Frankfurt/Main; published in Korrosion, Vol. 20, Verlag Chemie, Weinheim 1967.

[4] Cf. *e.g. H. A. Stuart*: Physik der Hochpolymeren. Springer, Berlin 1955, Vol. III; *W. Holzmüller* and *K. Altenburg*: Physik der Kunststoffe. Akademie-Verlag, Berlin 1961.

[5] Cf. *P. H. Geil*: Polymer Single Crystals. Interscience, New York 1963; *H. A. Stuart*, Kolloid-Z. *165*, 3 (1959).

annealing. Thus it is characteristic of macromolecular materials that they are always removed to some extent from the thermodynamic equilibrium state. Their molecular order and hence their properties tend to change continuously in one direction, *i.e.* the materials tend to "age".

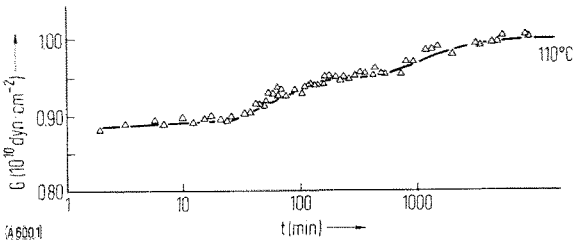


Fig. 1. Shear modulus of the polycarbonate of bisphenol A below the glass transition temperature as a function of annealing time.

II. Internal Thermodynamic Causes of Aging

It is generally known that changes in the crystallization state mainly influence the mechanical properties of a material (*e.g.* hardening or embrittlement). It is not so well known that similar phenomena can also occur in noncrystalline substances, such as amorphous polyethylene terephthalate, polymethyl methacrylate, polycarbonate, and polystyrene, on storage or after prolonged use. Since these processes can take place far below the glass transition temperature, they cannot be due to crystallization, but must involve an improvement in the short-range order characteristic of the amorphous state.

The completely disordered amorphous state can never be reached in liquids or melts, or even in somewhat compressed gases above the critical temperature. Even the close-packed spherical or rod-shaped molecules of a liquid exhibit a characteristic short-range order, *e.g.* approximately hexagonal close packing or a substantially parallel arrangement over very small regions. Since this statistical order extends only to the immediate surroundings of any given molecule (in the case of small molecules it has disappeared within a few intermolecular distances), it is known as short-range order. In substances consisting of chain molecules, there is always a certain amount of parallel arrangement of adjacent chain segments; the extent to which this occurs increases with the extent to which the chain segments are in the *trans* or zig-zag form as opposed to the *cis* and *gauche* forms. Since the width of X-ray reflections increases with decreasing dimensions of the crystallites, a substance having minute crystallites or crystal nuclei with an edge length of about 10 Å, gives, like an ordinary liquid or chain molecules in the melt or in the glassy state, only an amorphous halo. These systems are amorphous to X-rays, and will be referred to here simply as "amorphous", though it should be understood that this merely means that details of the short-range order at present defy investigation by X-ray methods. In my opinion, however, it is probable that information about the packing of the molecules in the noncrystalline regions can be obtained by accurate intensity measurements on the halo.

For some years we have been conducting experiments designed to measure and interpret structural changes in the amorphous region [6, 7]. Thus the increase in the shear modulus as a function of time at elevated temperatures was measured for the polycarbonate from bisphenol A, which is particularly suitable because of its high glass transition temperature (≈ 150 °C). When the polycarbonate is annealed *e.g.* at 110 °C (cf. Fig.1), the modulus increases in two stages. If it is then cooled to 20 °C, the modulus no longer returns to its old, room-temperature value, but remains constant between room temperature and the annealing temperature, *i.e.* the material has become stable in one of its mechanical properties. We might also say that it has been "artificially aged" to a final state that depends on the annealing temperature. The modulus returns to its original value only when the polycarbonate is heated for a short time at about 15 °C above its glass transition temperature and then quenched to 20 °C.

This effect is also exhibited by other high polymers, such as noncrystalline polyethylene terephthalate and polymethyl methacrylate. Similar phenomena are observed when the density or the rate of swelling is determined (i) at room temperature, (ii) after annealing below the glass transition temperature, and finally (iii) after heating above the glass transition temperature [7].

Investigations with an electron-microscope gave some very surprising results [8]. Figure 2 shows the surface replica of a polycarbonate film that had been etched with fast argon ions [9] after having been annealed in accordance with the program indicated in the figure. After annealing at 110 °C, the grain structure is coarser [a], and this difference disappears again when

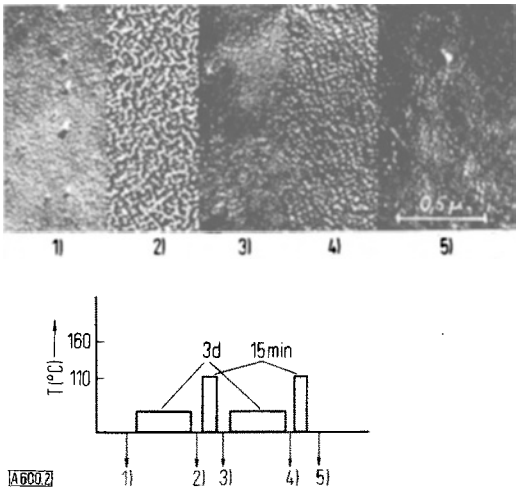


Fig. 2. Electron micrographs of the surface replica of an ion-etched amorphous polycarbonate film as a function of previous thermal history.
1) Original sample;
2) annealed for 3 days at 110 °C;
3) as 2), then heated for 15 min at 160 °C; quenched.
4) as 3), then annealed for 3 days at 110 °C;
5) as 4), then heated for 15 min at 160 °C; quenched.

[6] *W. Frank*, Dissertation, Universität Mainz, 1966.

[7] *W. Frank, H. Goddar*, and *H. A. Stuart*, Kolloid-Z., Z. Polymere, in preparation.

[8] *W. Frank, H. Goddar*, and *H. A. Stuart*, Polymer Letters, in press.

[9] For details see, *e.g. L. Reimer*: Elektronenmikroskopische Untersuchungs- und Präparationsmethoden, Springer, Berlin 1967.

[a] Grain structures have recently also been directly detected by *Geil* [10] in amorphous, extremely thin, quenched polyethylene terephthalate films by electron microscopy with a transmitted beam.

[10] *P. H. Geil* and *G. S. Y. Yeh*, Lecture Meeting Amer. physic. Soc., March 27–30, 1967, Chicago; Bull. Amer. physic. Soc., in press.

the material is subsequently annealed above the glass transition temperature ($\approx$ 150 °C). These phenomena are obviously due to a substantially reversible change in the morphological structure of an amorphous substance. When etched with ions, the amount of material removed from the surface depends on the density of the region, so that regional differences in density become recognizable. Thus annealing below the glass transition temperature evidently leads to a change in the packing density on the submicroscopic level.

A theoretical treatment of the modulus curves at various temperatures shows that the two stages correspond to two activated rate processes having somewhat different activation energies.

This means that the change in molecular order in the glassy state takes place in two stages, and can be reversed by heating for a short time above the glass transition temperature. Crystallization begins only at much higher temperatures, *i.e.* the phenomena in question do not involve precrystallization or nucleation. The effect is most readily explained by changes in the conformations of the chain molecules. Suppose that the temperature-dependent degree of coiling of the chain molecules in the melt or just above the glass transition temperature depends on an equilibrium between *trans* and *gauche* conformations [b] along the chain. If the polymer is cooled below the glass transition temperature, the ratio of these conformations present in the melt is "frozen in". This ratio can be brought closer to the equilibrium value by annealing. As is shown by the increase in density, this leads to better packing, an increase in the parallelism of the chains, and an increase in the order of the short-range order regions with respect to one another, *i.e.* to an increase in the grain size. The modulus increases, and the rate of swelling decreases [6, 7].

Geymeyer [11] and *Hendus* [12] recently found that a plasticized commercial PVC (suspension polymer Vinoflex 531) that is 55 % syndyotactic and random, *i.e.* practically atactic, contained lamellae of folded chain molecules such as have hitherto been found only in high polymers that crystallize well; *Hendus* also detected a low-angle X-ray scattering giving the same period. It has been further known for some time that spherulites, which are admittedly very poorly formed, occur in PVC [13, 14].

All the observations mentioned show that morphological structures, which can change with time and temperature, occur not only in crystallizable materials, where they have been known for a long time, but also in typically amorphous substances, such as quenched PET (polyethylene terephthalate) and PC (polycarbonate) or in atactic PMA (polymethyl methacrylate) and PVC below the glass transition temperatures. This explains certain aging phenomena that were previously incomprehensible, such as gradual exbrittlement without crystallization.

[b] An extended chain would contain only *trans* conformations.

[11] *W. Geymayer*, Radex-Rundschau (1965).

[12] *H. Hendus*, personal communication.

[13] *A. Utsuo* and *R. S. Stein*, Polymer Letters *3*, 49 (1965).

[14] *R. J. Clark*, J. Polymer Sci. *51*, 71 (1961).

III. External Factors Affecting Aging

1. Stress Crazing

a) Pure Stress Crazing

A well-known and feared phenomenon is the formation of cracks on the surfaces, *i.e.* crazing, of materials that are subjected to mechanical stress in the presence of a wetting agent. If chemical reactions with gases, vapors, or liquids play any part in the crack formation, the process is known as stress-crack corrosion. This case will not be considered here. The limiting case of "pure stress crazing", *i.e.* without the simultaneous influence of the environment hardly ever occurs in practice, since even small quantities of moisture or carbon dioxide in the air affect the process.

Nevertheless, we have studied this limiting case in some detail [15–17] in order to obtain a better insight into the processes involved in crazing. The crazing stress, the number of crazes, the rate of crack growth, and the induction time were measured under vacuum for amorphous 120 micron polyethylene terephthalate film (Hostaphan, produced by Messrs. Kalle). These quantities are defined as follows:

The crazing stress is the critical stress at which the first crazes become visible to the naked eye; it increases appreciably with the rate of stretching of the film. A certain induction time is therefore required for a weak spot or defect [c] to develop into a visible crack. The crazing stress, like the tensile strength, decreases rapidly with rising temperature. Furthermore, as the temperature is raised, the increasing mobility of the chains, and hence the decreasing relaxation time, in amorphous materials leads to disappearance of crack formation (*i.e.* the 'number of cracks', or number of visible cracks per cm^2, consequently tends toward zero) with increasing proximity to the glass transition temperature.

For any given stress and at a constant temperature, a plot of the crack number against time tends toward a limiting value, which increases rapidly with increasing stress. This is evidently because at a given stress, visible cracks can develop only from weak spots whose notch number [d] lies above a certain minimum value.

[15] *H. A. Stuart, D. Jeschke*, and *G. Markowski*, Materialprüfung *6*, 77 (1964).

[16] *G. Markowski, H. A. Stuart*, and *D. Jeschke*, Materialprüfung *6*, 236 (1964).

[17] *H. A. Stuart, G. Markowski*, and *D. Jeschke*, Kunststoffe *54*, 618 (1964).

[c] The defect may even be a submicroscopic crack. Any inhomogeneity can lead to a crack or to rupture.

[d] The notch number is the ratio of the maximum stress occurring at a defect, *i.e.* the "notch stress", to the macroscopic stress. The notch number was originally defined and calculated for a crack oriented at right angles to the tensile stress.

Another important observation is that the length of the cracks on the surface always tends toward a limiting value; thus the growth of the cracks is accompanied by a reinforcing mechanism, which is evidently due to substantially reversible orientation of the molecular chains. Thus three stages can be distinguished in the crazing process: (a) conversion of the defect into a visible crack, (b) the growth phase, and (c) the reinforcement or termination phase.

As can be seen from Figure 3, the rate of crack growth $\Delta l/\Delta t$ and the ultimate crack length decrease as the induction time increases. This has also been observed by other authors [18], and is evidently related to the structure of the original defect; the greater the notch number of the defect, the shorter is the induction time, and the greater is the rate of growth and the ultimate crack length.

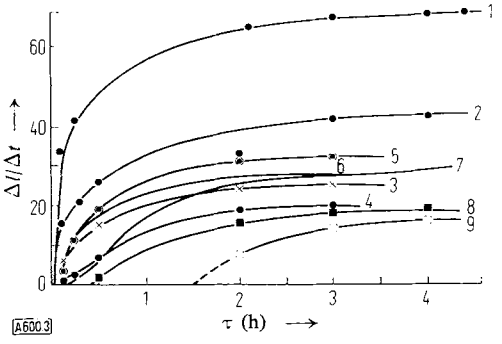


Fig. 3. Induction times τ and rates of crack growth $\Delta l/\Delta t$ for individual cracks in polyethylene terephthalate in air under constant stress. The figures 1 to 9 on the curves denote measurements on different cracks.

It is important to note that the cracks formed in vacuum or in an inert medium are largely reversible [18–20]. If an unstressed Hostaphan film covered with surface cracks is heated to 10 to 15 °C above its glass transition temperature, the cracks (provided that they are not longer than 10 μ) can no longer be recognized under the optical microscope after only a few minutes. However, this does not mean that they have completely disappeared, but only that they have become submicroscopic, since they again become visible on application of a tensile load. Moreover, the "cracks" observed on polycarbonate films in the presence of air are not true cracks, but are partly filled with oriented polymeric material [21]. As a result of the flow processes, the walls of the cracks are evidently joined by stretched fibrous material. This also explains the reversibility of crack formation.

b) Environmental Stress Crazing

If one disregards chemical reactions, crack formation depends mainly on three properties of a medium (apart from temperature, time, and the distribution of the stresses in the surface) *i.e.* the wetting, the rate of diffusion or of swelling, and the maximum degree of swelling, *i.e.* the equilibrium degree of swelling. Crazing can be caused only by wetting and moderately swelling liquids and by vapors that penetrate into the material. Comparison of such results with those obtained in vacuo shows several differences, even in the case of media that do not induce crystallization (*e.g.* methanol):

1. The crazing stress decreases; 2. the number of crazes is generally decreased by one to three orders of magnitude; 3. the rate of crack growth increases considerably. The cracks generally spread out over the entire surface and are much wider and deeper. Thus there is no self-limitation of crack growth. Crack formation under the action of a wetting and swelling medium involves both irreversible and reversible processes. This can be seen from the fact that when the material is heated above the glass transition temperature, the cracks disappear to a large extent, but never completely.

Considerable assistance in the explanation of crazing can be obtained *e.g.* from the curve of the crazing stress of stretched Hostaphan film at constant strain velocity as a function of the time of action of liquid methanol and methanol vapor (see Fig. 4).

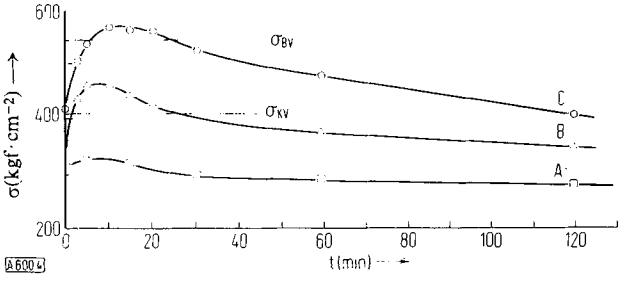


Fig. 4. Crazing stress as a function of the time of action in the presence of liquid methanol (curve A) and of methanol vapor (curve B: 150 mm Hg; curve C: 50 mm Hg) [16].

At very short times of action, the crazing stress is considerably lower than the value found in vacuum (σ_{KV}) (adverse effect of methanol). After a longer period of action, however, the properties appear to improve; for example, at a CH_3OH vapor pressure of 50 mm Hg (curve C), the crazing stress even rises above the value found for the tensile strength under vacuum (σ_{BV}). When the time of action is still further increased, however, the improvement is reversed by the progressive swelling of the material, and the crazing stress and the tensile strength decrease. The number of cracks after short times of action is also characteristically lower by a factor of 100 than in dry air [e]. In the course of time, *i.e.* with increasing swelling, the crack number again increases, but always remains much lower than in vacuum or in dry air.

[e] The decrease in the number of cracks under the influence of a wetting and swelling medium may seem surprising at first, but can be explained as follows: The higher the rate of crack growth and the wider the cracks become, the more rapidly will the stresses in the surface be relaxed in comparison with pure stress crazing. This is particularly pronounced when cracks have already formed over the entire width of the film. In this case the external stress in the crack profile decreases from the bottom of the crack toward zero at the surface of the film. Consequently, since cracks always originate at the surface of the film, new cracks, can no longer be formed. One could also say that the surface areas between cracks are no longer affected by external stresses ("islands" on a stressed surface).

[18] *O. K. Spurr jr.* and *W. D. Niegisch*, J. appl. Polymer Sci. *6*, 585 (1962).
[19] *S. B. Newmann* and *J. Wollock*, J. Res. nat. Bur. Standards *58*, 339 (1957).
[20] *C.C.Hsiao* and *J.A.Sauer*, J. appl. Physics *21*, 1071 (1950).
[21] *R. P. Kambour*, Polymer *5*, 143 (1964); Nature (London) *195*, 1299 (1962).

Thus when a wetting medium is allowed to act on a polymer surface subjected to external or internal stress, at least three effects come into play. Though these effects frequently cannot be distinguished experimentally, except by detailed measurements, we shall distinguish them in the following discussion as the instantaneous effect (effect I), the healing effect (effect II), and the swelling effect (effect III).

c) Models of Surface Crack Formation

α) Instantaneous Increase in the Notch Stress at a Defect (Instantaneous Effect or Effect I)

The fact that the energy required to extend a crack is lowered by a wetting medium can be formally expressed by an additional stress that leads to an increase in the notch stress. This additional stress will be referred to as the wetting medium stress [f].

The rapidly arising differences in the concentration of swelling agent in the immediate vicinity of the base of a crack and the resulting difference in the degree of swelling can also lead immediately to additional internal stresses, which have not so far been directly measured, and which we shall call "swelling stresses". The more slowly the surface layer swells, the smaller are the swelling stresses. However, if these stresses are very high, the application of an external load can lead to immediate rupture, or at least to intensified surface crack formation, which can be caused even by internal stresses. If the penetrating swelling agent also induces crystallization of the polymer, crack formation will be further promoted by the shrinkage stresses. If the wetting medium is allowed to act for a long time, the instantaneous increase in the notch stress [d] is accompanied by that of effect III (see Section III.1.c.γ). However, the surface crack formation or the rupture usually takes place so rapidly that no swelling of the surface layer has taken place even at a depth of only a few microns.

Since the instantaneous effect arises only in the presence of very small, possibly even invisible cracks, and better still from defects, the material can obviously be made more resistant to crack formation by healing of surface cracks and defects (*e.g.* by heating, polishing, or irradiation).

β) Diffusion within the Region of a Defect with Stress Relaxation in Submicroscopic Regions (Healing Effect or Effect II)

If the wetting agent eventually penetrates into deeper zones of a weak spot, plasticization takes place in submicroscopic regions. Under the influence of internal or external stresses, this leads to "microflow", and hence to relaxation of the stresses in the vicinity of the defect, *i.e.* to lowering of the notch number or to healing of the weak spot. However, this is true only if the external stress and the wetting-medium stress are not too high, since the weak spot otherwise develops into cracks, which then grow further.

If the material contains amorphous but stressed regions as well as crystalline regions, the diffusion of the swelling agents will proceed preferentially in the non-crystalline zones, and will again lead to the dissipation of internal stresses.

It is clear that these healing effects, which take time, occur only in certain stress ranges and only with some swelling agents. Effect II cannot occur with swelling agents that penetrate very strongly and very rapidly.

γ) Diffusion into the Interior (Swelling Effect or Effect III)

If the molecules of the swelling agent eventually penetrate into the interior of the polymer between the long chain molecules, macroscopic softening takes place, and the material becomes more plastic. At the same time, the kinetic inhibition in the widening of cracks and the activation energies decrease. This favorable influence on the crack formation and crack widening is eliminated only when the temperature is raised sufficiently far above the glass transition temperature, *i.e.* when all stresses relax sufficiently rapidly.

Effects I, II, and III are certainly not sufficient to explain the stress-crazing complex, and the effects cannot always be separated from one another. Thus according to *Charles* and *Hillig* [22], the development of a notch into a crack also depends on whether the action of the wetting medium makes the notch base sharper or rounder (*e.g.* on slow swelling, or on microflow under stress (effect II)) [g]; if it becomes rounder, the notch number decreases.

It can be seen, therefore, that no definite relationship can be expected between the parameters of crack formation and a single physical constant of a swelling agent. Attempted further quantitative studies have so far been unsuccessful [17].

2) Attempts to Improve Crazing Properties

a) Temporary Swelling Under Stress

If a Hostaphan film is wetted for about 5 min with liquid methanol and then evacuated for 24 hours at 50 °C, the crazing stress and the crack number return to the values found before wetting. Thus the number and distribution of defects in the surface have not changed. When partial swelling is carried out under an external stress, the crack number decreases [17] by about two orders of magnitude, so that there is a

[f] The term "wetting stress" has already been reserved in the literature for another purpose.

[22] *R. J. Charles* and *W. B. Hillig*, Symposium sur la résistance mecanique du verre, Florence 1961. Union Scientific Continental du Verre, Charleroi 1962, p. 511.

[g] If the glass transition temperature of a mechanically stressed and swollen surface is below the experimental temperature, surface and interfacial tensions will cause smoothing of the surface. Rounding-off is probably important in the etching or dissolving-away of the surface of rock salt by water. Under water, the strength of the rock salt almost reaches its theoretical value, *i.e.* 500 times its normal value (Joffé effect) [23].

[23] *A. Joffé*, Trans. Faraday Soc. *24*, 65 (1928).

considerable permanent improvement in the quality of the material. Thus where the surfaces have internal stresses, as in the case of injection-molded articles, the quality can be improved simply by swelling for a short time followed by drying.

It is known that the quality can also be improved by heating slightly above the glass transition temperature; however, internal stresses are evidently again necessary. The quality of films that are substantially free from stresses can be improved by heating only if an external stress is also applied. Annealing in the presence of a weak swelling agent (*e.g.* in the form of a vapor), either with or without external stresses, should lead both to the relaxation of internal stresses in the surface and to the elimination of defects.

b) Wetting with Long-Chain Molecules

When polymer films are wetted with long-chain silicones, the crazing stress becomes higher than for the free film in air. The crack number decreases by three orders of magnitude or more (see Table 1). This

Table 1. Improvement of crazing quality by wetting with long polymethylsiloxane chains.

Wetting medium	Tensile strength (kgf cm^{-2})	Crazing stress (kgf cm^{-2})	Crack number N_R [*]
Air	630—650	490—510	$\approx 10^3$
Octamethyltrisiloxane	560—580	360—380	15—20
Silicone oil 50 cSt	580—600	520—540	0.2—1
Silicone oil 240 cSt	600—620	570—590	0.2—0.6
Silicone oil 100000 cSt	640—660	570—590	0.2—0.6

[*] Number of cracks per cm^2.

effect, which is strongly dependent on the molecular weight of the silicone, cannot be explained by diffusion within the region of a defect or by microflow, but is probably due to the fact that the strongly wetting and very mobile silicone chains cover the film surface with a molecular layer and probably also fill out holes or submicroscopic cracks, and so "bridge" the weak spots. This hypothesis is supported by the observation that the rate of crack growth remains the same as that in air, *i.e.* the spreading of cracks is not facilitated by penetrating molecules of the wetting liquid. This *coating* effect disappears only when a more strongly wetting or swelling liquid such as methanol is applied after the silicone.

IV. Morphological Structure, Diffusion, Swelling, and Crack Formation

1. Morphological Structure and Crack Formation

It has been known for some time that for a given degree of crystallinity, a polymer containing spherulites is more brittle than a finely crystalline polymer [24].

[24] *E.g. H. A. Stuart* in: Physik der Hochpolymeren. Springer Verlag, Berlin 1956, Vol. IV, p. 626.

Fracture along the radial fibers of the spherulites and the decrease in dielectric strength as compared with a material containing no spherulites indicate that molecular or capillary cracks must exist between the spherulites. Figure 5 shows [17] the free surface of a 1 mm isotactic polypropylene film; the melt was heated to 220 °C and kept at 120 °C for 3 hours to allow crystallization, and the material was then cooled. Shrinkage during crystallization led to distinct cracks along the radii and along the boundaries of the spherulites [25]. These cracks became larger on cooling, so that the shrinkage due to crystallization could be distinguished from the shrinkage due to cooling.

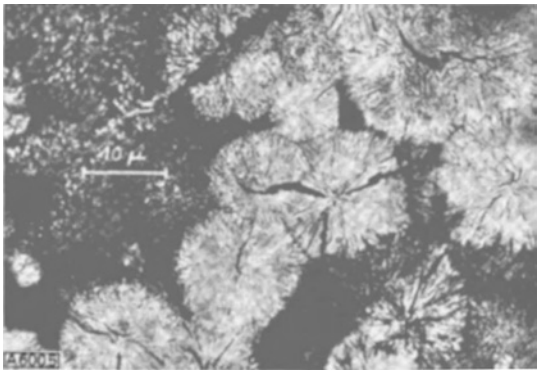


Fig. 5. Crack formation caused by crystallization of isotactic polypropylene.

Figure 6 shows the crack formation caused by the annealing of a polypropylene film that has been kept at 130 °C for more than 60 hours [26]. According to *Inoue* [26], the large cracks between the spherulites are due to oxidative degradation in the regions of low order between the spherulites (cf. also *Kavafian*'s experiments below). However, since the author himself found an increase in density, *i.e.* an increase in crystallinity within the spherulites, shrinkage must also have made an important contribution.



Fig. 6. Crack formation caused by annealing a polypropylene film for 60 hours at 130 °C [26].

On the basis of such observations, it might be concluded that materials containing spherulites are generally poorer in quality. However, the situation is

[25] *S. Van Schooten*, J. appl. Polymer Sci. *9*, 122 (1960).
[26] *M. Inoue*, J. Polymer Sci. *55*, 443 (1961).

not quite so simple as this, since according to *Reding* and *Walter*[27] the order within the spherulites is very important. Thus it is found that both branched and very high molecular weight polyethylenes are very resistant to stress cracking. Both branched and very long chains evidently prevent the attainment of a high degree of order inside the spherulites. Electron micrographs show that the spherulites in a high molecular weight polyethylene are still in a poorly ordered state after annealing. Ethylene-propylene block copolymers are also extremely resistant to crack formation, even after prolonged annealing[27]. The formation of large and well ordered spherulites is prevented in this case by the "elastomeric" chain segments, which are not incorporated into lattice zones. Thus to avoid crack formation, it is necessary to avoid a high degree of order within the spherulites and the formation of large spherulites.

2. Morphological Structure, Swelling, and Chemical Reactivity

Since the supramolecular order strongly influences diffusion and swelling processes, it is possible to develop details of the morphological structure and very fine, possibly even invisible cracks, *i.e.* to magnify them and make them visible, by means of a swelling agent. Figure 7 shows a highly ordered spherulite in a polyethylene sebacate film in transmitted polarized light. Its ring structure is due to bundles of single-crystalline lamellae which are twisted regularly along the radius. After treatment with xylene for a short time at room temperature, examination in transmitted unpolarized light reveals deep cracks, from which the period of the spherulite rings can still be recognized. Small cracks, which are shorter than the ring period and which are themselves arranged in rings, have also been formed (see Fig. 8).

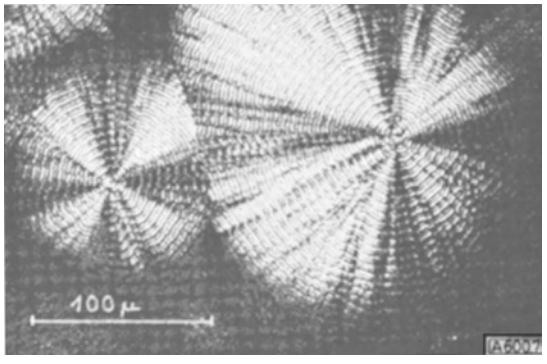


Fig. 7. Polyethylene sebacate spherulite with ring structure, photographed in transmitted polarized light [17].

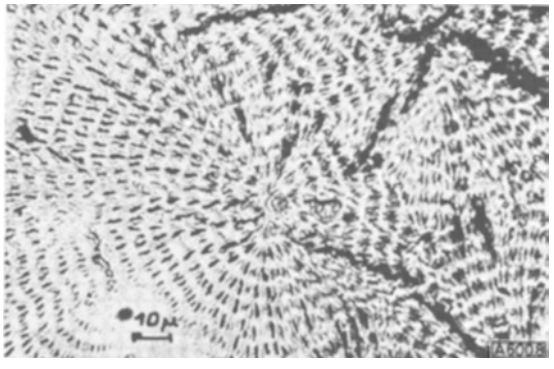


Fig. 8. The spherulite shown in Figure 7 after treatment with xylene [17].

Any orientation of the chains leads to reduced transverse strength, and hence to a greater tendency toward crack formation, *i.e.* toward preferential diffusion and swelling between the parallel, extended molecular chains or bundles of molecular chains. This is very clearly recognizable in a stretched film of amorphous polycarbonate from bisphenol A; the swelling agent, was eugenol, which dissolves the amorphous polycarbonate to a small extent, but at the same time induces spherulitic crystallization.

The stretched films were stuck to a cover glass with an epoxy resin and the projecting portions were cut off. The film was then exposed to the eugenol from the edge, and crack formation was followed under the microscope. Crack formation took place only from the edges perpendicular to the stretching direction, the cracks running parallel to the stretching direction. If the film is stuck on obliquely, the cracks also run obliquely into the interior, again exactly parallel to the stretching direction.

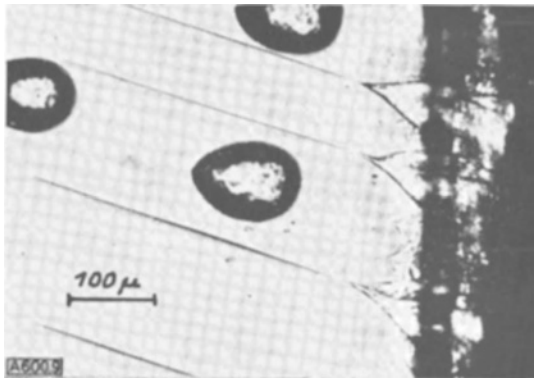


Fig. 9. Crack formation in a stretched amorphous polycarbonate film wetted with eugenol [17]. An irregular turbidity due to spherulitic crystallization and to the crystallization of the polycarbonate that first went into solution is seen at the edges of the film and in the eugenol itself.

The effects of chemical processes on aging vary in intensity according to the morphological structure. Thus *Kavafian*[28] has shown that tough specimens of polyethylene become completely embrittled on annealing in air at 100 °C for only 48 hours. New specimens prepared by melting and recrystallization of these brittle samples had practically the same properties as the original material, in agreement with the fact that viscometric and spectroscopic measurements show that only very slight chemical degradation of the chains has taken place. *Kavafian* considers that the attack by oxygen takes place mainly in the looser packed regions between the spherulites. Transport processes of every type, particularly diffusion, are greatly facilitated in these regions. Thus chemical reactions such as oxidation, which are practically

[27] *F. P. Reding* and *E. R. Walter*, J. Polymer Sci. *38*, 141 (1951).

[28] *G. Kavafian*, J. Polymer Sci. *24*, 499 (1957).

impossible in a perfect crystal zone, can take place in interposed amorphous regions and on internal surfaces. The temperature-dependence of the rate of a chemical reaction in high molecular weight solids will therefore depend partly on changes in molecular order and on internal crack formation with temperature and time. Consequently the temperature-dependence of the overall reaction rate can become considerably greater than in solution.

In many cases, it is impossible to make quantitative predictions, simply because of the unknown crack formation and the possibility of additional diffusion. This should always be borne in mind when information gained for artificially accelerated aging is applied to aging processes in practice.

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Potential and Charge Distribution at Semiconductor-electrolyte Interfaces

BY R. MEMMING AND G. SCHWANDT [*]

The present article deals with the basic concepts of charge and potential distribution at semiconductor-electrolyte interfaces. The authors use examples to show how external polarization and the variation of the electrolyte composition can change the potential drop across the space-charge region in the semiconductor and in the Helmholtz double layer at the interface. The article also contains a detailed discussion of the effects exerted by surface properties and by injection of carries on the distribution of charge and potential.

Introduction

Problems connected with semiconductor-electrolyte interfaces were approached originally from two different branches, from electrochemistry and solid state physics. Semiconductor electrodes found electrochemical applications a long time ago, *e.g.* in semiconducting oxide electrodes in batteries. However, the electrical properties of semiconductor electrodes were then virtually unknown, and therefore systematic studies of the electrode processes were not possible. Only the preparation of high-purity single crystals of semiconductors gave a new impetus to research in this field. The basic electrochemical processes have been described by *Gerischer* [1] in a review article.

Surface effects are of great importance in solid state physics, because they exert a great influence on the electrical properties of many semiconductor devices. The properties of clean surfaces produced by cleaving single crystals in high vacuum have been investigated, and the electrical properties of the surfaces could be altered by the adsorption of gases or the formation of surface films. Furthermore, certain conditions can be created on the surface of the semiconductors by bringing these into contact with electrolytes. *Harten* [4] has lately discussed in a review article the electrical properties of such "wet" surfaces, particularly from the viewpoint of semiconductor physics, and has compared the distribution of charge and potential at the semiconductor-electrolyte interface with the corresponding distribution in a semiconductor-vacuum system.

The present article is devoted to a discussion of the charge and potential distribution mainly from the electrochemical viewpoint, and particularly to the description of the typical properties of semiconductor electrodes as distinct from the properties of metal electrodes. The three parts of this article deal respectively with the basic theoretical concepts of the distribution of charge and potential, the principal methods of measurement, and experimental results. Reactions at semiconductor electrodes will be discussed only in so far as they play a part in the distribution of charge and potential.

1. Theory

1.1. General Considerations

A double layer is formed at the semiconductor-electrolyte interface in the same way as at the metal-electrolyte interface. A double layer consists of opposite charges in the two phases and aligned dipoles at the interface. This results in a potential difference (Galvani potential) between the two phases whose interiors contain no charge. The corresponding charges

[*] Dr. R. Memming and Dr. G. Schwandt
Philips Zentrallaboratorium GmbH.
Laboratorium Hamburg
Postfach 13545
2 Hamburg-Stellingen (Germany)

[1] *H. Gerischer* in *P. Delahay*: Advances in Electrochemistry and Electrochemical Engineering. Vol. I, Interscience, New York 1961.

are electrons on the metal or the semiconductor surface and ions in the electrolyte. The distance between these two charges is mainly determined by the radius of the solvation shell of the ions. Therefore, the double layer, which is also known as the Helmholtz layer, can be considered as a charged capacitor. On the assumption that the charges are uniformly distributed over the surface, the capacitance of this condenser should be constant; however, this picture can only be applied in the case of concentrated electrolyte solutions, otherwise the capacity varies with the electrolyte concentration. *Gouy*[2] and *Chapman*[3] have improved this model by regarding the charge of the condenser on the side of the electrolyte not as a continuous surface charge, but as a space charge (Gouy-Chapman layer) for which the well-known Poisson equation holds.

1.2. Space-charge Region in Semiconductors

Metal electrodes and semiconductor electrodes do not differ in the Helmholtz double layer and the Gouy-Chapman layer; the main difference between them is that the concentration of mobile charge carriers is much lower in semiconductors than in metals. As in dilute electrolytes, the charges in semiconductors are not confined to the surface, but extend over a certain region below the surface, and thus form a space charge. The relationship between the space charge density $\rho(x)$ and the potential at the surface φ is given by the Poisson equation:

$$\Delta\varphi = (d^2\varphi)/(dx^2) = -(\rho(x))/(\varepsilon\varepsilon_0) \qquad (1)$$

where Δ is the Laplace operator, ε is the dielectric constant, ε_0 is the influence constant, and x is a distance normal to the surface.

The space charge density ρ is given by the total number of mobile and non-mobile charges, *i.e.* electrons $n(x)$ and holes $p(x)$ on the one hand, and ionized donors n_D and acceptors n_A on the other. The following formula, where e is the unit charge, holds in the case of semiconductors with homogeneous doping:

$$\rho(x) = e(n_D - n_A - n(x) + p(x)) \qquad (2a)$$

The charge is zero in the inside of the bulk (*i.e.* $\rho = 0$), and the number of electrons and holes is given by the doping of the crystal: $n(x) = n_o$ and $p(x) = p_o$. In this case, we have

$$\rho(x) = 0 = e(n_D - n_A - n_o + p_o) \qquad (2b)$$

The concentration of electrons in the conduction band and of the holes in the valence band can be calculated using the energy gap model of semiconductors. Non-degenerate semiconductors – the only type to be discussed – are characterized by a Boltzmann distribution of the electrons and the holes. The following formula shows how the electron concentration in the conduction band depends on the Fermi potential E_F:

$$n = N_c \exp[-(E_e - E_F)/(kT)] \quad (E_c \gg E_F) \qquad (3a)$$

(N_c is the density of states in the conduction band, E_c is the lowest energy level in the conduction band, k is the Boltzmann constant, and T is the temperature).

The closer the Fermi level to the conduction band, the greater the number of electrons in the latter. An analogous formula applies to the concentration of holes:

$$p = N_v \exp[-(E_F - E_v)/(kT)] \qquad (3b)$$

(N_v is the density of states in the valence band and E_v is the highest energy level in this band).

Thermodynamic equilibrium between electrons and holes prevails inside the semiconductor, *i.e.*

$$n_o \cdot p_o = n_i^2$$

(where n_i is the intrinsic number of electrons).

The distribution of the potentials in the space-charge region below the surface can in principle be calculated from eqs. (1)–(3). The set of equations does not admit a closed solution, and a qualitative picture of the potential distribution in the space-charge region is obtained as described below.

In the equilibrium state, the Fermi level is the same inside the semiconductor and on its surface (Fig. 1). If the electron concentration on the surface and in the space-charge region is lower than in the interior, then the distance between the Fermi level and the bottom of the conduction band is greater. This leads to upward bending of the energy bands (Fig. 1).

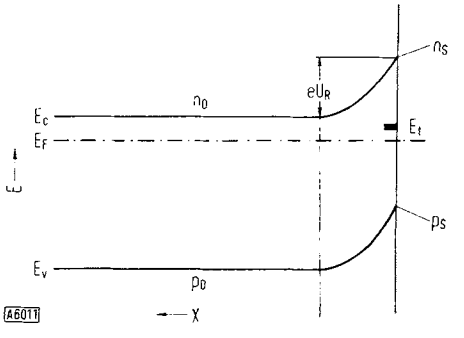


Fig. 1. Energy gap model of the semiconductor's surface.
E_c - bottom of the conduction band; E_v - top of the valence band; E_F - Fermi level; n_o and p_o - density of electrons and holes in the bulk; n_s and p_s - density of electrons and holes at the surface of the semiconductor; U_R - band bending at the surface; E_t - surface state: E - energy of electrons; x - vertical distance from the surface.

The use of eq. (3a) gives the following relationship between the electron density at the surface n_s and in the bulk n_o:

$$n_s = n_o \exp(-eU_R)/(kT) \qquad (4a)$$

where U_R is the band bending at the surface. An analogous relationship holds for the hole concentrations:

$$p_s = p_o \exp(eU_R)/(kT) \qquad (4b)$$

[2] *G. Gouy*, J. Physique [4], 9, 457 (1910).
[3] *D. L. Chapman*, Philos. Mag. Ser. 6. 25, 475 (1913).

Thermodynamic equilibrium normally prevails also in the space charge region, *i.e.*

$$n_s p_s = n_o p_o = n_i^2 \tag{5}$$

The upward bending of bands in an n-type semiconductor leads to an exhaustion layer ($n_s < n_o$) or an inversion layer ($p_s > n_s$), whereas if $n_s > n_o$, then the energy bands are bent downwards and an accumulation layer is formed.

1.3. Surface States

The charges on the semiconductor side of the interface need not all be distributed in the space-charge region; they may also be trapped in surface states. These are energy states E_t lying at the surface within the forbidden zone of the energy gap model (see Fig. 1). The surface states may arise *e.g.* by the interruption of the periodic structure of the lattice at the surface, or from the adsorption of impurity atoms or ions. The position of these states with respect to the Fermi level E_F will decide whether or not they will be occupied by electrons: if they are above E_F, they will not be occupied by electrons (though they may be occupied by holes), if they are below the Fermi level, on the other hand, then the surface states will be filled with electrons. By changing the band bending, *e.g.* by applying an external voltage, one can shift the surface states across the Fermi level, and thus change their charge.

1.4. Distribution of Potential

The charge distribution at the semiconductor-electrolyte interface shows a certain symmetry in that there are two opposite surface charges at an atomic distance (Helmholtz double layer), followed by the space-charge regions, beyond which extend the neutral bulks of the two phases. The corresponding charge and potential distributions are shown in Fig. 2.

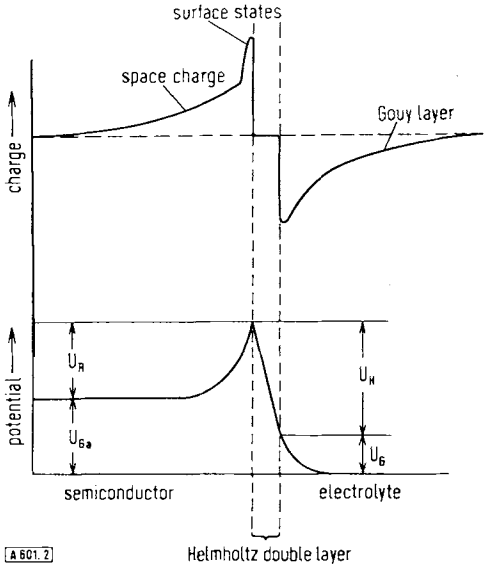


Fig. 2. Distribution of charge and potential around the interface between a semiconductor and an electrolyte.
U_R - potential drop across the space charge (band bending);
U_{Ga} - Galvani potential; U_H - potential drop across the Helmholtz double layer; U_G - potential drop across the Gouy layer.

The charge in the surface states is taken to be positive here. Since the density of these states is generally low and they are located only at the surface no remarkable potential drop occurs across the first atomic layers of the semiconductor. The Galvani potential U_{Ga} between the two phases is thus composed of three terms, namely the potential drop U_R across the space charge region in the semiconductor, the potential drop U_G across the Gouy layer, and the potential drop U_H across the Helmholtz double layer, *i.e.*

$$U_{Ga} = U_R + U_G + U_H \tag{6}$$

As with metal-electrolyte interfaces, the Galvani potential itself is not measurable. It can be determined except for an additive constant, when the electrode potential U_E is measured against a standard electrode such as the calomel electrode. Therefore, changes in the Galvani potential can be reliably determined. It holds that

$$\Delta U_E = \Delta U_{Ga} = \Delta U_R + \Delta U_G + \Delta U_H \tag{7}$$

or

$$U_E = U_R + U_G + U_H + \text{const.}$$

The constant contains the sum of all the Galvani potentials at all other phase boundaries of the electric circuit, and thus U_E is identical with the EMF of the galvanic cell.

It should be mentioned that the potential distribution shown in Fig. 2 is not quite satisfactory. Solids (metals or semiconductors) and electrolytes are treated as continua in the space-charge region. The potential is thus a "macro-potential" composed of the "micro-potentials" of the individual atoms. In the atomic dimensions of the Helmholtz double layer, a corresponding averaging is no longer permissible. The various definitions of potential have been discussed by *Harten*[4] and will not be dealt with here. In any case, they play no part in the measurement of the changes in the Galvani potential in a given system, since only potentials of the same definition are being compared. We shall deal in the following only with measurements of this type.

2. Methods of Measurement

Whereas only changes in the potential drop U_H can be measured in the Helmholtz layer, the potential drop U_R across the space-charge layer in the semiconductor can be determined as an absolute value. This can be done by measuring either the surface conductivity or the capacitance. The theoretical relationship between these and the band bending U_R can be derived as follows: The number of excess electrons ΔN and holes ΔP in the whole space charge region are defined respectively by

[4] *H. U. Harten* in: Festkörperprobleme III. Vieweg, Braunschweig 1964.

$$\Delta N = \int_0^l [n(x)-n_0]\,dx \text{ and } \Delta P = \int_0^l [p(x)-p_0]dx \qquad (8)$$

(where l is the thickness of the space-charge region).

The variations in the concentrations of electrons and holes in the space-charge region of an intrinsic semiconductor are shown in Fig. 3a. The hatched areas correspond to the excess or the missing charge carriers ΔN and ΔP. The attending potential-dependence

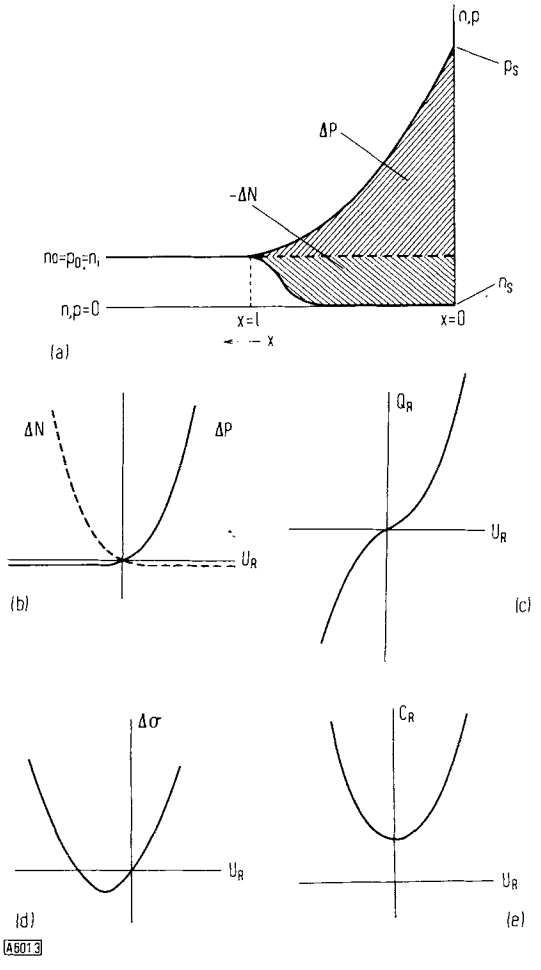


Fig. 3. a) Variation in the concentration of charges (n,p) in a p-conducting space-charge layer ($U_R > 0$) — Schematic representation; the hatched areas denote the excess charges. — b) Excess charge densities ΔN and ΔP as a function of the band bending U_R. — c) Surface density of the space charge Q_R as a function of the potential drop across the space region U_R. — d) Surface conductivity $\Delta\sigma$ as a function of the band bending U_R. — e) Space-charge capacity C_R as a function of the band bending U_R.

is illustrated in Fig. 3b. If the bands are flat ($U_R = 0$) up to the surface in an intrinsic semiconductor ($n_0 = p_0 = n_i$), then by definition $\Delta N = \Delta P = 0$. In the case of a p-conducting surface (upward band bending, $U_R > 0$), p_s increases exponentially with U_R according to eq. (4b) and ΔP also rises rapidly in a corresponding manner. On the other hand, ΔN becomes negative, though it cannot reach high values, since n_s tends to zero. These roles of ΔN and ΔP are reversed on n-conducting surfaces. The surface charge density Q_R in the space-charge region is given by

$$Q_R = e(\Delta P - \Delta N) \qquad (9)$$

(see Fig. 3c).

The change in the carrier concentration in the space-charge region alters also the conductivity parallel to the surface. The surface conductivity $\Delta\sigma$ is defined by

$$\Delta\sigma = e\,(\mu_n\,\Delta N + \mu_p \Delta P) \qquad (10)$$

(where μ is the mobility of electrons or holes).

The surface conductivity $\Delta\sigma$ is related to the measurable conductance ΔG of the space-charge region *via* a geometric factor. The dependence of the surface conductivity on the potential follows directly from Fig. 3b and eq. (10), and is illustrated in Fig. 3d. The minimum of the curve is not necessarily at $U_R = 0$, since electrons and holes usually differ in their mobility [5–7]. The accurate values of the excess charges ΔN and ΔP can be determined from the Poisson equation.

A similar connection may be found between the space charge capacity and the band bending U_R. This capacity is made up of two components, namely the Helmholtz capacity C_H and the space-charge capacity C_R. A differential capacity can be defined for the space-charge layer in exactly the same way as for the Helmholtz double layer. The opposite charge to the space charge is located in the electrolyte. The space-charge capacity is defined as follows:

$$C_R = \mathrm{d}\,Q_R/\mathrm{d}U_R \qquad (11a)$$

The charge per unit surface area (Q_R) of the space-charge layer is given by eq. 9, and is shown in Fig. 3c as a function of the band bending U_R. The slope of this s-shaped curve corresponds to the capacity C_R. When there is no space-charge layer (*i.e.* $U_R = 0$), the charge curve shows a turning point and the capacity C_R goes through a minimum (Fig. 3e). According to *Bohnenkamp* and *Engell* [8], the quantitative relationship between C_R and U_R for an intrinsic semiconductor ($n_o = p_o$) is as follows:

$$C_R = C_{min} \exp\,(e\,U_R)/(2\,kT) \qquad (11b)$$

Similar equations may be derived for doped (n- or p-type) semiconductors. This results in a small change in the shape of the curve for the U_R-dependence of the surface conductivity and the capacity.

As mentioned above, the potential-dependence of the surface conductivity can be directly determined from conductivity measurements [9]. The measurement of the space-charge capacity C_R is more difficult, since the equivalent circuit diagram contains some other RC terms as well. In the equivalent circuit diagram (see Fig. 4), the space-charge capacity is in series with the Helmholtz capacity C_H (the latter is generally much greater than C_R [*]) and with a series

[5] *H. Flietner* and *G. Hundt*, Ann. Physik *3*, 396 (1959).

[6] *R. F. Greene*, *D. R. Frankl*, and *J. Zemel*, Physic. Rev. *118*, 967 (1960).

[7] *J. R. Schrieffer*, Physic. Rev. *97*, 641 (1955).

[8] *K. Bohnenkamp* and *H. J. Engell*, Z. Elektrochem., Ber. Bunsenges. physik. Chem. *61*, 1184 (1957).

[9] *H. U. Harten*, Z. Naturforsch. *16a*, 459 (1961).

[*] The space charge in the Gouy layer is neglected in the equivalent circuit diagram as well as in the investigations. This layer is suppressed in practice by increasing the concentration of electrolyte by the addition of a conducting salt.

resistance which basically represents the bulk resistance of the system. Parallel to this, there is a complex resistance Z_P, basically corresponding to the Faraday impedance. The equivalent circuit diagram should therefore be analysed in every case. This diagram generally reduces at high frequencies to one containing only C_R and R_S.

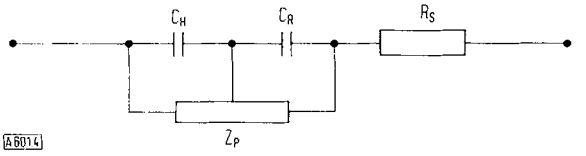


Fig. 4. Equivalent circuit diagram for the semiconductor-electrolyte interface.

The simplest of the many established methods uses an a-c bridge. However, this is not really suitable, because the potential-dependence of the space-charge capacity C_R must be measured within a few seconds so as to avoid any possible changes of the surface coverage. One uses therefore pulse techniques [10], or records the phase angle with an oscilloscope [11, 12]. A difficulty is introduced by the fact that the a-c voltage used must have a small amplitude ($\ll kT/e$), since the capacity itself depends on the voltage. The individual methods will not be described here in detail.

Applying an a-c field, the charge in the space-charge region is altered at a certain frequency. Since charges Q_o are also located in surface states, these too can be influenced by the a-c field, and can contribute to the total capacity.

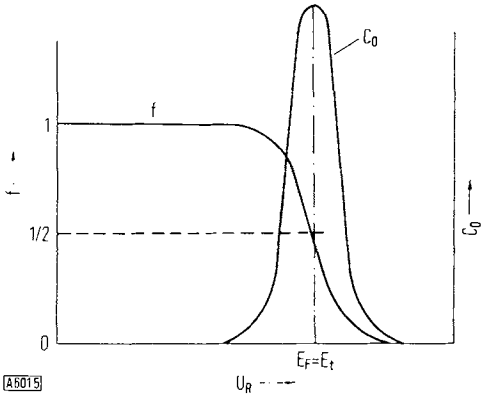


Fig. 5. Fermi function f and the capacity of the centers C_o (in arbitrary units) as a function of the band bending U_R.

As with space-charge capacity, we define a pseudo-capacity for the surface states:

$$C_o = (\mathrm{d}\, Q_o)/(\mathrm{d}\, U_R) \qquad (12)$$

The charge per unit area Q_o in the surface states is determined by the density of states N_t and their probability f of being filled by an electron:

$$Q_o = e\, N_t f \qquad (13)$$

Differentiation with respect to U_R gives the capacity C_o of the surfaces states, while f is given by the Fermi function whose dependence on U_R is shown qualitatively in Fig. 5. At a certain value of the band bending U_R, the energy of the surface state E_t coincides with the Fermi level E_F. The Fermi function has a turning point at this value, as shown in Fig. 5. It is here that the change ΔQ_o produced in the charge by a small a-c voltage is the greatest, and thus the capacity C_o reaches its maximum. Since the change in the charge of the surface states and the space charge region is of the same sign when the band bending is varied, the pseudo-capacity C_o in the equivalent circuit diagram is parallel to the space-charge capacity C_R. In the presence of surface states, therefore, an additional capacity must appear in the measurement of the space-charge capacity C_R.

3. Experimental Results

3.1. Space Charge and Surface States

Bohnenkamp and *Engell* [8] were the first to observe a minimum in the capacitance of a germanium electrode, and it was some years later that quantitative results were published about the potential distribution at germanium-electrolyte phase boundaries [13, 10]. Some data obtained by capacity and surface conductivity measurements are shown in Figs. 6a and 6b.

The experimental points are plotted against the electrode potential U_E (lower scale), and the theoretical curve features as a function of the band bending U_R (upper scale). The difference between the two potentials, which cannot be obtained by any theory, was determined by displacing the scales with respect to each other. The theoretical values are in addition multiplied by a factor of 1.3 corresponding to a linear

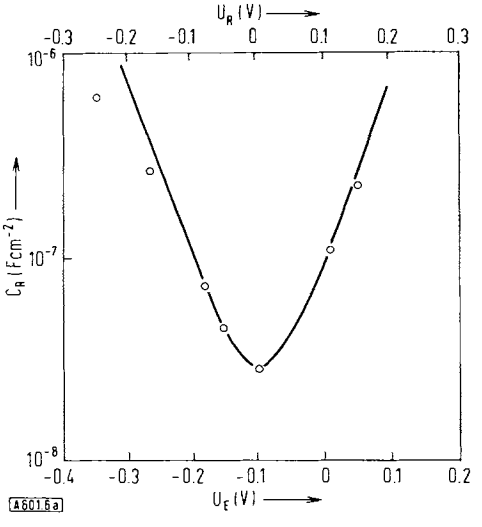


Fig. 6a. Space-charge capacity C_R as a function of the electrode potential U_E of a p-type germanium electrode (49 ohm. cm), as measured against a saturated calomel electrode. Solid line: theoretical capacity values calculated with the aid of the band bending U_R (upper scale); open circles: experimental values (a roughness factor of 1.3 was taken into account) (lower scale) [11].

[10] *W. H. Brattain* and *P. J. Boddy*, J. electrochem. Soc. *109*, 574 (1962).

[11] *R. Memming*, Philips Res. Rep. *19*, 323 (1964).

[12] *H. Gerischer*, *M. Hoffmann-Perez*, and *W. Mindt*, Ber. Bunsenges. physik. Chem. *69*, 130 (1965).

[13] *H. U. Harten* and *R. Memming*, Physics Letters *3*, 95 (1962).

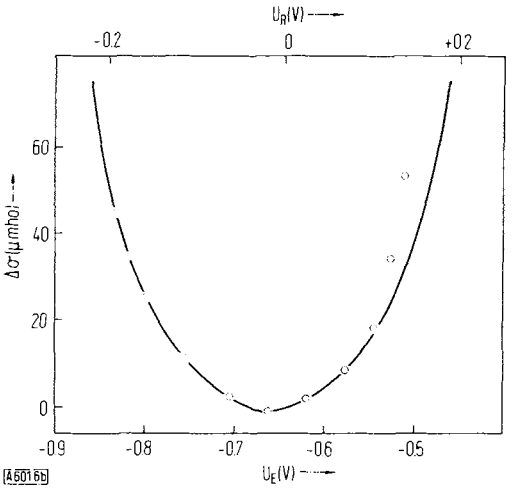


Fig. 6b. Surface conductivity $\Delta\sigma$ as a function of the electrode potential U_E of a germanium electrode (intrinsic), as measured against a saturated calomel electrode [13].

displacement on a logarithmic scale. This roughness factor is regarded as a correction for the roughness of the surface in contact with the electrolyte.

The agreement between theory and experiment means that the band bending U_R follows exactly the change in the electrode potential ΔU_E produced by an external voltage. Thus, in accordance with eq. (7), $\Delta U_E = \Delta U_R$. However, this result was obtained with a germanium electrode only when it was anodically polarized before the measurement, and when the potential change required for the measurement was rapidly achieved (within 10 sec). This suggests that otherwise chemical changes, too, occur at the interface (see below). Under the specified conditions, therefore, the potential drop U_H across the Helmholtz layer remains unchanged ($\Delta U_H = 0$). It has been found also with other electrodes (*e.g.* silicon [9,14] and zinc oxide [15]) that the external voltage is fully taken up by the space charge in the semiconductor.

The measurement of the interfacial capacity of germanium has led to another important result. The good agreement between the measurements and the theoretical values calculated for the space charge indicates that no surface states (*i.e.* fewer than $10^9/cm^2$) are present after anodic polarization. Using a term of *Brattain* and *Boddy*, one can describe the surface as "perfect". However, this is not a general property of semiconductor electrodes, as shown by the observations that surface states are present in silicon after anodic or cathodic polarization [9,14]. It has been found in the case of germanium [16,17] that the addition of copper, silver, or gold ions (10^{-7} M) raises the capacity in a certain potential region (see Fig. 7), which means that these ions give rise to surface states (about $10^{11}/cm^2$).

[14] *R. Memming* and *G. Schwandt*, Surface Sci. *5*, 97 (1966).

[15] *J. F. Dewald*, Bell System techn. J. *39*, 615 (1960).

[16] *P. J. Boddy* and *W. H. Brattain*, J. electrochem. Soc. *109*, 574 (1962).

[17] *W. H. Brattain* and *P. J. Boddy*, Rep. Internat. Conf. on Physics of Semiconductors. (The Inst. of Physics and the Physical Soc., London, 1962), 797.

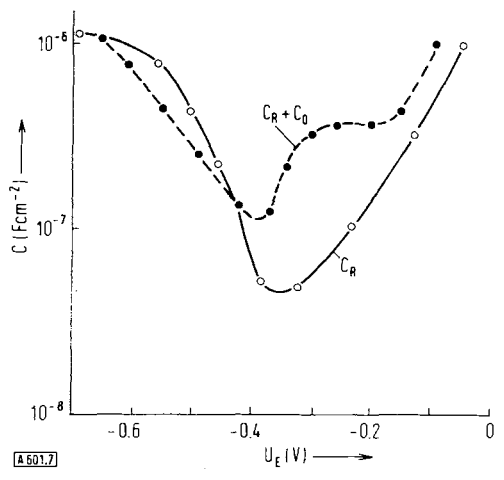


Fig. 7. Interfacial capacity as a function of the electrode potential of a p-type germanium electrode (45 ohm.cm) at pH 8 in a 0.1 M solution of Na_2SO_4 [18].

Solid curve: clean surface; dashed curve: after addition of cupric ions in a concentration of 10^{-7} M.

The properties of Cu, Ag, and Au impurity centers have been investigated in detail, particularly as regards their chemical nature. Since these elements are more electropositive than germanium, they readily deposit on the surface. This circumstance was used in the first attempt at explaining the formation of surface states at the interphase. Later investigations [18] have shown however, that below pH 4 surface states are no longer present, although these metals are still deposited (at rest potential). It seems therefore that the mechanism is much more complicated. Thus, only little is yet known of the actual chemical nature of the impurity centers. The formation of the surface states will be re-encountered in Section 3.4.2. in connection with other investigations.

3.2. Helmholtz Double Layer

The potential distribution at a germanium electrode was also investigated using electrolytes of various pH values. After anodic polarization and during a rather high sweeping rate, the band bending was only varied by the external voltage whereas the position of the capacity curve and the surface conductivity curve on the electrode potential (U_E) scale depends on the pH value of the electrolyte. Since the electrode potential is determined by the potential drop across the space-charge layer and across the Helmholtz double layer (we ignore the additive constant here), the above result suggests that the potential drop U_H across the Helmholtz double layer varies with the pH of the electrolytic solution.

A quantitative connection between U_H and the pH is established experimentally in the following way: In the case of an intrinsic semiconductor, the space charge in the semiconductor vanishes ($U_R = 0$) where the surface conductivity curve and the capacity curve reach their minimum. At this point, the electrode

[18] *R. Memming*, Surface Sci. *2*, 436 (1964).

potential U_E depends only on the potential drop across the Helmholtz double layer, and thus on the pH of the medium, *i.e.*

$$U_{E\,min} = U_H\,(pH) + \text{const.}\quad (U_R = 0) \qquad (14)$$

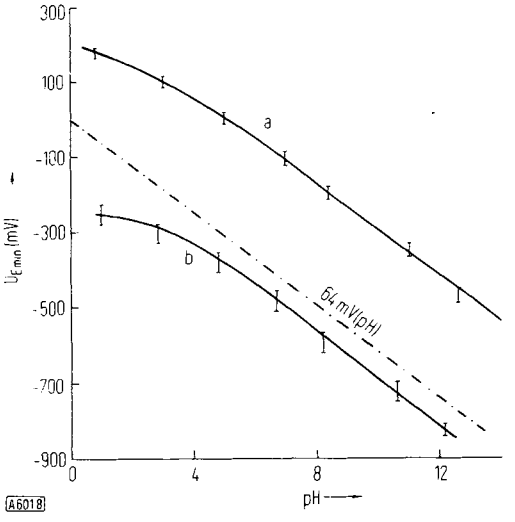


Fig. 8. pH-Dependence of the electrode potential at minimum capacity (on the standard hydrogen electrode scale) after a) anodic and b) cathodic polarization, measured on the <111> surface of germanium at 50 °C [19]. At pH > 4, the slope of the curves is 64 mV/pH.

The pH-dependence of the electrode potential has been determined by several authors [13, 19, 20]; curve (a) in Fig. 8 representing the results of *Gerischer* and *Mindt*. At pH > 4, the slope of this curve is 64 mV/pH, which means that the potential drop across the Helmholtz double layer must be fairly large, since it can be varied by a few hundred millivolts. *Gerischer* [19] has explained this by assuming that a dissociation double layer is present. It follows from the mechanism of the anodic dissolution of germanium [21] that the surface after anodic polarization is covered with OH groups. The dissociation on a <111> surface is then as follows:

$$\diagdown\!\!\diagup\!\!\text{Ge–OH} + OH^{\ominus} \rightleftharpoons \diagdown\!\!\diagup\!\!\text{Ge–O}^{\ominus} + H_2O \qquad (15)$$

and the equilibrium condition is given by

$$\mu_{Ge-OH} + RT \ln x_{Ge-OH} =$$
$$\mu_{Ge-O^{\ominus}} + RT \ln x_{Ge-O^{\ominus}} - F\,\Delta U_H + \mu_H + 2.3\,RT\text{pH} \qquad (16)$$

(where x_i is the mole fraction and μ_i is the chemical potential).

For electrostatic reasons, the proportion of $Ge-O^{\ominus}$ groups on the surface must be small, so that x_{Ge-OH} is practically 1. We thus obtain in the following form the pH-dependence that has also been found experimentally:

$$\Delta U_H = (RT/F)\,\text{pH} + \text{const.} \qquad (17)$$

[19] *M. Hoffmann-Perez* and *H. Gerischer*, Z. Elektrochem., Ber. Bunsenges. physik. Chem. *65*, 771 (1961).

[20] *P. J. Boddy* and *W. H. Brattain*, J. electrochem. Soc. *110*, 570 (1963).

[21] *F. Beck* and *H. Gerischer*, Z. Elektrochem., Ber. Bunsenges. physik. Chem. *63*, 500 (1959).

All these investigations discussed above have been carried out after anodic polarization. The potential drop across the Helmholtz double layer depends also on the polarization. If the germanium surface at a given pH is subjected not to anodic but to cathodic polarization, the capacity curve was observed in a more cathodic potential range (see Fig. 9a). The capacity minimum (no space charge layer, $U_R = 0$), therefore also appears at a different electrode potential. It follows therefore that, after cathodic polarization, the potential drop across the Helmholtz double layer assumes a different value.

It emerges from the current-voltage characteristic of the phase boundary [22] that, when U_E is changed externally in the cathodic direction, the surface coverage with OH groups is replaced by a surface coverage with hydrogen groups (see Fig. 9b) [12].

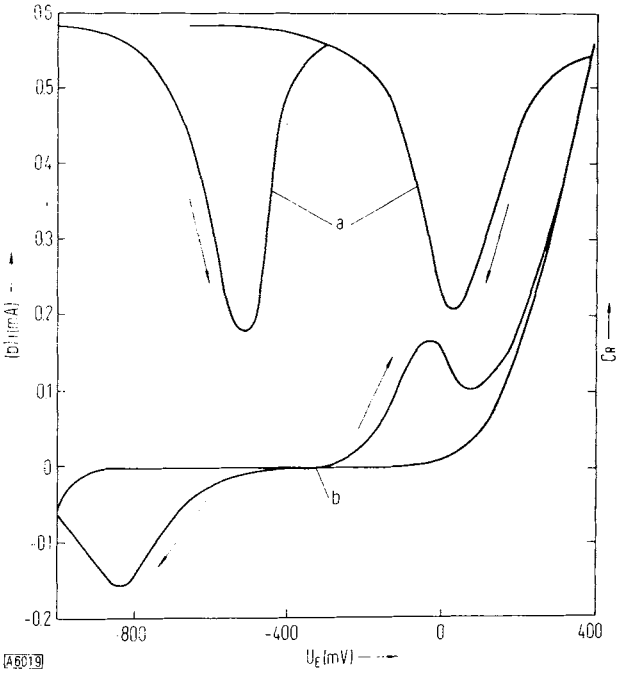


Fig. 9. a) Space-charge capacity C_R as a function of the electrode potential U_E after anodic (right) and cathodic (left) polarization of an n-type germanium electrode (15 ohm.cm), measured on the <111> surface against a saturated calomel electrode in a 0.01 N solution of H_2SO_4 (since only the position of the C_R - minimum is of interest here, the absolute values of C_R were not determined). — b) Current-voltage characteristic of an n-type germanium electrode (15 ohm.cm) (<111> plane), measured against a saturated calomel electrode, in a 0.01 N solution of H_2SO_4 [36].

Cathodic polarization is thus followed by the formation of a new Helmholtz double layer that is characteristic of hydride surfaces. This of course results in a change in the potential drop U_H across this double layer. The pH-dependence of the capacity minimum is similar to that after anodic polarization (cf. curves (a) and (b) in Fig. 8). Accordingly, there is a dissociation double layer also for hydride surfaces, the dissociation equilibrium being expressed as follows:

$$\diagdown\!\!\diagup\!\!\text{Ge–H} + OH^{\ominus} \rightleftharpoons \diagdown\!\!\diagup\!\!\text{Ge}^{\ominus} + H_2O \qquad (18)$$

[22] *H. Gobrecht*, *O. Meinhardt*, and *M. Lerche*, Ber. Bunsenges. physik. Chem. *67*, 486 (1963).

Investigations on silicon [14] have shown that the potential distribution across the Helmholtz double layer must again depend on the pH, but quantitative measurements are difficult, because the silicon electrode is covered with a silicon dioxide layer in aqueous solutions, with the exception of hydrofluoric acid.

In contrast to silicon, the picture concerning the potential distribution inside the Helmholtz double layer in germanium can be further refined [12]. Figure 8 shows that it is only at pH > 4 that the position of the capacity minimum is a linear function of the pH. At very low pH values, the position of the capacity minimum and the potential drop across the Helmholtz double layer are virtually independent of the pH. This is readily explained by the fact that the dissociation equilibrium in eq. (15) and that in eq. (18) are fully displaced to the left at such pH values. This does not mean that the potential drop disappears in the Helmholtz layer, since – as Fig. 9a shows – there is a great difference between the position of the capacity minimum of a hydroxide surface (*ca.* −500 mV) and that of a hydride surface (*ca.* +30 mV).

This behavior can be explained only by assuming that the two types of surface differ in their electrical moment. The Helmholtz double layer on the surface of germanium is therefore composed of two parts, namely a dissociation double layer and a dipole layer which lies inside the surface compound.

3.3. Application to Investigations of Reaction Kinetics

The distribution of potential at the semiconductor-electrolyte interphase is of interest in connection with electrochemical reactions at such electrodes. This will be shown by two examples.

Example 1. p-Type silicon is electrochemically dissolved in hydrofluoric acid when subjected to anodic polarization. The current-voltage characteristic (Tafel slope) plotted in a semilogarithmic coordinate system has a slope of $dU_E/d \log i = 60$ mV/decade [23]. Knowing the number of carriers (Z) participating in the rate determining step, one can calculate from the above value of the slope the transition factor α. In the present case, the value $\alpha Z = 1$ emerges from the equation:

$$\alpha Z = \frac{2.3\,RT}{F} \cdot \frac{1}{d\,U_E/d \log i} \qquad (19)$$

(where R is the universal gas constant and F is the Faraday constant).

On the assumption that $Z = 1$, *i.e.* that only one charge is involved in the rate-determining step, the transition factor itself has a value of one, which does not occur in practice in the case of metal electrodes. It should be added that this factor can be one only when the Helmholtz layer does not take up an external voltage. This is possible in semiconductors (silicon in this example), since the applied voltage can be taken up completely by the space-charge region in the semiconductor. This can be easily shown by measuring the interfacial capacity (see Fig. 10).

Measurements at the silicon-hydrofluoric acid interface have in fact shown that the potential drop across the Helmholtz layer does not change in anodic polarization [14], that is to say,

[23] *R. Memming* and *G. Schwandt*, Surface Sci. *4*, 109 (1966).

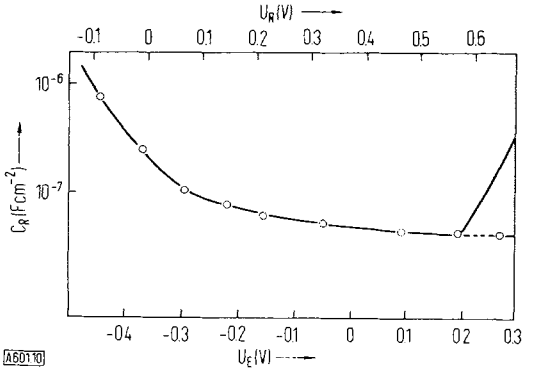


Fig. 10. Interfacial capacity C_R as a function of the electrode potential U_E of an n-type silicon electrode (1 ohm.cm) in 10 M hydrofluoric acid (measured on the saturated calomel electrode scale) [14].

Solid line: theoretical values (upper scale U_R); ○ - experimental values.

$\alpha = 1$. A further consequence of this result is: The concentration of holes at the surface is increased in accordance with eq. (4b) *i.e.* $p_s = p_o \exp (eU_R)/(kT)$ by a change in the band bending caused by the anodic polarization (this effect is shown as the upward bending of the energy bands). Since the external voltage appears only across the space-charge region, one can put $U_R = U_E + \text{const.}$ Substitution of this in eq. 4b gives

$$p_s = p_o \exp (e\,U_R)/(kT) = p_o \exp [e(U + \text{const.})]/(kT) \qquad (20)$$

Since the anodic dissolution current follows the same exponential law (eq. 10) it therefore increases in proportion to the hole concentration at the surface.

Example 2. As mentioned above, the surface of germanium subjected to cathodic polarization becomes coated with hydride groups instead of hydroxyl groups. This is indicated in the current-voltage curve (Fig. 9b) by the fact that a potential change in the cathodic direction is accompanied by a maximum in the cathode current [12, 22]. An anodic current maximum appears in the other sweeping direction. *Gerischer* and *Mindt* [24] have found that the reaction involved proceeds in two steps, one over the conduction band, and the other over the valence band [*]:

$$\text{Ge–OH} + \text{H}^{\oplus} + \text{e}^{\ominus} \rightleftharpoons \text{Ge}^{\bullet} + \text{H}_2\text{O} \qquad (21a)$$

$$\text{Ge}^{\bullet} + \text{H}^{\oplus} \rightleftharpoons \text{Ge–H} + \text{p}^{\oplus} \qquad (21b)$$

(where $e^{\ominus}$ is an electron in the conduction band and $p^{\oplus}$ is a hole in the valence band).

The authors assume that the reaction proceeds *via* an intermediate state represented by a surface radical. As shown before, the corresponding change of the potential drop ΔU_H in the Helmholtz layer is found from capacity measurements (Fig. 9a).

If H_2O_2 is added to the solution, an additional cathodic current (reduction of H_2O_2) can be expected. *Gerischer* and *Mindt* [25] have found however that the reduction of hydrogen peroxide (high redox potential) occurs only at that potential at which the hydroxide surface is changed into hydride surface. This leads to the assumption that the reduction occurs at the germanium radical by an electrochemical process:

$$\text{Ge}^{\bullet} + \text{H}^{\oplus} + \text{H}_2\text{O}_2 + \text{e}^{\ominus} \rightleftharpoons \text{Ge–OH} + \text{H}_2\text{O} \qquad (22)$$

[24] *H. Gerischer*, *A. Mauerer*, and *W. Mindt*, Surface Sci. *4*, 431 (1966).

[*] Electrochemical reactions basically involve either the conduction band or the valence band, depending on various factors which will not be discussed here.

[25] *H. Gerischer* and *W. Mindt*, Surface Sci. *4*, 440 (1966).

or that the following chemical reaction takes place:

$$\text{Ge–H} + H_2O_2 \rightarrow \text{Ge–OH} + H_2O \qquad (23)$$

This means that the hydroxide surface is re-formed continually in a cyclic process. The proof of this assumption is again based on the potential distribution[25]. Thus, a capacity curve typical of hydride formation is obtained after cathodic polarization without added H_2O_2 (see Fig. 9a), whereas the same polarization in the presence of H_2O_2 leads to a capacity minimum whose position is characteristic of a hydroxide surface (see the curve on the right in Fig. 9a). We shall return to this reaction mechanism in a different context.

3.4. Influence of Injection Processes on the Distribution of Charge and Potential

After the above description of the basic results pertaining to the potential distribution, an effect typical of semiconductor electrodes will now be discussed. The concentration of carriers is much smaller in semiconductors than in metals and the carriers in semiconductors are not only electrons in the conduction band, but also holes in the valence band. The number of carriers, particularly of the minority carriers (*e.g.* holes in an n-type semiconductor) is relatively small, but it can be increased by optical excitation or the injection of carriers during an electrochemical reaction. The following is a description of how the distribution of potential and the charge at the interphase is changed by these processes.

3.4.1. Surface Photovoltaic Effect

When a semiconductor electrode is exposed to light, the electrode potential U_E will assume a value different from that in the dark. The direction of this shift depends on the doping of the semiconductor. It has been found that the rest potential generally becomes cathodic in an n-type sample and anodic in a p-type sample. This difference indicates that the shift in the electrode potential is due to a change in the potential drop U_R across the space-charge region of the semiconductor, *i.e.* it is due to a change in the band bending. The cause of this effect is illustrated in Fig.11.

It will be assumed that the energy bands in the original state curve upward at the surface, *i.e.* that the space charge is positive (the corresponding negative charge is in the electrolyte). The optical excitation of electrons from the valence to the conduction band leaves behind holes in the valence band (Fig. 11a). The electron-hole pairs are separated by the electric field across the space-charge layer, and the electrons are drawn to the interior of the crystal, while the holes are drawn to the surface. The result is that the field is lowered and thus the band bending becomes smaller.

As shown before, this reduction in the positive space charge (change of the band bending downward in Fig. 1) is equivalent to a shift in the electrode potential in the cathodic direction. If the energy bands are bent downward in the dark (negative space charge), then the illumination causes a change of the band bending in the opposite direction, *i.e.*

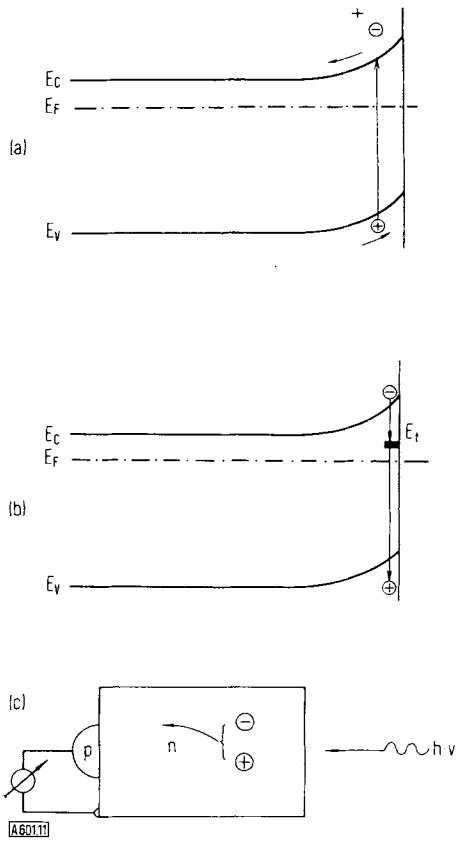


Fig. 11. (a) Energy gap model of a semiconductor illustrating the production of electron-hole pairs at the surface. — (b) Energy gap model of a semiconductor illustrating surface recombination *via* surface states. — (c) Semiconductor electrode with p-n junction on the reverse side of the electrode for detecting injected electron-hole pairs (schematic representation).

the photovoltaic effect has the opposite sign. It has already been seen that the type of band bending prevailing before illumination can be identified *e.g.* by measuring the interfacial capacity.

Brattain and *Boddy*[26] have investigated on germanium electrodes the quantitative relationship between the light-induced change in the electrode potential ΔU_E^L (and the change in the band bending ΔU_R^L) and the original band bending U_R. The variation of the photovoltage ΔU_R^L (change in the band bending) with the band bending U_R in the absence of light is given by the Poisson equation. Assuming that the concentration change is small ($dp = dn \ll n_o$, p_o) just outside of the space-charge region (between the bulk and the space-charge region), we find that the following equation holds for this variation:

$$\frac{d\,U_R^L}{dp} = \frac{1 - \exp(eU_R)/(kT)}{p_o + n_o \exp(eU_R)/(kT)} \cdot \frac{kT}{e} \qquad (24)$$

One can measure primarily only the light-induced change in the electrode potential ΔU_E^L (under galvanostatic conditions). The various band bendings in the dark are adjusted by an external voltage (see Fig. 12)[26], and determined by measuring the interfacial capacity. The experimental values satisfy eq. (24), which proves that $\Delta U_E^L = \Delta U_R^L$.

[26] *W. H. Brattain* and *P. J. Boddy*, Conf. On Clean Surfaces, New York Academy of Sci., Vol. *101*, Art. 3, 683 (1963).

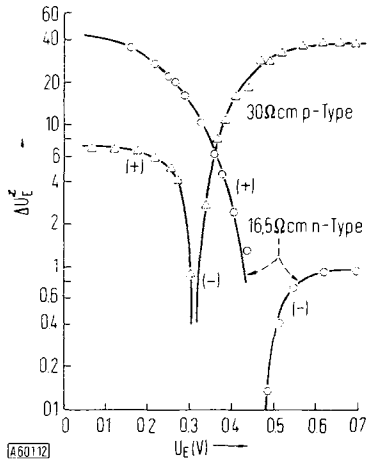


Fig. 12. Photovoltage ΔU_E^L (in arbitrary units) as a function of the electrode potential U_E (measured against a saturated calomel electrode) of p-type germanium (30 ohm.cm) and n-type germanium (16.5 ohm. cm) [26].

Similar investigations have been carried out on the variation of the photovoltage ΔU_E^L with the number of the injected carriers, particularly in the case of Ge, Si, GaP[27], and CdS[28]. Experiment again agrees well with theory in the case of germanium, but the relationships appear to be more complicated with other semiconductors examined.

The same effect can take place when carriers are not created by light, but are injected instead in electrochemical reactions. To produce electron-hole pairs in this manner, two reactions must in fact proceed simultaneously in opposite directions, *i.e.* in the anodic and the cathodic direction.The anodic process is mostly the electrochemical dissolution of the semiconductor electrode. If for example the atoms of the semiconductor go into solution with a valence of one, the equation of the reaction is as follows:

$$A + \lambda p^{\oplus} \xrightarrow{j^+} A^{\oplus} + (1-\lambda)e^{\ominus} \qquad (25)$$

(where λ is the distribution factor; if the reaction proceeds wholly *via* the valence band for example, then $\lambda = 1$).

This dissolution process is thought to involve both energy bands, *i.e.* $(1-\lambda)e^{\ominus}$ electrons are given off into the conduction band and $\lambda p^{\oplus}$ holes are extracted from the valence band. This means that the holes are neutralized by the liberation of electrons into the valence band. The corresponding anode current is given by j^+. When an oxidizing agent is introduced into the solution, it is reduced in a cathodic process. We shall assume that this reduction involves only valence-band electrons, in accordance with equation:

$$Ox \xrightarrow{j^-} Red + Zp^{\oplus} \qquad (26)$$

i.e. holes are injected into the valence band.

At equilibrium, the anode current j^+ is equal in magnitude to the cathode current j^-, *i.e.*

$$j^+ = j^- = j_{corr}. \qquad (27)$$

The partial currents are proportional to the charges transferred in unit time. However, λj_{corr} of holes injected in the reduction are consumed in the dissolution, so that $(1-\lambda)j_{corr}$ holes will be left behind. At the same time, however, $(1-\lambda)j_{corr}$ electrons are injected during the dissolution process, in accordance with eq. (25). These two reactions thus give rise to an equal number of electrons and holes, *i.e.* electron-hole pairs at the surface. The current corresponding to the pair production is given as

$$jp = (1-\lambda)j_{corr}. \qquad (28)$$

This pair production must exceed the thermal pair production i_s if it is to have an effective influence on the band bending.

This "electrochemical photovoltaic effect" was first detected by *Beck* and *Gerischer*[29] on germanium. A very large change (of several hundred millivolts) in the electrode potential (*i.e.* in the band bending) has been found to result from this pair formation in semiconductors with a wide band gap (*e.g.* GaP), in which the thermal pair production is insignificant[27].

3.4.2. Recombination Processes *via* Surface States

It has been shown in connection with the charge distribution inside the space-charge region that charge can also be stored in surface levels. Another property of such centers is that electron-hole pairs produced by light excitation or electrochemical reactions can recombine *via* such surface states (Fig. 11).

The mechanism of recombination *via* a lattice imperfection has been treated theoretically by *Shockley* and *Read*[30], and extended to surface processes by *Stevenson* and *Keyes*[31] and *Koc*[32]. The rate of recombination R' is proportional to the density of centers N_t and the change in the concentration Δn_o ($= \Delta p_o$) at the boundary between the interior of the crystal and the space-charge region. It depends furthermore on the position of the surface level with respect to the Fermi level, *i.e.* on the band bending. To obtain a magnitude characteristic of the surface recombination and independent of the change in the concentration Δn, the surface recombination velocity s is defined as

$$s = R'/\Delta n = N_t f(U_R) \qquad (29)$$

where s has the dimensions of velocity. The function $f(U_R)$ will not be discussed; suffice it to say here that s has about its maximum when the center passes through the Fermi level in the change of the band bending.

[27] *R. Memming* and *G. Schwandt*, Elektrochim. Acta, in press.
[28] *R. Williams*, J. chem. Physics *32*, 1505 (1960).
[29] *H. Gerischer* and *F. Beck*, Z. physic. Chem. *23*, 113 (1960).
[30] *W. Shockley* and *W.T. Read*, Physic. Rev. *87*, 835 (1952).
[31] *D.T. Stevenson* and *R. J. Keyes*, Physica *20*, 1041 (1954).
[32] *S. Koc*, Czechoslov. J. Physics Sect. B, *10*, 579 (1960).

Recombination in surface levels is important in the investigations of the carrier injection. It affects the surface photovoltaic effect, and must also be considered in connection with the injection of minority carriers occurring in electrochemical processes at semiconductor electrodes. Furthermore, the measurement of the surface recombination can also be of use in the analysis of the surface states. This offers a further possibility of finding out something about the chemical nature of these states. This will be illustrated below by an example, but a method used for investigating the recombination process will first be described briefly.

The light-induced electron-hole pairs diffuse into the interior of the crystal provided that they do not recombine *via* traps. If there is a p-n junction on the reverse side of the electrode, then the electron-hole pairs are separated in the internal field of this junction. When the p-n junction is short-circuited (Fig.11c) *e.g.* by an ampere meter, then the corresponding short-circuit current is a direct measure of the number of the arriving electron-hole pairs[*]. At strong surface recombination at the semiconductor-electrolyte interface, only relatively few electron-hole pairs diffuse to the p-n junction, *i.e.* the corresponding short-circuit current i_K is small. A more accurate treatment[33] gives the following relationship for i_K

$$i_K \approx 1/s \qquad (30)$$

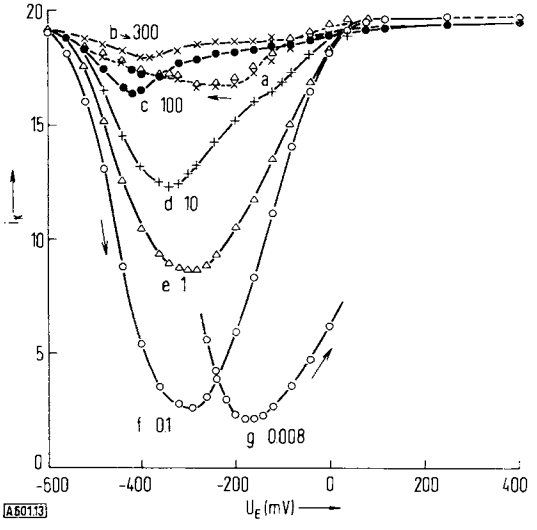


Fig. 13. Short-circuit current i_K as a measure of the surface recombination s ($s \approx 1/i_K$), determined as a function of the electrode potential U_E (on the saturated calomel electrode scale) of an n-type germanium electrode (15 ohm.cm) with a <111> surface in a 0.01 N solution of H_2SO_4 [36]. (a) After anodic polarization. — (b) - (g) after cathodic polarization. With curves (a)-(f), the sweeping time τ in the measurement was 1 sec, for (g) 2 msec; the polarization times t_k are given by the curves in sec.

provided that the depth of penetration of the light is sufficiently small. Fig. 13 shows the curve of recombination measured by this method as a function of the electrode potential.

In principle, the energy of the recombination center can be determined from such curves, but this will not be discussed here. It is sufficient to point out that the minimum short-circuit current $i_{k,\,min}$ (or the maximum of recombination) is a measure of the number of the recombination centers:

$$i_{k\,min} \approx 1/s_{max} \approx 1/N_t \qquad (31)$$

Germanium will again be used as an example. The recombination curves shown in Fig. 13 were measured under the following conditions: After anodic polarization (curve a), the short-circuit current has no minimum, *i.e.* there are practically no centers present. This was to be expected, since the centers were undetectable also in the capacity measurements (Fig. 9a). The same result was obtained after fairly prolonged cathodic polarization, during which the hydroxyl groups on the surface were replaced by hydride groups, this result indicating that the hydride surface, too, was practically perfect[36]. Surface recombination occurred only after a shorter duration of cathodic polarization (curves c–g in Fig. 13). At longer polarization times, the number of recombination centers was found to decrease (the sweeping time τ in the measurement was much smaller than t_k).

Capacity measurements have shown that the time in which the centers are present is exactly the same as is needed for the changing of a hydroxide surface to a hydride surface. It seems feasible to assume on the basis of eq. (21) that the recombination centers are identical with $\equiv$Ge$^\bullet$ surface radicals postulated as intermediate state. As mentioned before the addition of H_2O_2 to the electrolyte changes the hydride surface back to the hydroxide surface in a cyclic process. Thus, radicals are continuously re-formed [see eqs. (21)–(23)], so that they are present at a certain concentration in the stationary state[37]. As proved experimentally the recombination centers show the same behavior; even after a very long cathodic polarization, the recombination is as high as found without H_2O_2 after very short polarization times (curve f, Fig. 13).

Comparison between the experimentally observed kinetic properties of the centers and the theoretical properties of the radicals suggests that the surface states are identical in this case with the radicals. Capacity measurements show that the number of surface states or radicals amounts only to about 0.01 % of the total surface coverage.

It has been suspected before that surface states are brought about by surface atoms with unpaired electrons. Though such proposals remain largely hypothetical, the electric and electrochemical investigations of germanium electrodes give an excellent insight into the nature of surface states.

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Translated by Express Translation Service, London

[*] Refs. [33,34,35] contain a more accurate description of this method, which can also be used for measuring the minority carriers injected by electrochemical process.

[33] *W. H. Brattain* and *C. G. B. Garrett*, Bell System techn. J. *35*, 1019 (1956).

[34] *R. Memming*, Surface Sci. *1*, 88 (1964).

[35] *H. U. Harten* and *W. Schultz*, Z. Physik *141*, 319 (1955).

[36] *R. Memming* and *G. Neumann*, Physics Letters *24 A*, 19 (1967).

[37] *R. Memming* and *G. Neumann*, Surface Sci., in press.

Cyclopentadienylgold(I) and Cyclopentadienyl-(triphenylphosphine)gold(I) [1]

By *R. Hüttel, U. Raffay*, and *H. Reinheimer* [*]

Pure cyclopentadienyl-metal compounds involving elements of the first sub-group have not been described hitherto. Only (triethylphosphine)cyclopentadienylcopper(I) is known [2].

We have now synthesized cyclopentadienylgold(I). The success of the method depends on preparing solutions of AuCl in organic solvents in which it is normally insoluble. This may be accomplished by means of a loose addition of a cyclic olefin. Dicyclopentadienylgold(I) chloride [3] and *trans,trans, cis*-1,5,9-cyclododecatrienegold(I) chloride [3] are soluble in tetrahydrofuran (THF) and on treatment with cyclopentadienylsodium afford the desired C_5H_5Au.

About 1 g of the olefin-gold(I) chloride is dissolved in 100 ml of THF/ether (1:4) and treated at −60 °C under nitrogen with a solution of C_5H_5Na (3 molar equiv.) in THF. A yellow precipitate is at once formed but dissolves in the excess of C_5H_5Na solution to give a colorless solution. The yellow substance separates again on addition of dry ice. After centrifugation at −30 °C the precipitate is washed three times with 96 % alcohol and twice with ether and then taken up in n-pentane. All solvents are precooled to −70 °C. On evaporation of the pentane under vacuum at −30 °C there remains a powdery, yellow insoluble substance whose elemental composition corresponds to the formula C_5H_5Au.

The substance is sensitive to heat and friction. It is stable for about an hour at room temperature but often deflagrates on gentle warming.

The same compound was obtained by treating the olefin-gold(I) chloride with cyclopentadiene (Cp) and triethylamine but was then not analytically pure.

Since the insolubility and instability of C_5H_5Au prevent its closer study, the soluble and more stable cyclopentadienyl-(triphenylphosphine)gold(I) was prepared.

About 1 g of (triphenylphosphine)gold(I) chloride [4] was made into a slurry in 20 ml of ether and treated at −30 °C under nitrogen with an excess of C_5H_5Na solution in ether (5×10^{-3} mole/liter). The temperature was slowly raised to 0 °C and the mixture was stirred for an hour. The whole was poured into 200 ml of ice-water with vigorous stirring and then filtered. The residue was washed first with water, then with cold acetone, and finally with ether. For purification it was dissolved in THF/acetone at 0 °C and treated dropwise with ice-water. Colorless rhombohedral crystals of the composition $C_{23}H_{20}AuP$ were obtained; they decompose above 100 °C.

The same compound was detected by NMR spectroscopy in the products of the following reactions:

C_5H_5Au + triphenylphosphine (TPP)
TPP·AuCl + Cp + triethylamine
TPP·AuCl + Cp + KOH
TPP·AuCl + Cp + $NaOCH_3$.

The IR spectrum (KBr disc) of cyclopentadienyl(triphenylphosphine)gold(I) (TPP·AuC_5H_5) contains the following bands in addition to those that occur in the spectrum of TPP·AuCl:

642 w, 734 s, 803 s, 922 w–m, 970 m, 998 m, 1404 m (cm^{-1})[5]

An ionic cyclopentadienyl-metal bond is excluded because there are two bands in the region around 1000 cm^{-1} [6]; it is questionable whether a π bond of the ferrocene type is present because the intense bands at about 1100 cm^{-1} are missing [6]. The only remaining possibility is a σ bond.

The UV spectrum of TPP·AuC_5H_5 resembles the spectra of σ-cyclopentadienyl(triethylphosphine)copper(I) and di(cyclopentadienyl)mercury(II) [2]. Its maximum lies at 236.6 nm (ε = 33400 in dioxane); TPP and TPP·AuCl give no maximum near this wavelength.

Only a few ^1H–NMR measurements of σ-cyclopentadienyl-metal compounds are available [7]. For TPP·AuC_5H_5 we find only one sharp signal (τ = 3.7) [8] for the protons on the five-membered ring, corresponding to a σ-bonded cyclopentadienyl ligand undergoing rapid exchange of the carbon-metal bond [9].

The NMR spectrum of (methylcyclopentadienyl)-TPP-gold(I), which we have so far obtained only in solution – by treating TPP·AuCl with methylcyclopentadienylsodium or with methylcyclopentadiene + $NaOCH_3$ – shows three signals, namely at τ = 3.9, 4.15, and 7.7 (2:2:3). This indicates that in this instance the metal is σ-bonded to the carbon atom carrying the CH_3 group [10].

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[*] Prof. Dr. R. Hüttel, Dipl.-Chem. U. Raffay, and Dipl.-Chem. H. Reinheimer
Institut für Organische Chemie der Universität,
Abteilung für Technische Chemie
Karlstr. 23
8 München 2 (Germany)

[1] Part 5 of Olefin-Gold Complexes. – Part 4: *R. Hüttel, H. Reinheimer*, and *K. Nowak*, Tetrahedron Letters *1967*, 1019.

[2] *G. Wilkinson* and *T. S. Piper*, J. inorg. nuclear Chem. *2*, 32 (1956).

[3] *R. Hüttel, H. Reinheimer*, and *H. Dietl*, Chem. Ber. *99*, 462 (1966).

[4] *M. Levi-Malvano*, Atti Reale Accad. naz. Lincei, Ser. 5, *17* I, 847 (1908).

[5] s = strong, m = medium, w = weak.

[6] *H. P. Fritz* in *F. G. A. Stone* and *R. West*: Advances in Organometallic Chemistry. Academic Press, New York, London 1964, Vol. 1.

[7] *G. Wilkinson* and *F. A. Cotton*, Progr. inorg. Chem. *1*, 51 (1959); *H. P. Fritz* and *K. E. Schwarzhans*, Chem. Ber. *97*, 1390 (1964); *H. P. Fritz* and *C. G. Kreiter*, J. organometallic Chem. *4*, 313 (1965).

[8] Recorded in $DCCl_3$ with a Varian A 60.

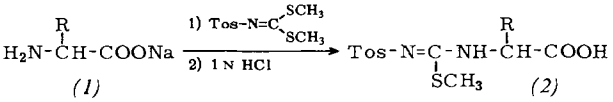
[9] *T. S. Piper* and *G. Wilkinson*, J. inorg. nuclear Chem. *3*, 104 (1956).

[10] *H. P. Fritz* and *K. E. Schwarzhans*, Chem. Ber. *97*, 1390 (1964).

N-[(Methylthio)-*N*-tosylformimidoyl]amino Acids [1]

By *J. Gante* [*]

Heating the sodium salts of the amino acids *(1a)–(1d)* with *S,S*-dimethyl *N*-tosyldithiocarbonimidate [2] (molar ratio 1:1) in boiling ethanol/water (2:1) for five to six hours and then adding an equivalent amount of 1 N HCl gives the hitherto unknown *N*-[(methylthio)-*N*-tosylformimidoyl]-amino acids *(2a)–(2d)*. In the case of *(1d)* (L-glutamic acid the disodium salt is used.



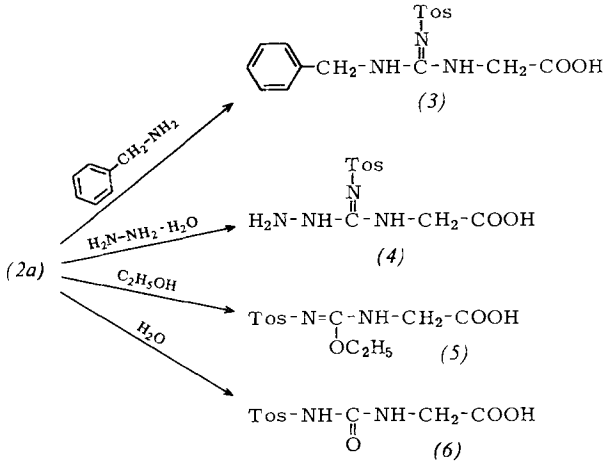
(1) *(2)*

Tos = *p*-toluenesulfonyl

	R	Yield (%)	M.p. (°C)	Optical rotation
(2a)	$-H$	76	173–175	
(2b) DL-Form	$-CH_3$	61	135–136	
(2c) DL-Form	$-CH_2-C_6H_5$	85	168–170	
(2d) L-Form	$-CH_2-CH_2-COOH$	64	151–153	$[\alpha]_D^{25} = -24.4°$ (c = 1, ethanol)

Compounds *(2a)–(2d)* are colorless, crystalline substances that react weakly acidic and dissolve readily in ethanol but only slightly in water; they can be readily recrystallized from mixtures of these two solvents from which they often separate first as oils.

These compounds are susceptible to aminolysis, ethanolysis, and hydrolysis. Thus *(2a)* (as the sodium salt) reacts with an excess of benzylamine in boiling ethanol/water (3:1) within 8 h to give *N*-(*N*^{1}-benzyl-*N*^{2}-tosylamidino)glycine *(3)* (yield 41 %, m.p. 196–198 °C), and with an excess of hydrazine hydrate on six hours' heating with water under reflux to give *N*-(hydrazino-*N*-tosylformimidoyl)glycine *(4)* (yield 50 %, m.p. 146–147 °C).



When the sodium salt of *(2a)* (obtained by adding an equivalent amount of 1 N $NaOC_2H_5$) is heated for 30 h in boiling ethanol, ethanolysis occurs to yield *N*-(ethoxy-*N*-tosylformimidoyl)glycine *(5)* (yield 28 %, m.p. 166–168 °C). When, however, double the amount (100 % excess) of sodium ethoxide is used and the mixture is boiled for 15 h, *N*-(tosylcarbamoyl)glycine *(6)* (yield 22 %, m.p. 187–188 °C) is obtained, probably under the hydrolytic influence of small amounts of water present in the ethanol.

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[*] Dr. J. Gante
Institut für Organische Chemie der Freien Universität
Thielallee 63–67
1 Berlin 33 (Germany)

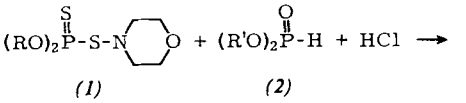
[1] This work was supported by the Deutsche Forschungsgemeinschaft.

[2] *R. Gompper* and *W. Hägele*, Chem. Ber. *99*, 2885 (1966).

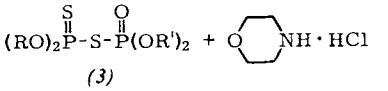
Synthesis of Asymmetric *O,O,O,O*-Tetraalkyl Dithiopyrophosphates

By *L. Almasi* and *L. Paskucz* [*]

We have found a simple process for preparing asymmetrical *O,O,O,O*-tetraalkyl dithiopyrophosphates *(3)* that have powerful anticholinesterase activity. This method affords a 95 % yield and avoids the high-vacuum distillation necessary for purification in all previous preparations of these compounds [1–3]. *O,O*-Dialkyl *S*-morpholinodithiophosphate *(1)* is treated with a dialkyl phosphite *(2)* in a stream of anhydrous HCl [4].



(1) *(2)*



(3)

	R	R'
(3a)	C_2H_5	C_2H_5
(3b)	C_2H_5	C_4H_9
(3c)	C_2H_5	i-C_4H_9
(3d)	i-C_4H_9	C_2H_5

	R	R'	n_D^{20} [a]	d_4^{20}	Mol. refraction Calc. Found	Yield (%)
(3a)	C_2H_5	C_2H_5	1.5000	1.2175	77.95 77.87	95
(3b)	C_2H_5	C_4H_9	1.4892	1.1351	96.54 96.26	96
(3c)	C_2H_5	i-C_4H_9	1.4880	1.1322	96.54 96.30	94
(3d)	i-C_4H_9	C_2H_5	1.4870	1.1302	96.54 96.33	95

[a] Values in the literature: For *(3a)* n_D^{20} = 1.5008 [1], 1.4964 [3], n_D^{25} = 1.4969 [2]; for *(3b)* n_D^{20} = 1.4920 [3].

The elemental compositions, molecular refractions, and IR spectra (maxima at 555, 653, and 1270 cm^{-1}, which correspond to P–O–P, P=S, and P=O groups) prove the purity and structure of the compounds *(3a)–(3d)*.

Experimental:

The thioamide *(1)* (0.04 mole) in anhydrous ether (100 ml) is treated at room temperature with an equivalent amount of *(2)* in a two-necked flask fitted with a $CaCl_2$ tube and a tube for introduction of gas. A stream of anhydrous hydrogen chloride is passed into the ice-cooled solution. After saturation of the solution with HCl, the precipitated morpholine hydrochloride is filtered off and the etheral solution is concentrated (at 10 mm) to half its volume, treated with 50 ml of petroleum ether, and washed successively with 20 ml of water, 20 ml of sodium hydrogen carbonate solution, and 20 ml of water. The organic layer is dried for 2 h over anhydrous $MgSO_4$, and the solvent is removed at room temperature (1 mm, 1 h). The residue *(3)* is a colorless liquid.

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[*] Dr. L. Almasi and Dipl.-Chem. L. Paskucz
Academia Republicii Socialiste Romania
Filiala Cluj
Institutul de Chimie
Str. Donath No. 59–65
Cluj (Roumania)

[1] *N. N. Melnikoff, K. D. Shevzova-Schilovskaya*, and *M. I. Kagan*, Ž. obšč. Chim. *30*, 200 (1960).

[2] *W. Lorenz* and *G. Schrader*, German Pat. 1159934; Chem. Abstr. *60*, 11898b (1964).

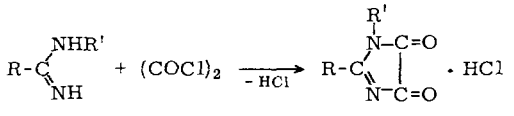
[3] *J. Michalski* and *J. Wassiak*, J. chem. Soc. (London) *1962*, 5056.

[4] The course of the reaction will be discussed in a paper to be published later.

α-Iminoalkyl Isocyanates

By *L. I. Samaraj, V. A. Bondar,* and *G. I. Derkatsch* [*]

We recently ascertained that amidines *(1)* react very readily with oxalyl dichloride to give imidazoline-4,5-dione hydrochlorides *(2)* [1,2].

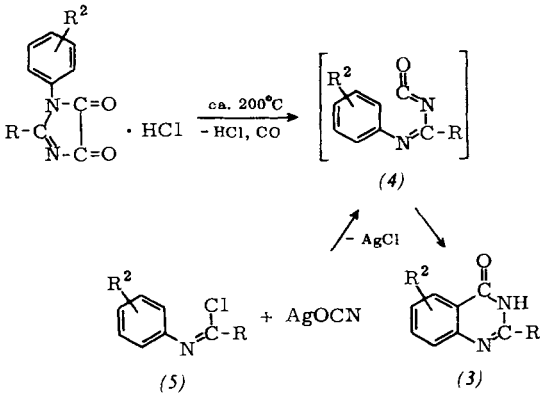


(1) *(2)*

R = Alkyl, Aryl

R' = H, Alkyl, Aryl

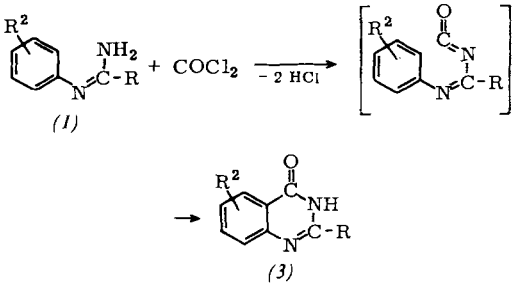
The products *(2)*, R' = aryl, lose HCl and CO when heated and are converted into 4-quinazolones *(3)*. These are formed by way of iminoalkyl isocyanates *(4)* as intermediates.



(4) *(5)* *(3)*

The same 4-quinazolones are obtained on treatment of the *N*-(chloroalkylidene)anilines *(5)* with silver cyanate.

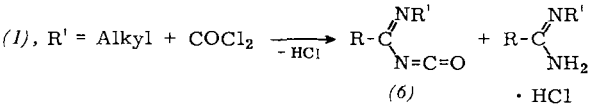
N-Arylamidines *(1)*, R' = aryl, react with phosgene in hot inert solvents (benzene, toluene, xylene, chlorobenzene, *etc.*) (80–110 °C), again yielding 4-quinazolones *(3)* in almost quantitative yields [3].



(1) *(3)*

This reaction permits the one-stage preparation of 4-quinazolones containing various substituents in the benzene ring.

On the other hand, *N*-alkylamidines *(1)*, R' = alkyl, react with phosgene under the same conditions to give iminoalkyl isocyanates *(6)*. These products are relatively stable; they are colorless liquids with a powerful odor, with the exception of *(6d)* which is odorless. Reaction of the iminoalkyl isocyanates with amines or alcohols gives substituted ureas or urethanes, respectively. The compounds *(6)* react very slowly with water; their IR spectra are in accord with the structures assigned.



(6)

	R	R'	Yield (%)	B.p. (°C/mm)	n_D^{20}	d_4^{20}
(6a)	CCl_3	CH_3	40	63/8	1.5042	1.4658
(6b)	CCl_3	C_2H_5	30	76/12	1.4954	1.3711
(6c)	CCl_3	n-C_4H_9	44	53/0.2	1.4892	1.2734
(6d)	CCl_3	$CH_2CH_2C_6H_5$	63	90/0.03	1.5498	1.3312

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[*] L. I. Samaraj, V. A. Bondar, and Prof. G. I. Derkatsch
Institute for Organic Chemistry of the Ukrainian Academy of Sciences
str. Vyborhskaja h. 80/17 z. 76
Kiev-67 (USSR)

[1] *L. I. Samaraj, W. A. Bondar,* and *G. I. Derkatsch,* Ž. org. Chim. *1*, 2004 (1965).

[2] *L. I. Samaraj, W. A. Bondar,* and *G. I. Derkatsch,* Chim. geterocikličeskich Soedinenij, in press.

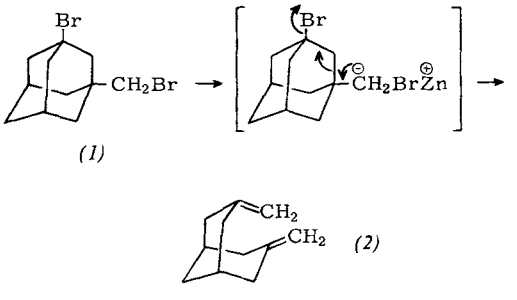
[3] *L. I. Samaraj, W. A. Bondar,* and *G. I. Derkatsch,* Chim. geterocikličeskich Soedinenij, in press.

A New Fragmentation in the Adamantane Series

By *F. N. Stepanov* and *V. D. Sukhoverkhov* [*]

We recently reported [1] the preparation of 1-bromo-3-(bromomethyl)adamantane *(1)*, which was later synthesized also from 3,7-bismethylenebicyclo[3.3.1]nonane *(2)* by *Stetter* and *Gärtner* [2].

We have now found that, unlike 1-bromoadamantane, the dibromide *(1)* reacts readily with magnesium in ether. The main product is a resinous mass that we have not investigated in detail. The reaction takes a different course when the dibromide *(1)* is treated with zinc in dimethylformamide. In the latter case, two bromine atoms are removed and 3,7-bismethylenebicyclo[3.3.1]nonane *(2)* is obtained. The reaction is thus the reverse of the synthesis of *(1)* from the hydrocarbon *(2)* and bromine [2].



(1) *(2)*

A mixture of dibromide *(1)* (10 g), Na_2CO_3 (6.5 g), NaI (0.3 g), zinc dust (5 g), and dimethylformamide (10 ml) is boiled for 5 h. After dilution with water the hydrocarbon formed is distilled off in steam. Yield 3.6 g (75 %), m.p. 78–79 °C (from methanol) (lit. [2], m.p. 75 °C).

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[*] Prof. F. N. Stepanov and Dipl.-Ing. V. D. Sukhoverkhov
Polytechnic Institute
Kiev 56 (U.S.S.R)

[1] *F. N. Stepanov, W. F. Baklan,* and *S. D. Issaev,* Ž. org. Chim. *1*, 280 (1965).

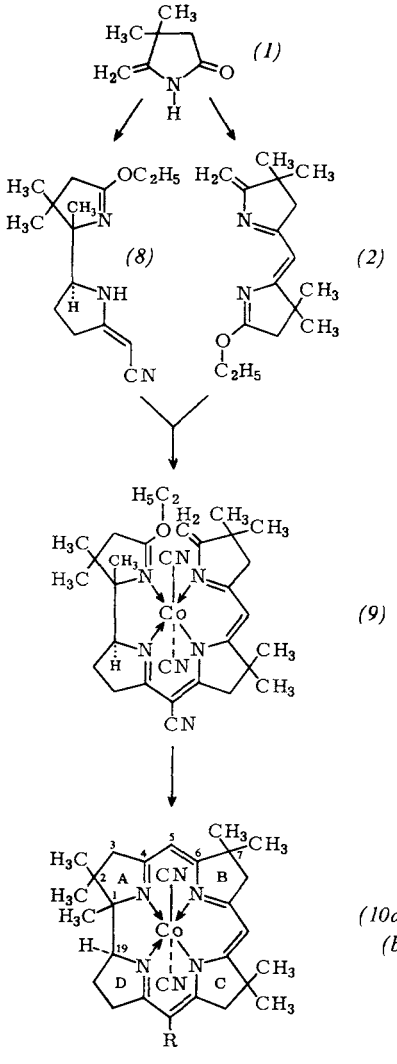
[2] *H. Stetter* and *J. Gärtner,* Chem. Ber. *99*, 3888 (1966).

rac.-Dicyano-(1,2,2,7,7,12,12-heptamethylcorrin)-cobalt(III) [**]

By *I. Felner, A. Fischli, A. Wick, M. Pesaro, D. Bormann, E. L. Winnacker,* and *A. Eschenmoser* [*]

In our earlier work on the synthesis of corrin complexes the enamide *(1)* served as precursor of ring C of nickel(II) and cobalt(III) complexes of *rac.*-7,7,12,12,19-pentamethylcor-

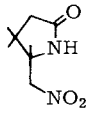
rin[1]. Since that time, methods have been developed which permit use of this readily accessible enamide as precursor, not only of ring C, but also of rings A and B[2] of correspondingly methylated corrin derivatives. We now report the preparation of the (A)–(D) intermediate *(8)*. Corrin(III)-cobalt complexes of type *(10)* are now readily accessible by two-stage condensation of this compound with the component *(2)* used previously[1].



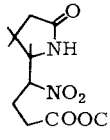
The impulse to work out the reaction sequence *(1)* → *(3)* → *(8)* was provided by the observation that nitromethane reacts readily and almost quantitatively with the enamide *(1)* in the presence of potassium t-butoxide. The product *(3)* doubtless arises by nucleophilic addition of deprotonated nitromethane to the *N*-acylketimine tautomer of the enamide[***]. The mixture of diastereoisomers *(4a,b)* formed on Michael addition of *(3)* to methyl acrylate is the result of thermodynamic control; they are separable by fractional crystallization and equilibrate to the same mixture of diastereoisomers under the conditions of the addition. Since the corresponding diastereoisomeric dilactams are very readily separated by virtue of their differing solubilities, the mixture *(4a,b)* is directly submitted to catalytic hydrogenation for preparative purposes. The series of steps *(5a)* → *(8)* carried out with the lower-melting dilactam isomer *(5a)* reflects types of reaction that were worked out earlier[1a,c]. The structural selectivity of the condensation step *(6)* → *(7)* is explained on steric grounds; the structure of the product *(7)* is unambiguously proved by the mass spectrum. As usual with compounds of this type[1], the (A–D) intermediate *(8)* exists in solution as a 1:1 mixture of the two isomers with the diastereoisomeric arrangement of substituents on the double bond.

Assignment of the *anti*-configuration[3] to the lower-melting dilactam isomer *(5a)* is for the moment unproved. The assignment was originally[4] made on the basis of IR-spectroscopic comparison with known *anti*- and *syn*-dilactams of the same type[1a,c]; it is supported in particular by the fact that the dicyanocobalt(III) complex *(9)* derived from the lower-melting lactam *(5a)* can be cyclized to a dicyano-(corrin)cobalt(III) complex whose UV, IR, and NMR spectroscopic data correspond to those of authentic 1,19-*anti*-dicyano(corrin)cobalt(III) complexes[1b,c]. The condensation *(8)* + *(2)* and subsequent complex formation to give *(9)*, the cyclization to *(10a)*, and hydrolytic removal of the cyano groups from the chromophore, yielding the corrin complex *(10b)* named in the title, parallel results obtained previously [1b,c] in the tetramethyl and pentamethyl series.

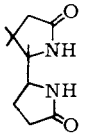
(1)
↓ 84 %
+ 0.3 equiv. of t-BuOK in nitromethane/18 h/60 °C

(3)

M.p. 140 °C (from CH_2Cl_2-petroleum ether)
IR (cm^{-1}): 3420m, 1700s, 1555s ($CHCl_3$) [5]
NMR (ppm): 1.11(S/3H), 1.16(S/3H), 1.31(S/3H), 2.23(D/16.5/1H), 2.33(D/16.5/1H), 4.49(D/12/1H), 4.57(D/12/1H), 6.5–7.0(B/1H) ($CDCl_3$)

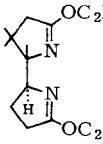
↓ 78 %
+ 0.1 equiv. of 40 % methanolic solution of benzyltrimethylammonium hydroxide in methyl acrylate, 4 h/RT

(4)

M.p. 100–105 °C (from CH_2Cl_2-hexane, diastereoisomer mixture a, b);
anti: *syn* [3] = 45:55)
a) 130 °C (*anti*); b) 124 °C (*syn*)
IR (cm^{-1}): (*anti*) 3410m, 1725s, 1700s, 1555s ($CHCl_3$)
NMR (ppm): (*anti*) 1.19(S/3H), 1.23(S/3H), 1.33(S/3H), 1.92–2.67(M/6H), 3.70(S/3H), 4.66–5.0(M/1H), 6.3–6.4(B/1H) ($CDCl_3$)

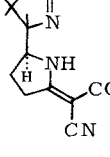
↓
Raney nickel in CH_3OH/H_2/100 atm/RT [40 % of *(5a)* from diastereoisomer mixture *(4a,b)*, 88 % of *(5a)* from pure *anti*-isomer *(4a)*]

(5)

M.p. a): 212 °C (*anti* [3]; from CH_2Cl_2-hexane)
b): 292 °C (*syn*; from CH_3OH, insol. in CH_2Cl_2)
IR (cm^{-1}): (*anti*) 3330s, 3220s, 1681s (with side bands at 1708m and 1641m) (Nujol)
(*syn*) ν̃(C=O) single band at 1679s (Nujol)
NMR (ppm): (*anti*) 1.30(S/6H),1.39(S/3H), 1.9–3.2(M/6H), 4.25–4.66(M/1H), 7.9–8.3(2H) (CF_3COOH)

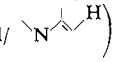
(5a)
↓ 82 %
(5a) [3] + 3 $(CH_3CH_2)_3O^{\oplus}BF_4^{\ominus}$ in CH_2Cl_2/4 h/RT

(6)

B.p. 77–79 °C/0.01 mm; $n_D^{22} = 1.4721$
IR (cm^{-1}): ν̃(C=N) double band 1645s/1628s ($CHCl_3$) (*syn*: single band 1629s)
NMR (ppm): 0.9–1.4(3S + 2T/*J ca.* 7/15H), 1.85–2.50(M/4H), 1.90/3.05(2AB–D/*J ca.* 15/2H), 3.70–4.05(M/1H), 4.16(Q/*J ca.* 7/4H) ($CDCl_3$)

↓ 82 %
+ 0.1 equiv. of $(CH_3CH_2)_3N$ in 2 equiv. of t-butyl cyanoacetate /140 h/40 °C

(7)

M.p. 147 °C (from hexane)
UV (nm): 277(4.38) (C_2H_5OH)
IR (cm^{-1}): 3410w, 3320m, 2200s, 1664s, 1640s, 1586s ($CHCl_3$)
m/e: 154(100 %/$C_9H_{16}ON$, ring A), 126(42 %/154–C_2H_4)

↓ 87 % CF_3COOH/10 min/RT

(8) M.p. 117–120 °C (from CH_2Cl_2-hexane and sublimed at 100 °C/0.002 mm)
UV (nm): 265(4.39) (C_2H_5OH)
IR (cm^{-1}): 3410m, 2180s,1640s,1610s ($CHCl_3$)
NMR (ppm): 3.63 (S broad/ )
3.95  ($CDCl_3$)
m/e: 261(11 %/M^+), 154(100 %, ring A), 126(81 %, ring A–C_2H_4), 107(14 %, ring D)

60 % a) *(8)* + 1.03 equiv. of $NaOC_2H_5$ + 1.0 equiv. of *(2)* in diglyme/5 h/60 °C
b) $Co(II)(H_2O)_6(ClO_4)_2$ in C_2H_5OH/2.5 h/RT + 3 equiv. of KCN in C_2H_5OH–H_2O

(9) M.p. 258 °C(decomp.; from methanol-ethyl acetate)
UV (nm): 310(4.08), 318(4.10), 340(3.57), 358(3.49), 461(4.08), 480(4.03/shoulder) (C_2H_5OH)
IR (cm^{-1}): 2220m, 2140w, 1618s, 1550s, 1485s, *etc.* ($CHCl_3$)

↓ 65 % 3.5 equiv. of t-BuOK in DMF-t-BuOH (1:4)/17 h/50 °C (exclusion of air)

(10a) Decomp. pt. 250 °C (from methanol-diisopropyl ether)
UV (nm): 271(4.14), 296(3.85), 307(3.89), 320(3.89/shoulder), 337(4.19/shoulder), 351(4.38), 388(3.81) 413(3.75), 465(3.65/shoulder), 496(3.85/shoulder) 527(4.04), 560(4.00) (C_2H_5OH)
IR (cm^{-1}): 2200m, 2118w, 1640m, 1598s, 1572 m, 1510s, 1480s, *etc.* ($CHCl_3$)
NMR (ppm): 1.20–1.50(5S/21H), 1.7–2.4 (M/2H), 1.5–2.5(2S+ 1AB(*J ca.* 17) + M/8H), 4.31(M/1H), 5.60(S/1H), 5.64(S/1H), ($CDCl_3$)
m/e: 488(22 %), 487(M^+–2CN/60 %), 471(21 %)

↓ 86 % 0.1 N HCl–H_2O, 40 h/230 °C (under N_2)

(10b) M.p. 270 °C (decomp.; from $CHCl_3$-hexane)
UV (nm): 268(4.01), 286(3.77), 296(3.85), 310(3.82), 338(4.09/shoulder), 353(4.41), 384(3.50), 406(3.51), 487(3.66), 521(3.86), 559(3.96) (C_2H_5OH)
IR (cm^{-1}): 2118w, 1635w, 1597s, 1571s, 1518s, 1500s, *etc.* ($CHCl_3$)
NMR (ppm): 1.24/1.31(2S/21H), 1.5–2.3(M/2H), 1.45–3.30(2S + 1 AB (*J ca.* 17) + M/8H), 4.10–4.40(M/1H), 5.40(S/1H), 5.44(S/1H), 5.56 (S broad/1H) ($CDCl_3$)
m/e: 463(33 %), 462(100 %/M^+ – 2 CN), 466(52 %/M^+ – 2CN – CH_4)

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[*] I. Felner-Caboga, dipl.-Ing. Chem. ETH, A. Fischli, dipl.-Ing. Chem. ETH, Dr. A. Wick, Dr. M. Pesaro, Dr. D. Bormann. E. L. Winnacker, dipl.-Ing. Chem. ETH, and Prof. A. Eschenmoser
Organisch-chemisches Laboratorium
der Eidg. Techn. Hochschule
Universitätsstr. 6
CH-8006 Zürich (Switzerland)

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[1] a) *E. Bertele, H. Boos, J. D. Dunitz, F. Elsinger, A. Eschenmoser, I. Felner, H. P. Gribi, H. Gschwend, E. F. Meyer, M. Pesaro,* and *R. Scheffold,* Angew. Chem. *76*, 393 (1964); Angew. Chem. internat. Edit. *3*, 490 (1964);
b) *A. Eschenmoser, R. Scheffold, E. Bertele, M. Pesaro,* and *H. Gschwend,* Proc. Roy. Soc. (London) *A 288*, 306 (1965);
c) *M. Pesaro, I. Felner-Caboga,* and *A. Eschenmoser,* Chimia *19*, 566 (1965).

[2] *P. Wehrli* and *D. Miljkovic,* unpublished work.

[***] Note added in proof: A similar reaction was described by *J. W. Cornforth* at the Corrin Symposium in Nottingham (July 17–19, 1967).

[3] Hydrogen and methyl group at the ring-junction *anti* in the conformation with synplanar arrangement of the two nitrogen atoms.

[4] *I. Felner,* Dissertation, ETH Zürich. 1967.

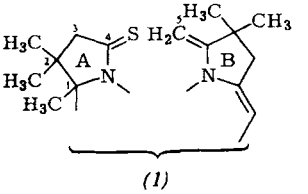
[5] RT = room temperature; UV data, log ε values in parentheses; IR data, rel. intensities, s = strong, m = medium, w = weak; NMR data, δ values referred to δ (tetramethylsilane) = 0, S = singlet, D = doublet (absolute value of the coupling constants *J* in Hertz), T = triplet, Q = quadruplet, M = multiplet, B = broad signal; mass spectrum, rel. intensities in parentheses. Compounds *(3)–(10b)* gave correct analytical values on combustion. A detailed description of the reaction series *(3)* → *(8)* is given in ref. [4].

A Synthetic Route to Metal-free Corrins [**]

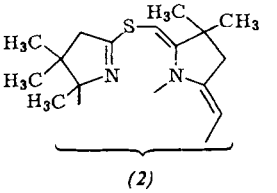
By *A. Fischli* and *A. Eschenmoser* [*]

Cobalt-free corrinoid compounds have recently been isolated from photosynthesizing bacteria [1]. However, it has not yet been possible to remove the cobalt solvolytically or reductively from cobalt-corrin complexes of either natural or synthetic origin whilst still retaining the ligand system [2]. The final cyclizing step in the route used by us hitherto for the synthesis of corrin complexes [3] requires the template effect of metal ions such as cobalt(III) and nickel(II). These metals form robust planar complexes with the polydentate ligand system to be cyclized and cannot be removed later [4]. We now describe a modified method of cyclization whereby the synthesis of metal-free corrins becomes possible: our example is *rac.*-15-cyano-1,2,2,7,7,12,12-heptamethylcorrin hydrochloride *(9)*.

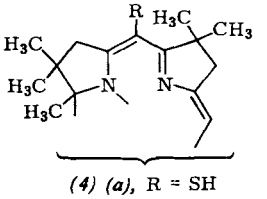
The process rests on a new type of condensation for formation of vinylogous amidine systems that was developed in our laboratory in another connection [6]. Formulae *(1)–(4)* illustrate the concept for the present case.



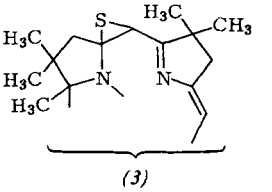
(1)



(2)



(4) (a), R = SH
(b), R = H



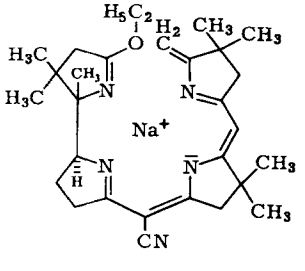
(3)

The two condensation centers C-4 and C-5 [cf. *(1)*] are first linked by a sulfur bridge [cf. *(2)*] and the bridged system is then either isomerized to *(4a)* by way of the hypothetical

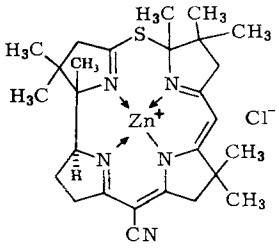
intermediate of type *(3)* or desulfurized to *(4b)*. In contrast to base-induced cyclization by the imino-ester procedure [7], the sulfur bridging does not require fixation of the ligand system into a robust metal complex but can be carried out on the labile zinc(II) complex; the zinc ion can be removed from the cyclized corrin complex very easily by acidolysis. Experimental details are given in the reaction scheme *(5)* → *(9)*. The attempt to convert the tetracyclic condensation product *(5)* [8] by acid-catalysed reaction with hydrogen sulfide into the corresponding thiolactam derivative of type *(1)* and to isolate the latter as zinc complex gave the crystalline macrocyclic isomer *(6)* whose structure was recognized from, in particular, the NMR spectrum (eight methyl groups, one vinyl proton). The series of operations, a) oxidation with benzoyl peroxide in the presence of trifluoroacetic acid at room temperature, b) warming with trifluoroacetic acid in dimethylformamide in the presence of ethylenediaminetetraacetic acid, and c) re-formation of the complex with zinc(II) perchlorate and finally chromatography on silica gel, all effected without isolation of the intermediate products, yielded 15-cyano-1,2,2,7,7,12,12-heptamethyl-5-mercaptocorrinzinc(II) *(7)* together with smaller amounts of the already desulfurized complex *(8)*; the complex *(7)* was crystallized as its chloride. We assume that the trifluoroacetic acid equilibrates the reactant *(6)* with the corresponding open thiolactam [cf. *(1)*], and that this is oxidized by dibenzoyl peroxide [9] to the *O*-benzoyl-*S*-oxide in which the sulfur bridge to the methylidene group of ring B is formed. It is treatment b) that causes formation of the corrin chromophore (UV spectrum!), it being remarkable that intermediate decomplexing of the ligand system seems to be necessary for this reaction [11]. The product *(7)* can be converted by acid-catalysed desulfurization with triphenylphosphine into the zinc(II)-corrin complex *(8)*, and the latter can be decomplexed by treatment with trifluoroacetic acid in acetonitrile to yield *rac.*-15-cyano-1,2,2,7,7,12,12-heptamethylcorrin *(9)*, the reactions occurring very smoothly. Compound *(9)* was crystallized as the hydrochloride.

The structure of the metal-free corrin derivative is shown unambigously by the NMR and mass-spectroscopic results (cf. scheme). The UV spectrum in ethanol corresponds in structure and relative intensity of the absorption bands to that of the natural cobalt-free corrin derivatives measured by *Toohey* [1] for aqueous solutions at pH = 7; the hypsochromic position of the absorption maxima in the spectrum of *(9)*, ascribable to the differing substitution of the chromophore, accords with previous observations [3,8] in the series of natural and synthetic dicyanocobaltcorrin(III) complexes. The free corrin ligand corresponding to the hydrochloride *(9)* is a moderately strong base; the pK^*_{MCS} [12], determined in dimethylcellosolve-water (4:1 w/w) is 8.6 (pK^*_{MCS} of piperidine = 9.7). Treatment of the hydrochloride *(9)* with an excess of $Co(II)(ClO_4)_2 \cdot (DMF)_6$ in acetonitrile (2 h at room temperature), re-oxidation with air in a mixture of 1 N aqueous hydrochloric acid and acetonitrile (15 min at room temperature), and finally treatment with aqueous potassium cyanide afforded crystalline *rac.*-dicyano-(15-cyano-1,2,2,-7,7,12,12-heptamethylcorrin)cobalt(III) [8] in more than 90 % yield [13].

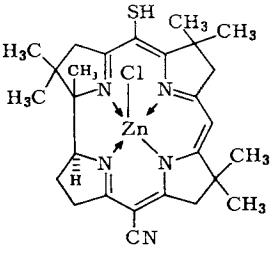
Spectroscopic and structural characterization of the mono- and di-protonated derivatives of *(9)*, as well as other questions arising from the above results, are currently under investigation.



(5)



(6)



(7)

a) $DMF-H_2S$ (1:2)–CF_3COOH/ 50 °C/20 h

60 %

b) $Zn(ClO_4)_2/NaOC_2H_5/C_2H_5OH$/RT (ref. [14])

M.p. 268 °C (from $CHCl_3-C_2H_5OH$)

UV (nm): 234(4.22), 266(4.32/shoulder), 275(4.49), 416(4.26/shoulder), 429(4.30) (C_2H_5OH)

IR (cm^{-1}): 2200s, 1610m, 1595s, 1570s, 1545s, 1470s, *etc.* ($CHCl_3$)

NMR (ppm): 1.05–1.43(6S/7CH_3), 1.98(S/1CH_3), 1.50–1.70(M/2H), 1.80–3.25(M/8H), 3.84(T/*J* 8/1H), 5.02(S/1H) ($CDCl_3$)

m/e: 529(9 %/M^+–H/^{68}Zn), 527(14 %/^{66}Zn), 525(21 %/^{64}Zn), 388(41 %), 386(63 %), 384(100 %/M^+– $C_7H_{12}NS$/^{64}Zn) (*ca.* 170 °C)

a) 1.2 equiv. of $(C_6H_5COO)_2$, 6.0 mol. equiv. of CF_3COOH in CH_2Cl_2/75 min/RT/under N_2; working up with $KHCO_3/H_2O$/NaCl

b) 6.0 mol. equiv. of CF_3COOH, 2.0 mol. equiv. of ethylenediaminetetraacetic acid in DMF/7 h/70 °C/under N_2

48 % *(7)*

7 % *(8)*

c) 15 mol. equiv. of ethyldiisopropylamine, 3.0 equiv. of $Zn(II)(ClO_4)_2$/30 min/RT/under N_2; working up pH 7/ NaCl/H_2O/CH_2Cl_2

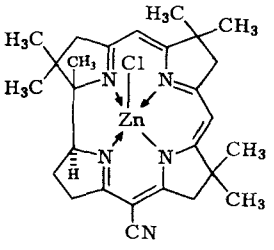
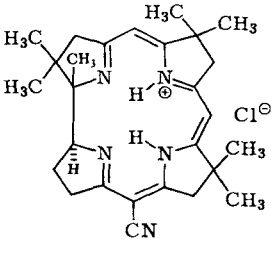
Decomp. pt. *ca.* 300 °C (from $CH_3OH-CHCl_3$-hexane)
Found: S 5.75 %;
Calc.: S 5.71 %.

UV (nm): 229(4.16), 263(4.31), 324(4.41), 376(3.78), 457(3.81/shoulder), 495(4.16/shoulder), 528(4.27/shoulder), 550(4.29) (C_2H_5OH)

IR (cm^{-1}): 2200m, 1630w/1610m (shoulders), 1580s, 1525w, 1492s, *etc.* ($CHCl_3$)

NMR (ppm): overlapping of the signals of α- and β-chloro-complex in intensity ratio *ca.* 2:3
5.36/5.34(S/1H/=C–H), 4.9/3.9(M tripletoid/ 1H/–N–C–H) ($CDCl_3$)

m/e: 532(12 %), 531(31 %), 530(20 %), 529(47 %/M^+–S/^{66}Zn, ^{35}Cl/^{64}Zn, ^{37}Cl), 528(18 %), 527(50 %/^{64}Zn, ^{35}Cl), 492(96 %/M^+–(S + Cl)/^{64}Zn), 491(59 %/M^+–(S + HCl)/^{64}Zn) + corresponding isotopic peaks; 476 (100 %/ M^+– (S + HCl + CH_3)/ ^{64}Zn) + corresponding isotopic peaks;
34(34 %/H_2S), 33(20 %/HS), 32(23 %/S) (*ca.* 210 °C)

↓ 86 %	1.5 mol. equiv. of triphenylphosphine, *ca.* 0.1 mol. equiv. of CF_3COOH in $CHCl_3$/4 h/60 °C
(8) 	M.p. 332–338 °C (from ethanol/ethyl acetate/hexane) UV (nm): 225(3.88), 260(4.28), 306(4.31/shoulder), 316(4.43), 363(3.45), 382(3.26), 454(3.89/shoulder), 480(4.04), 502(3.95/shoulder) (C_2H_5OH) IR (cm^{-1}): 2200s, 1625m, 1608m, 1586s, 1570s (shoulder), 1508s, 1470s, *etc.* ($CHCl_3$) NMR (ppm): a) in $CDCl_3$, overlapping of signals from the α- and β-complex in intensity ratio *ca.* 3:1 5.36/5.33(S/2H), 3.8/4.9(M/1H), 3.3–2.5(M/8H), 2.3–1.6(M/*ca.* 2H), 1.5–0.9 (*ca.* 21H) b) in $CDCl_3$ after treatment with $AgBF_4$ in $CHCl_3$ and filtration from AgCl (tetracoordinated complex), 1.08/1.20/1.30/1.36/1.37 (5S/21H), 1.5–2.5(M/2H), 2.70–3.25(M/8H), 4.26(M tripletoid/1H), 5.50(S/1H), 5.60(S/1H) *m/e*: 527(10 %/M^+/^{64}Zn, ^{35}Cl), 492(38 %/M^+–Cl/^{64}Zn), 491(37 %/M^+–HCl/^{64}Zn), 476(100 %/M^+–(HCl + CH_3)/^{64}Zn) + corresponding isotope peaks; no peak at 32–34 (*ca.* 140 °C)
↓ 94 %	12 mol. quiv. of trifluoroacetic acid in acetonitrile/5 min/RT/under N_2; repeated after working up with $NaCl–H_2O–CH_2Cl_2$
(9) 	M.p. 211 °C (decomp.; from ethanol/ethyl acetate/hexane) UV (nm): 224(4.11), 260(4.37), 272(4.18/shoulder), 290(4.20/shoulder), 303(4.43/shoulder), 314(4.53), 365(3.85), 440(3.85/shoulder), 470(3.97), 496(3.89/shoulder) (in C_2H_5OH); same spectrum in $CH_3OH–H_2O$ (2:1) in region pH 1–8 (HCl) pK^*_{MCS} (see [12]): 8.64 (titrated with 0.1 N TMAH), 8.65 (back-titrated with 0.1 N HCl; 25 °C); equiv. wt. 487/497 (calc. 466) IR (cm^{-1}): 3400–3000w, 2450w, 2210m, 1610s, 1588s, 1564s, 1482s, *etc.* ($CHCl_3$) NMR (ppm): 1.19/1.24/1.31/1.39/1.47(5S/21H), 1.6–2.6(M/2H), 2.76–3.48(M + AB system 2.87/3.37 (*J ca.* 19)/8H), 4.56(M tripletoid/1H), 5.75(S/1H), 5.83(S/1H), 12.0(B/1H), 13.2(B/1H) ($CDCl_3$) *m/e*: 430(32 %), 429(94 %/M^+–H), 415(32 %), 414(100 %/M^+–(H + CH_3)) (*ca.* 90 °C)

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[*] A. Fischli, dipl.-Ing.-Chem. ETH and Prof. A. Eschenmoser
Organisch-chemisches Laboratorium
der Eidg. Techn. Hochschule
Universitätsstr. 6
CH-8006 Zürich (Switzerland)

[**] This work was supported by the Schweizerische Nationalfonds zur Förderung der wissenschaftlichen Forschung.

[1] a) *J. I. Toohey*, Proc. nat. Acad. Sci. USA *54*, 934 (1965); b) *J. I. Toohey*, Feder. Proc. *25*, 1628 (1966).

[2] Cf. *R. Bonnett*, Chem. Rev. *63*, 573 (1963), and [1a].

[3] *A. Eschenmoser, R. Scheffold, E. Bertele, M. Pesaro*, and *H. Gschwend*, Proc. Roy. Soc. (London) *A* 288, 306 (1965).

[4] The corrinoid reduction products of tetradehydrocorrin derivatives obtained synthetically by *A. W. Johnson et al.* [5] have also been recorded so far only as nickel(II) or cobalt(III) complexes.

[5] *R. Grigg, A. W. Johnson*, and *O. van den Broek*, Chem. Commun. *1967*, 502; *A. W. Johnson*, Chem. Britain *1967*, 253.

[6] *B. Golding* and *P. Löliger*, unpublished work.

[7] Previous attempts to cyclize precorrinoid zinc complexes by the imino ester procedure were unsuccessful (*M. Pesaro* and *E. Bertele*, unpublished work).

[8] *I. Felner, A. Fischli, H. Wick, M. Pesaro, D. Bormann, E. L. Winnacker*, and *A. Eschenmoser*, Angew. Chem. *79*, 863 (1967); Angew. Chem. internat. Edit. *6*, 864 (1967).

[9] On oxidation with benzoyl peroxide, thioamides give disulfides [6, 10]. The use of benzoyl peroxide as reagent for S-bridging of thiolactams with enamides was developed by *B. Golding* when working with another example [6].

[10] *F. Hodosan*, Bull. Soc. chim. France *1957*, 633.

[11] This phenomenon, and the structure of the unstable intermediates formed in operation a), are under current investigation.

[12] *W. Simon*, Helv. chim. Acta *41*, 1835 (1958).

[13] Identification by thin-layer chromatography and UV and IR spectra.

[14] Cf. [5] in [8]. The approximate direct inlet temperature of the substance is given after the mass-spectrometric data. Compounds *(6)–(9)* were isolated in crystalline form, were homogeneous on thin-layer chromatography, and gave correct analytical values.

Reactivity of Ligands in Synthetic Cobalt(III)- and Nickel(II)-corrin Complexes [**]

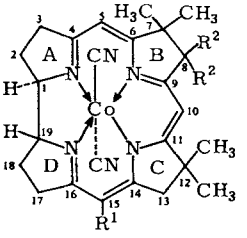
By *D. Bormann, A. Fischli, R. Keese*, and *A. Eschenmoser* [*]

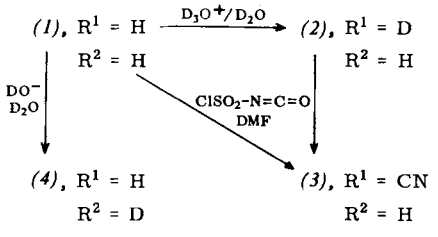
In investigations carried out so far, electrophilic substitution on the ligand chromophore of the synthetic corrin complexes *rac.*-dicyano-(7,7,12,12-tetramethylcorrin)cobalt(III) *(1)* [1] and *rac.*-7,7,12,12,19-pentamethylcorrinnickel(II) chloride *(5)* [2] occurs preferentially at position 15. In a basic medium, the periphery of the ligand system can be selectively deprotonated at position 8. These statements are based on the following findings.

Reaction of the cobalt complex *(1)* with three equivalents of chlorosulfonyl isocyanate at room temperature for 15 min and subsequent treatment of the reaction mixture with dimethylformamide for 15 min at room temperature (*Lohaus* and *Graf*'s method of cyanation [3]) gave an 80–90 % yield of the monocyano complex *(3)*. The structure of this complex is certain because it is an intermediate in the total synthesis of *(1)* [4].

In the NMR spectrum of the cobalt complex *(1)* (in $CDCl_3$), the signals of the three vinyl protons appear as singlets at 5.40, 5.44, and 5.56 ppm. The last of these signals is broadened (tripletoid) as a result of spin-spin coupling of the corresponding vinyl proton with the protons of the

neighboring allyl methylene groups, whose signal occurs as a broadened singlet at 2.84 ppm[5]. All three vinyl positions are completely deuterated in the mixture *t*-BuOD-D_2O(1:1)–CF_3COOD (pD *ca.* 2; room temperature; 5 days), the four allylic methylene groups being unaffected.

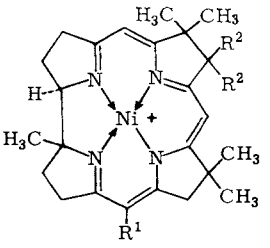


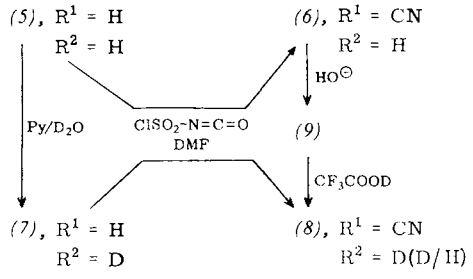


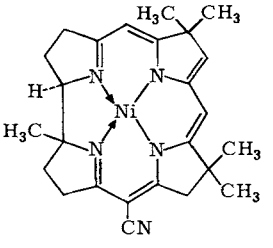
In the NMR spectrum of the trideuterio complex the methylene signal at 2.84 appears as a sharp singlet. According to the mass spectrum[6], the product of partial deuteration (*p*D *ca.* 3; room temperature; 24 h) contains 38 %, 40 %, 17 %, and 4 % of the D_0, D_1, D_2, and D_3 components respectively; most of the loss in intensity in the NMR spectrum is due to the tripletoid vinyl-proton signal at 5.56 ppm. The complex *(3)* obtained on reaction of this product with chlorosulfonyl isocyanate and dimethylformamide (yield 86 %) contains the components D_0 (79 %), D_1 (17 %), and D_2 (4 %)[6]. This leads to the conclusion that acid-catalysed deuteration of the chromophore system occurs most rapidly at position 15, and that in the NMR spectrum of the cobalt complex *(1)* the tripletoid signal at 5.56 ppm is to be assigned to the vinyl proton at position 15, and the signal at 2.84 ppm to the proton of the methylene group in ring C (position 13). A sharp doublet at 2.91/2.93 ppm can now be assigned to the protons of the allylic methylene group of ring B (position 8), and can, as a near-singlet AB signal system, be clearly distinguished from the broad multiplet at 3.1 ppm of the allylic methylene protons of rings A and D.

Base-catalysed partial deuteration of the dicyanocobalt(III) complex *(1)* in the system *t*-BuOD–D_2O(1:1)–NaOD-KCN ($c_{(1)}$ = 0.071 mole/l; pD *ca.* 12; 7 h; 31 °C; under N_2) leads to the dideuterio complex *(4)*, *i.e.* to selective disappearance of the signal at 2.91/2.93 ppm in the NMR spectrum; the structure and intensities of the remaining NMR signals are unchanged (within experimental error). The reaction, followed in several experiments by NMR spectroscopy, is first order with respect to *(1)* (half-life 99 ± *ca.* 5 min) and is independent of the cyanide concentration from 0.13 to 0.70 mole/l.

Cyanation of the 7,7,12,12,19-pentamethylcorrinnickel(II) cation *(5)*[2] by chlorosulfonyl isocyanate occurs as in the cobalt series and affords a yield of over 90 % of the cyano nickel complex *(6)*, a complex which is known from its total synthesis[2]. With this positively charged complex ion, deuteration of the allylic methylene group of ring B [cf. *(7)*] takes place even in the presence of a weak base; keeping the compound for 15 h in pentadeuteriopyridine-D_2O (1:1) ($c_{(5)}$ = 0.014 mole/l; 31 °C; under N_2) brings about selective disappearance of the methylene-singlet signal at 3.18 ppm in the NMR spectrum[7]. However, the structure and intensities of the two weakly coupled signals at 3.02 ppm (methylene protons of ring C, position 13) and 6.10 ppm (vinyl proton in position 15) are substantially unchanged; assignment of these signals is based







(9)

on the evidence provided for the cobalt complex *(1)* that the vinylic-allylic spin-spin coupling observable for one of the three vinyl protons refers to the proton at position 15. This is also in accord with the theoretically predicted correlation[8] between spin-spin coupling constants and π-bond order in vinyl-allyl systems. According to the results of X-ray structure analyses of various corrin complexes[9] the 5,6- and 14,15-bonds have the highest π-bond order of the (C,C)-π-bonds of the corrin chromophore.

In our earlier investigations[1b,2] a neutral complex formed on deprotonation of the 15-cyano nickel(II) complex *(6)* was isolated in crystalline form and was characterized. Findings recorded below show that this complex has structure *(9)*. Thus, with a cyano group at position 15 it is also the methylene group in ring B that is preferentially deprotonated by base. In the NMR spectrum of the 15-cyano nickel(II) complex *(6)* in trifluoroacetic acid the signals of the two allylic methylene groups in rings B and C appear as singlets at 3.27 and 3.37, respectively. The complexes *(6)* and *(9)* in trifluoroacetic acid[10] give identical NMR spectra, but in the spectrum of complex *(9)* in deuteriotrifluoroacetic acid the signal at 3.27 is broadened and its intensity is reduced by half. This signal is absent from the spectrum of the 15-cyano-8,8-dideuterio complex *(8)* (in trifluoroacetic acid) that is obtained by treating the 8,8-dideuterio complex *(7)* with chlorosulfonyl isocyanate-DMF.

Neither the preference of electrophilic substitutions for position 15 (or 5) nor the selectivity in base-induced deprotonation at position 8 of the corrin ligand system can be convincingly predicted or interpreted on the basis of qualitative resonance structure formalism. The experimental findings, however, agree qualitatively with the atom localization energies A^- (positions 5 or 15 and 10) and A^+ (positions 4, 9, and 14) calculated by the HMO method[11]. The dominance of position 15 over the electronically equivalent position 5, observed particularly in the reactions with chlorosulfonyl isocyanate, is presumably to be ascribed to steric shielding of position 5 by the neighboring *gem*-methyl groups in ring B. To what extent the steric non-equivalence of positions

10 and 15 causes the difference in reactivity of these two centers remains to be clarified by further experiments.

The results now reported indicate new possibilities for selective structural modification of the corrin ligand system and contribute to a better understanding of previous results on the oxidation and dehydrogenation of ring B of vitamin B_{12} [12].

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[*] Dr. D. Bormann, A. Fischli, dipl.-Ing.-Chem. ETH, Dr. R. Keese, and Prof. A. Eschenmoser
Organisch-chemisches Laboratorium
der Eidg. Techn. Hochschule
Universitätsstr. 6
CH-8006 Zürich (Switzerland)

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[1] a) *M. Pesaro, I. Felner*, and *A. Eschenmoser*, Chimia *19*, 566 (1965);

b) *A. Eschenmoser, R. Scheffold, E. Bertele, M. Pesaro*, and *H. Gschwend*, Proc. Roy. Soc. (London) *A 288*, 306 (1965).

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[4] Identification by UV, IR, and NMR spectra.

[5] This spin-spin coupling was confirmed by double resonance experiments. Cf. also theNMR spectrum of dicyano-(7,7,12,12,19-pentamethylcorrin)cobalt(III) reproduced in [1b], Fig. 14.

[6] Evaluated from the intensities of the (M^+-2 CN) signals (direct inlet, *ca.* 200 °C).

[7] The NMR spectrum of the complex *(5)* is shown in Fig. 7 of ref. [1b].

[8] *H. M. McConell*, J. molecular Spectr. *1*, 11 (1957); *M. J. S. Dewar* and *R. C. Fahey*, J. Amer. chem. Soc. *85*, 2704 (1963).

[9] *D. C. Hodgkin, J. Kamper, J. Lindsey, M. MacKay, J. Pickworth, J. H. Robertson, C. B. Shoemaker, J. G. White, R. J. Prosen*, and *K. W. Trueblood*, Proc. Roy. Soc. (London) *A 242*, 228 (1957); *J. D. Dunitz* and *E. F. Meyer, jr.*, *ibid. A 288*, 324 (1965); *R. Bonnett*, Chem. Rev. *63*, 573 (1963).

[10] In trifluoroacetic acid the complex *(9)* exists in the protonated form *(6)*. The signals of the methylene groups of rings B and C coincide in deuteriochloroform (cf. [1b], Fig. 5) but not in trifluoroacetic acid.

[11] Cf. a paper by *R. Keese* to be published shortly.

[12] *R. Bonnett, I. R. Cannon, V. M. Clark, A. W. Johnson, L. F. Parker, E. Lester Smith*, and *A. R. Todd*, J. chem. Soc. (London) *1957*, 1158; cf. *R. Bonnett*, Chem. Rev. *63*, 573 (1963); *F. Wagner*, Ann. Rev. Biochem. *35*, 405 (1966).

Thermal and Photochemical Behavior of a [16]Annulene

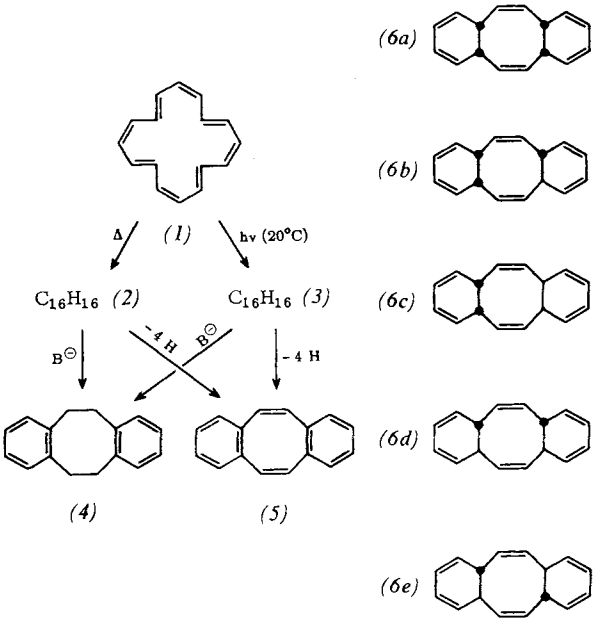
By *G. Schröder, W. Martin*, and *J. F. M. Oth* [*]

[16]Annulene *(1)* can be synthesized on the gram scale [3] by photolysis of the cyclooctatetraene dimer of m.p. 53 °C [1,2]. Both heat and UV light cause characteristic changes in this annulene. When warmed [4] in various solvents (benzene, ether, acetone, or CS_2) the compound rearranges to give a yield of over 90 % of an oil $C_{16}H_{16}$ *(2)* [5] which appears homogeneous on thin-layer chromatography (silica gel; cyclohexane, benzene, or CS_2).

In the UV region [6] the product *(2)* absorbs at λ_{max} = 261 nm (ε = 4900). The NMR spectrum [6] is unusually complex and shows twelve olefinic (τ = 4.0–5.1) and four aliphatic protons (τ = 5.8–7.5). No unambiguous result has so far been obtained from catalytic hydrogenation over Pd/C. The product is very sensitive to both oxygen and acids.

A solution of the annulene *(1)* in ether at 0 °C is unchanged on irradiation even for rather long periods (several days). However, at 20 °C a photoisomer $C_{16}H_{16}$ *(3)* [5] of m.p. 92 °C is obtained. When 2 g of *(1)* in 350 ml of ether is irradiated with a Philips high-pressure lamp HPK 125 W for 30 h, 0.8 g of pure *(3)* can be isolated. Its UV spectrum [6] shows several shoulders and a main band at 261 nm (ε = 8500) that is flanked by side bands. The NMR spectrum [6] discloses twelve olefinic (multiplet around τ = 4.45) and four aliphatic protons (pseudosinglet at τ = 6.8). Catalytic hydrogenation over Pd/C affords $C_{16}H_{28}$ [5].

On treatment with $KOC(CH_3)_3$ in dimethyl sulfoxide, both *(2)* and *(3)* yield 5,6,11,12-tetrahydrodibenzo[*a*,*e*]cyclooctatetraene *(4)* [5,7], and on dehydrogenation with chloranil yield dibenzo[*a*,*e*]cyclooctatetraene *(5)* [5,7] (yield in both cases, 60–70 %).

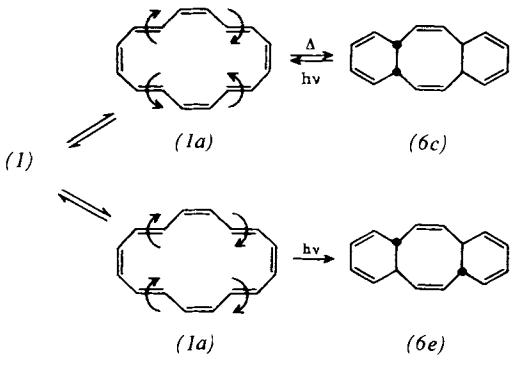


Compounds *(2)* and *(3)* are thus 4a,6a,10a,12a-tetrahydrodibenzo[*a*,*e*]cyclooctatetraene *(6)* and can differ only in their stereochemistry. Five isomers, *(6a)–(6e)*, are possible.

Which stereoisomers are we dealing with? – The products *(2)* and *(3)*, being 1,3-cyclohexadiene systems, should form Diels-Alder adducts. A diadduct $C_{28}H_{28}O_8$ [5], m.p. 232 °C (yield > 90 %), is formed surprisingly easily from *(3)* and dimethyl acetylenedicarboxylate (ADE) at 30–40 °C. A monoadduct $C_{22}H_{22}O_4$ [5], m.p. 93–94 °C, is obtained only when very dilute solutions and a several-fold excess of *(3)* [*e.g.* *(3)* 5.1 g, ADE 1.3 g, benzene 130 ml] at 65 °C are used [yields around 48 % calc. on the amount of *(3)* that reacts]. In the NMR spectra of the mono- and the di-adduct, the methyl protons of the ester groups give two singlets of equal intensity at τ = 6.2, which are separated by *ca.* 1.2 Hz. This results enables us to exclude the stereoisomers *(6a)*, *(6b)*, and *(6c)*. The methyl protons of the ADE adducts of *(6a)* and *(6c)* would be expected to give rise to one singlet, and those of the adduct of *(6b)* to give several singlets. Thus for the photoisomer *(3)* the decision lies between *(6d)* and *(6e)*. This is aided by the observation that formation of the diadduct is preferred to that of the monoadduct, a fact that is in accord only with the all-*trans*-configuration of the bridgehead protons as in *(6e)*. The photoisomer *(3)* is therefore *(6e)*.

The thermal isomer *(2)* does not react with ADE in a readily interpretable manner. This negative finding can be accommodated only by formula *(6c)* [8]. Consideration of models shows that the action radii of the two H atoms lying above the plane in the conformation with planar six-membered rings penetrate the π-orbitals of the other six-membered ring. The molecule will thus avoid this high-energy conformation which, however, is essential for a Diels-Alder reaction.

The behavior of [16]annulene on being warmed and on UV irradiation can be coordinated and understood on the basis of the Woodward-Hoffmann rule[9].



Structure *(1)* shows great conformational mobility[11]. Equilibration of *(1)* with *(1a)* is immediately understandable. The electrocyclic reactions of the two cisoid triene systems of *(1a)* are disrotatory in the thermal reaction and conrotatory in the photochemical reaction. The molecule undergoes two electrocyclic reactions in going from *(1a)* to *(6c)* or from *(1a)* to *(6e)*, and there are two possibilities for the second step: it can be in the same or in the opposite sense relative to the first. The opposing sense is dominant. However, we cannot yet decide whether the electrocyclic reactions of [16]annulene induced thermally or photochemically are synchronous or asynchronous.

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[*] Priv.-Doz. G. Schröder and Dipl.-Chem. W. Martin
Institut für Organische Chemie der Technischen Hochschule
Richard-Willstätter-Allee
75 Karlsruhe (Germany)
Dr. J. F. M. Oth
Union Carbide European Research Associates
Brussels 18 (Belgium)

[1] *G. Schröder* and *J. F. M. Oth*, Tetrahedron Letters *1966*,4083.

[2] *G. Schröder* and *W. Martin*, Angew. Chem. *78*, 117 (1966); Angew. Chem. internat. Edit. *3*, 130 (1966).

[3] It is advantageous to carry out the photolysis of $C_{16}H_{16}$, m.p. 53 °C, at 0 °C. Under otherwise identical conditions [1], this raises the yield of pure *(1)* to *ca.* 60 %.

[4] The half-life of *(1)* in benzene at 20 °C is 44 h. For the reaction *(1)* → *(2)* we found: activation energy $E_a \approx 22$ kcal/mole; reaction enthalpy $\Delta H \approx -9.0$ kcal/mole.

[5] Satisfactory C, H analyses were obtained for this compound.

[6] The UV spectra were measured with a Beckman instrument DK-2 for n-hexane solutions, and the NMR spectra with a Varian instrument A-60 for solutions in CCl_4 or CS_2 with tetramethylsilane as internal standard.

[7] Identical in melting point and spectral properties with authentic material: *(4)*, *L. F. Fieser* and *M. M. Pechet*, J. Amer. chem. Soc. *68*, 2577 (1946); *(5)*, *M. Avram*, *D. Dinu*, *G. Mateescu*, and *C. D. Nenitzescu*, Chem. Ber. *93*, 1789 (1960).

[8] We have identified *(1)* and *(6e)*, so far each in *ca.* 10 % yield, after photolysis of *(6c)* in ether at 20 °C.

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Preparation of Carbonyl and Fluorocarbonyl Pseudohalides in Molten Salts

By *W. Verbeek* and *W. Sundermeyer*[*]

When carbonyl fluoride is passed into a melt of lithium chloride and potassium chloride containing *ca.* 10 wt.-% of dissolved potassium cyanate at 400 °C, carbonyl diisocyanate *(1)*[1] and fluorocarbonyl isocyanate *(2)*[2], in the wt. ratio 78:22, are obtained in quantitative yield (calculated on the COF_2 consumed).

$$COF_2 + 2\,KOCN \rightarrow OC(NCO)_2 + 2\,KF \quad (1)$$

$$COF_2 + KOCN \rightarrow FCO(NCO) + KF \quad (2)$$

With lower concentrations of potassium cyanate the proportion of *(2)* becomes higher.

Compound *(1)* is a colorless liquid (m.p. −50.5 °C, b.p. 104 °C). It was identified by elemental analysis, IR spectrometry[11], and mass spectrometry. Alongside the molecular ion at $m/e = 112$, fragments occur at $m/e = 70$ (OCNCO), 42 (NCO), and 28 (CO). At room temperature, pure *(1)* polymerizes within a few days to a white crystalline solid, which is reconverted quantitatively into monomeric *(1)* when heated in a high vacuum to above 150 °C.

When carbonyl fluoride is passed into an equimolar potassium thiocyanate/sodium thiocyanate melt at *ca.* 140 °C, fluorocarbonyl isothiocyanate *(3)*[3] is obtained in 20 % yield.

$$COF_2 + KSCN \rightarrow FCO(NCS) + KF \quad (3)$$

Decomposition products are also formed, which are apparently derived from the carbonyl isothiocyanate that is formed as intermediate. *(3)* is a colorless liquid (m.p. −74 °C, b.p. 65.6 °C), which becomes yellow on storage. The compound was identified by elemental analysis and by mass spectrometry [m/e = 105 (molecular ion), 73 FCO(NC), 47 COF, 28 CO]. Its IR spectrum contains bands at 2049 (vs), 1961 (vs), 1848 (vs), 1232 (vs), 1010 (vs), 759 (m), 689 (m), and 635 (m) cm^{-1} [3a]. The vapor pressure curve accords with the equation

$$\log p = -17.697/T + 7.89$$

(Trouton constant 25.7). The ^{19}F–NMR spectrum includes a signal at −16.3 ppm (referred to $CFCl_3$ as external standard, −40 °C).

Compound *(3)* was also obtained, in quantitative yield, by treatment of trimethylsilyl isothiocyanate with carbonyl fluoride at 50 °C in an autoclave.

$$(CH_3)_3SiNCS + COF_2 \rightarrow FCO(NCS) + (CH_3)_3SiF \quad (3)$$

When carbonyl fluoride is passed into a lithium chloride/potassium chloride melt (LiCl:KCl = 58:42 mole-%) containing 10 wt.-% of dissolved potassium cyanide at 400 °C, a small yield of carbonyl dicyanide *(4)*[4] is obtained.

$$COF_2 + 2\,KCN \rightarrow OC(CN)_2 + 2\,KF \quad (4)$$

The expected fluorocarbonyl cyanide *(5)*[5] was, however, obtainable only by reaction of trimethylsilyl cyanide with carbonyl fluoride.

$$(CH_3)_3SiCN + COF_2 \rightarrow FCO(CN) + (CH_3)_3SiF \quad (5)$$

Reaction in an autoclave at room temperature gives only a 26 % yield. Compound *(5)* is a colorless liquid (m.p. −85 °C, b.p. −14.4 °C). The molecular weight was deduced by Dumas' method and from the mass spectrum. The ^{19}F–NMR spectrum includes a signal at −47.5 ppm (referred to $CFCl_3$ as external standard, −40 °C). The IR spectrum contains

bands at 2232 (s), 1852 (vs), 1156 (vs), 822 (m), 728 (m), and 547 (m) cm^{-1} [3a]. The vapor pressure curve accords with the equation

$$\log p = -1464/T + 8.54$$

(Trouton constant 25.9).

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[*] Dipl.-Chem. W. Verbeek and Priv.-Doz. Dr. W. Sundermeyer
Anorganisch-Chemisches Institut der Universität
Hospitalstr. 8–10
34 Göttingen (Germany)

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[3a] s = strong, vs = very strong, m = medium.

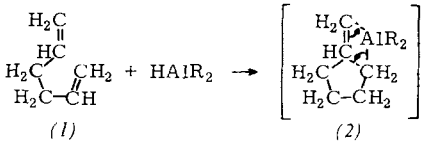
[4] *R. Malachowski, L. Jurkiewicz*, and *J. Wojtowicz*, Ber. dtsch. chem. Ges. *70*, 1012 (1937).

[5] Cf. *C. W. Tullock* and *D. D. Coffmann*, J. org. Chemistry *25*, 2016 (1960).

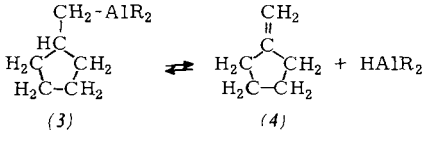
Diethyl-(5-hexenyl)aluminum-Ether [1]

By *R. Rienäcker* and *G. F. Göthel* [*]

On reaction of dialkylhydridoaluminum with 1,5-hexadiene *(1)*, *Ziegler* and *Gellert* [2] obtained the dialkyl(cyclopentylmethyl)aluminum *(3)* and methylenecyclopentane *(4)*. This cyclization can be regarded as an intramolecular analogue of the dimerization of α-olefins [3]. The dialkyl-(5-hexenyl)aluminum postulated as first intermediate has not been detected previously.



(1) *(2)*

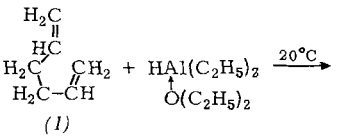


(3) *(4)*

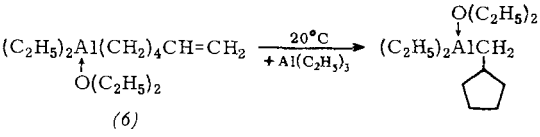
We have found that even at low temperatures ring closure is very much faster than addition of dialkylhydridoaluminum to the terminal double bonds. Thus on reaction of diethylhydridoaluminum *(5)* with an excess of *(1)* at 0 °C (experiment a) and hydrolysis, we found, alongside unchanged *(1)*, methylcyclopentane as almost the sole C_6 hydrocarbon.

If, however, the reaction is carried out with the ether adduct of *(5)* at 20 °C, no ring closure occurs and diethyl-(5-hexenyl)aluminum-ether *(6)* can be isolated (experiment b). The IR spectrum of this product shows intense absorption at 1638 cm^{-1} ($\nu_{C=C}$), which is not present in the IR spectrum of the product from experiment a. Obviously, intramolecular cyclization is prevented or strongly hindered when a lone pair of electrons of ether fills the vacancy in the octet of the aluminum in diethyl-(5-hexenyl)aluminum.

In a third experiment (experiment c) the product *(6)* was converted quantitatively into *(3)* (R = ethyl) by addition of catalytic amounts of $Al(C_2H_5)_3$ at room temperature (slight evolution of heat) (IR spectrum: no vinyl absorption). The ring closure occurs after exchange of ether molecules between *(3)* and $Al(C_2H_5)_3$.



(1)



(6)

Composition of the C_6 hydrocarbons of the hydrolysed products, without consideration of the excess of *(1)*. Gas-chromatographic analysis (mol.-%).

Experiment	a	b	c
n-Hexane	1.9	6.2	6.3
1-Hexene	4.1	92.7	0.2
Methylcyclopentane	94.0	1.1	93.5

Oxidation [4] of *(6)* by air at room temperature and subsequent hydrolysis afforded 5-hexen-1-ol, b.p. 60 °C/10 mm, n_D^{20} = 1.4355 (n_D^{20} = 1.4355 [5]). Similarly, from *(3)* we obtained cyclopentylmethanol, b.p. 87 °C/36 mm, n_D^{20} = 1.4578 (n_D^{20} = 1.4552 [6]).

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[*] Dr. R. Rienäcker and Dr. G. F. Göthel
Max-Planck-Institut für Kohlenforschung
Kaiser-Wilhelm-Platz 1
433 Mülheim/Ruhr (Germany)

[1] *G. F. Göthel*, Dissertation, Technische Hochschule Aachen, 1966.

[2] *K. Ziegler*, Angew. Chem. *68*, 729 (1956).

[3] *K. Ziegler* in *H. Zeiss*: Organometallic Chemistry. Reinhold Publishing Corp., New York 1960, p. 234.

[4] *K. Ziegler, F. Krupp*, and *K. Zosel*, Angew. Chem. *67*, 425 (1955).

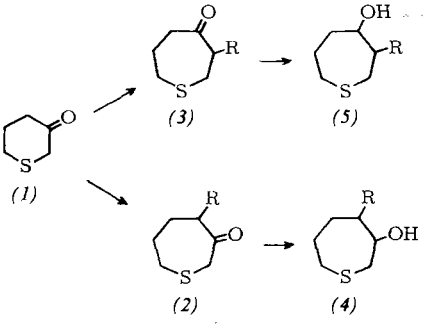
[5] *G. Zweifel, K. Nagase*, and *H. C. Brown*, J. Amer. chem. Soc. *84*, 183 (1962).

[6] *N. Turkiewicz*, Ber. dtsch. chem. Ges. *72*, 1060 (1939).

Transannular 1,4-Hydrogen Bridges in Thiepanols [1]

By *R. Borsdorf, H. Kasper*, and *H.-D. Repp* [*]

According to *Lüttringhaus et al.* [2] an intramolecular hydrogen bridge between the OH group and the sulfur of thianols (thiacyclohexanols) is formed only when the substituents are in the 1,3-position. We have found that in thiepanols (thiacycloheptanols) a hydrogen bridge between the sulfur and the OH group is formed also if these are in the 1,4-position.



(1) *(2)* *(3)* *(4)* *(5)*

(a), R = H; *(b)*, R = CH_3; *(c)*, R = $CH(CH_3)_2$

We obtained mixtures of 4-alkylthiepan-3-ones *(2)* and 3-alkylthiepan-4-ones *(3)* on ring expansion[3] of thian-3-one *(1)* by diazo-methane, -ethane, or -isobutane. These products were separated by distillation through a spinning-band column. Reduction with $LiAlH_4$ led to the alcohols *(4)* and *(5)*. When R = CH_3 or $CH(CH_3)_2$ the reduction gave mixtures of *cis-trans*-alcohols from which the pure *cis*-isomers were isolated by chromatography on silica gel with benzene/ethyl acetate.

The IR spectra of compounds *(4a)* and *(5a)* in CCl_4 ($<10^{-2}$ mole/l) each contained two ν_{O-H} bands – *(4a)* at 3623 and 3489 cm^{-1}, *(5a)* at 3623 and 3496 cm^{-1}, which shows that in both cases an equilibrium must be set up between a transannular-associated (lower frequency) and a non-associated conformation (higher frequency).

In *cis-(4b)*, *cis-(5b)*, *cis-(4c)*, and *cis-(5c)* the proportion of transannular-associated conformation is greater than in *(4a)* and *(5a)*. Thus the pseudoaxial position of the OH groups, which according to considerations of a model is necessary for transannular association, is favored by the alkyl group in the *cis*-position to the neighboring hydroxyl group.

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[*] Dr. R. Borsdorf, Dipl.-Chem. H. Kasper, and Dipl.-Chem. H.-D. Repp
Institut für Organische Chemie der Universität
Liebigstr. 18
DDR 701 Leipzig (Germany)

[1] Part VI of Seven- and Eight-membered Ring Compounds. – Part V: *R. Borsdorf* and *B. Olesch*, J. prakt. Chem., in the press.

[2] *A. Lüttringhaus, S. Kabuss, H. Prinzbach*, and *F. Langenbucher*, Liebigs Ann. Chem. *653*, 195 (1962).

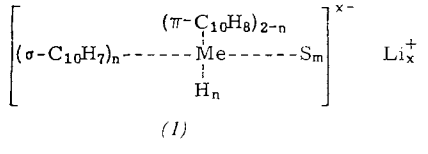
[3] Conditions: *in situ* method.

Synthesis of Tetramethylcyclobutadienenickel(II) Bromide with a New Nickel(0) Complex

By *G. Henrici-Olivé* and *S. Olivé*[*]

Transition metal salts such as VCl_3, $CrCl_3$, $NiBr_2$, and $PtCl_4$ can be reduced in tetrahydrofuran (THF) with lithium naphthalide (LiNp). On slow addition of the metal salt solution to the naphthalide[1,2], very stable, dark solutions of the corresponding reduced metals are obtained.

The high stability of these solutions can be interpreted on the assumption of complex formation of the reduced metal with naphthalene, and hydrogen transfer from the hydrocarbon to the metal[2]. Such complexes can carry up to 6 negative charges. Results of deuterolysis and EPR evidence suggest structure *(1)*[2]. ($0 \leqslant n \leqslant 2$; S = solvent; m = number of solvent molecules required as ligands by the corresponding symmetry of the metal complex. $x \leqslant 6$ = number of negative charges. The greater the excess of naphthalide the higher the value of x.)



(1)

Although the stable solutions do not contain the metal in colloidal form, minor amounts of colloidal metal are formed as a by-product, particularly during the reduction of transition metals with high population of the d orbitals[2].

Several species *(1)* having different values of x may be present in equilibrium. If the excess of LiNp is small, the bisarene complex ($n = x = 0$) takes part in the equilibrium, as EPR measurements with vanadium[2] and chromium[2a] have shown.

In the complexes *(1)*, transition metals behave as highly reactive metal(0) species, as in the metal carbonyls. The reaction of the nickel complex with tetramethylcyclobutene dibromide (TCD) to give tetramethylcyclobutadienenickel(II) (TCNi) clearly demonstrates this similarity. *Criegee et al.* prepared the chloride[3] and bromide[4] of $(TCNi)^{2+}$ from $Ni(CO)_4$; prolonged heating of the reactants was required. With the complex *(1)*, however, the reaction took a few minutes at room temperature, giving TCNi in quantitative yield (referred to reacted nickel).

A solution of $NiBr_2$ in THF (concentration 1.2×10^{-2} mole/l) is added to a solution of LiNp in THF (concentration 7×10^{-2} mole/l, 5 % excess over the amount necessary for the reduction Ni(II) → Ni(0)). An excess of TCD is then added under argon. Within 10–15 minutes at room temperature, the color changes from brown-black to dark violet. Elimination of the solvent from the filtered solution and extraction of the residue with water lead to the isolation of the complex salt $TCNiBr_2$.

Visible and IR spectra[4] as well as precipitation of the complex cation with sodium dicyanoethylenedithiolate[3] established the identity of the compound. Recrystallization from chloroform-butanol (1:1) gave solvent-free fine needles[5]. X-ray analysis on single crystals afforded the following crystallographic data: $a = 16.2$ Å, $b = 8.5$ Å, $c = 17.5$ Å, $\beta = 108°$; volume of the unit cell = 2292 Å^3; space group $P2_1/n(C_{2h}^5$, No. 14); 8 molecules in the unit cell[**]. Thus the dibromide appears isomorphous with the dichloride as reported by *Dunitz et al.*[5].

Another reaction in which the reported complexes behave in a similar manner to the carbonyls is the initiation of radical polymerization[6].

Compared with the carbonyls, the Me(0) complexes have the advantage that they are easier and safer to handle as well as more reactive.

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[*] Dr. G. Henrici-Olivé and Dr. S. Olivé
Monsanto Research S.A.
Binzstr. 39
CH-8045 Zürich (Switzerland)

[**] Our thanks are due to Dr. *P. J. Wheatley* and Dr. *J. J. Daly* for the crystallographic determinations.

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Nitrogen Fixation on New Transition Metal Complexes

By *G. Henrici-Olivé* and *S. Olivé*[*][**]

A number of the complexes that are obtained on reduction of a transition metal salt with lithium naphthalide (LiNp) in tetrahydrofuran (THF)[1–3] are capable of fixing and reducing molecular nitrogen. The ability to do this increases with the number of electrons carried by the complex (*i.e.* with increasing excess of LiNp) and, in favorable cases, results in the fixation of one N_2 molecule per molecule of metal complex. Since the number of electrons stored within the complex reaches a maximum of 6 per metal atom[2,3], it can be assumed that the nitrogen is present as N^{3-} in the complex:

$$N_2 + 6e \rightarrow 2\,N^{3-} \qquad (1)$$

The results of some fixation experiments are shown in Table 1 (20 °C, duration of reaction of N_2 with the complex in THF = 30 min).

Table 1. Nitrogen fixation on reduced transition metal salts in solution.

Salt	LiNp/ metal	N_2-pressure (atm)	NH_3/ metal
VCl_3	3	120	0.9
	5	120	1.2
	7	120	2.0
	10	1	0.9
$CrCl_3$	10	120	1.2
	10	1	0.4
$TiCl_4$ [a]	10	120	1.3
	15	120	1.7

[a] In toluene.

The solution of the metal salt was added to that of LiNp under N_2. After half an hour the reaction mixture was hydrolysed and analysed for ammonia according to reference [4]. At higher pressures, an ampoule containing the salt solution was broken (by the stirrer) in a solution of LiNp in an autoclave at the desired N_2 pressure No NH_3 was found in LiNp solution alone (120 atm, 24 h).

The mechanism of fixation and reduction indicated in eq. (1) finds support in the results of hydrolysis experiments. The electrons stored in the complex are consumed in decomposing water when the complex is hydrolysed. Thus the volume of hydrogen produced on hydrolysis gives an indication of the number of electrons available [2]. If the complexes are prepared under nitrogen the number of hydrogen atoms evolved on hydrolysis will be reduced by a quantity equal to the number of electrons that have been consumed in reducing the molecular nitrogen. This behavior is shown in Table 2. The ratio NH_3/metal in the last column was calculated according to equation (2), which follows from eq. (1):

$$NH_3/\text{metal} = 2\ (a-b)/3 \qquad (2)$$

Table 2. Hydrolysis of solutions of transition metals reduced under argon and under nitrogen.
LiNp/metal = 10; T = 20 °C; N_2-pressure = 1 atm.

Metal	H_2/metal under Ar = (*a*)	H_2/metal under N_2 = (*b*)	NH_3/metal (exp.)	NH_3/metal (calc.)
V	3.1	1.9	0.9	0.8
Cr	3.6	2.8	0.4	0.5
Ni	2.0	2.0		

It is worthy of note that Ni solutions, which under the given conditions did not fix any nitrogen, evolved the same amount of hydrogen when reduced under nitrogen as when reduced under argon.

Fixation of nitrogen under mild conditions by non-enzymatic systems which are based on transition metal salts and reducing agents such as Al-alkyls, Grignard compounds, or $LiAlH_4$ has been extensively investigated by *Volpin et al.* [4,5]. The highest yield was reported for the system bis(cyclopentadienyl)titanium dichloride/ethylmagnesium bromide, where 0.47 molecules of nitrogen per Ti atom were detected [5] after 31 hours at 150 atm nitrogen pressure.

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[*] Dr. G. Henrici-Olivé and Dr. S. Olivé
Monsanto Research S.A.
Binzstrasse 39
CH-8045 Zürich (Switzerland)

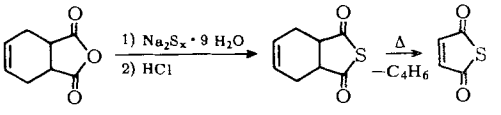
[**] We thank Mr. *F. Bangerter* for able and conscientious experimental work.

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Preparation of Maleic Thioanhydride [**]

By *H.-D. Scharf* and *M. Verbeek* [*]

Attempts to prepare maleic thioanhydride *(3)* have hitherto failed [1]. We have now succeeded in finding a method for preparing this substance and for studying its properties [2].

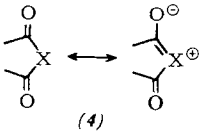


(1) *(2)* *(3)*

Starting from the readily accessible 1,2,3,6-tetrahydrophthalic anhydride *(1)*, we prepared the hitherto unknown thio derivative *(2)* as follows: The anhydride and $Na_2S_x \cdot 9H_2O$ were triturated in a mortar and then poured into 10 % hydrochloric acid; the thioanhydride *(2)* was extracted with ether and isolated by vacuum distillation in 40 to 50 % yield with b.p. 81–83 °C/0.1 mm [3]. It solidified to colorless crystals which melt at 29 °C [3]. It is sparingly soluble in toluene, from which it recrystallizes at room temperature. On treatment with an aqueous suspension of mercury(II) oxide it is converted into the known *cis*-1,2,3,6-tetrahydrophthalic acid. In the IR spectrum of *(2)* (in $CHCl_3$), the carbonyl vibration is at 1710 cm^{-1}, being shifted by 70 cm^{-1} towards lower wavenumbers in comparison with *(1)*.

Thermal retro-diene fission of *(2)* in an electrically heated quartz tube (2.5 cm × 30 cm) at 430 to 450 °C with nitrogen as carrier gas (between 6.0 and 6.2 liter/h) leads to maleic thioanhydride *(3)* with *ca.* 50 % conversion and more than 90 % selectivity. The mixed product contains small amounts of decomposition products with, mainly, the thioanhydrides *(2)* and *(3)*, which are separated by distillation. The compound *(2)* recovered is used for further cleavage experiments.

The thioanhydride *(3)* boils at 72–74 °C/10 mm [3]; it solidifies to pale yellow, translucent crystals of m.p. 28 °C [3]. It becomes deep brownish-yellow in air and is sensitive to moisture. UV absorption (in n-hexane): 318 nm (ε = 620) and 230 nm (ε = 9300). NMR spectrum ($CDCl_3$, tetramethylsilane as internal standard): the signal of the two protons is at τ = 2.8 (maleic anhydride, τ = 2.85). IR spectrum ($CHCl_3$): *(3)* shows typical anhydride splitting ($\Delta\gamma$ = 40 cm^{-1}) of the carbonyl vibration at 1690 cm^{-1} (high intensity) and 1730 cm^{-1} (low intensity); these bands are both shifted by *ca.* 100 cm^{-1} to lower wavenumbers in comparison with maleic anhydride ($\Delta\gamma$ = 70 cm^{-1}) at 1780 cm^{-1} (high intensity) and 1850 cm^{-1} (low intensity) [4].



(4)

According to *Mirone* and *Chiorboli* [5] the fairly large splitting of the IR carbonyl bands of maleic anhydride is due to participation of polar limiting structures (cf. *(4)*). In *(3)*

participation of such polar resonance forms must therefore be small.

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[*] Dr. H.-D. Scharf and cand. chem. M. Verbeek
Organisch-Chemisches Institut der Universität
Meckenheimer Allee 168
53 Bonn (Germany)

[**] We are grateful to Prof. *F. Korte* for his interest in this work. Thanks are also due to the Deutsche Forschungsgemeinschaft for their support.

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H/D Exchange in *N,N*-Dimethylformamide Acetals and Orthoformic Esters [**]

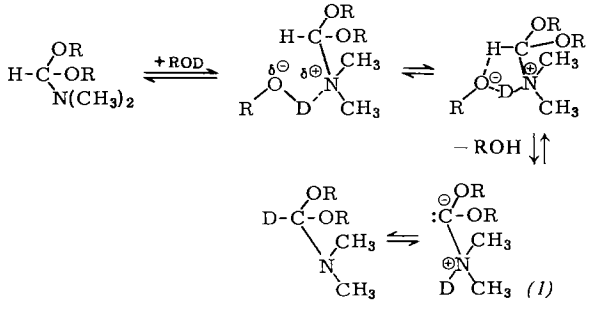
By *G. Simchen, S. Rebsdat,* and *W. Kantlehner* [*]

In connection with electrophilic substitution at the formyl-carbon atom of orthoformamides[1] we have studied the kinetic acidity of the formyl-hydrogen atom by means of H/D exchange reactions. It is known that the H atom of chloroform can be exchanged for deuterium within a few hours in the presence of bases[2], whereas analogous experiments with orthoformic esters were negative[3]. It was thus all the more surprising that, when dissolved in deuterioalcohols, most *N,N*-dialkylformamide acetals exchange their formyl proton for deuterium within a few minutes. The rate of exchange depends on the acidity of the alcohol used.

Overall velocity constants R^+ (sec^{-1}) [4] for H/D exchange between amide acetals and deuterated alcohols.

N,N-Dimethylformamide acetal	R in ROD	R^+
Dimethyl acetal	CH_3	1.63×10^{-2}
Diethyl acetal	C_2H_5	1.37×10^{-2}
Di-n-propyl acetal	n-C_3H_7	1.10×10^{-2}
Diisopropyl acetal	iso-C_3H_7	0.90×10^{-2}
Di-n-butyl acetal	n-C_4H_9	0.78×10^{-2}

The exchange reactions could be followed by NMR spectroscopy, using the diminishing CH-proton signal and the increasing intensity of the OH-proton signal of the alcohol formed. We assume that the exchange occurs by way of an ylide *(1)*.



(1)

We found that trimethyl orthoformate exchanges its formyl-hydrogen for deuterium if deuteriomethanol is allowed to react with the ester in the presence of deuterated sulfuric acid.

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[*] Dr. G. Simchen, Dr. S. Rebsdat, and
Dipl.-Chem. W. Kantlehner
Institut für Organische Chemie der Technischen Hochschule
Azenbergstr. 14–16
7 Stuttgart 1 (Germany)

[**] The Kinetic Acidity of Orthoformic Acid Derivatives.

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Synthesis and Properties of Diphenylphosphinous Amide

By *O. Schmitz-Du Mont, B. Ross,* and *H. Klieber* [*]

On ammonolysis of the triphenyl derivatives of arsenic, antimony, and bismuth in liquid ammonia in the presence of KNH_2 all the phenyl groups are removed as benzene to give $K[As(NH)_2]$, $K[Sb(NH)_2]$, and BiN, respectively[1]. Triphenylphosphine behaves differently. Even when it is heated in an autoclave at 130 °C, only one C_6H_5 group is eliminated as benzene, and the potassium salt *(1)* of diphenylphosphinous amide results:

$$P(C_6H_5)_3 + KNH_2 \rightarrow \underset{(1)}{(C_6H_5)_2PNHK} + C_6H_6$$

Treatment of *(1)* with NH_4Cl in liquid NH_3 affords the free amide *(2)*:

$$(C_6H_5)_2PNHK + NH_4Cl \rightarrow \underset{(2)}{(C_6H_5)_2PNH_2} + KCl + NH_3$$

This amide is also formed on ammonolysis of $(C_6H_5)_2PCl$ *(3)*[2]. It is obtained in a very pure state by reaction of *(3)* with a solution of KNH_2 in liquid NH_3:

$$\underset{(3)}{(C_6H_5)_2PCl} + KNH_2 \rightarrow \underset{(2)}{(C_6H_5)_2PNH_2} + KCl$$

Diphenylphosphinous amide *(2)* is an almost colorless oil (m.p. −54 °C), which is very soluble in liquid NH_3 and on cooling to −76 °C crystallizes in large needles. When warmed it eliminates NH_3 even below 100 °C, losing 0.5 mol. equiv. within 24 h at 150 °C with formation of tetraphenyldiphosphazane *(4)*[3]:

$$2\ \underset{(2)}{(C_6H_5)_2PNH_2} \rightarrow \underset{(4)}{(C_6H_5)_2P{-}NH{-}P(C_6H_5)_2} + NH_3$$

When recrystallized from benzene this product melts at 152 °C; it is difficulty soluble in liquid NH_3 but dissolves more readily on addition of KNH_2 indicating salt formation.

Hydrolysis of *(2)* in the presence of HNO_3 affords diphenylphosphinic acid $(C_6H_5)_2PO(OH)$.

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[*] Prof. Dr. O. Schmitz-Du Mont, Dr. B. Ross, and Dipl.-Chem. H. Klieber
Anorganisch-Chemisches Institut der Universität
Meckenheimer Allee 168
53 Bonn (Germany)

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Addition of R_3Ge and R_3Si Radicals to Multiple Bonds

By *K. Kühlein, W. P. Neumann*, and *H. P. Becker* [*]

Compounds $(R_3Ge)_2Hg$ *(1)*, which are quite stable thermally, react rapidly and exothermally with radical trapping agents even at room temperature, *e.g.* [1,2]:

$$[(C_2H_5)_3Ge]_2Hg + I_2 \xrightarrow{-Hg} 2\,(C_2H_5)_3GeI$$

$$+ \tfrac{1}{2}\,O_2 \xrightarrow{-Hg} (C_2H_5)_3Ge\text{-}O\text{-}Ge(C_2H_5)_3$$

$$+ BrCH_2\text{-}CH_2\text{-}Br \xrightarrow{-Hg} 2\,(C_2H_5)_3GeBr + H_2C{=}CH_2$$

It thus follows that induced decomposition is possible in which trialkylgermyl radicals occur as intermediates; this has been demonstrated by ESR spectroscopy [3].

We have now found that *(1)*, R = C_2H_5 [4], also reacts readily with compounds that contain C=C, C≡C, or N=N groups. The triethylgermyl groups always add to the unsaturated system with separation of Hg. Silyl compounds $[(CH_3)_3Si]_2Hg$ *(2)* react similarly [5,6]. Tables 1 and 2 present a selection of the compounds prepared.

We treated 10 mmoles of each compound listed in the tables with 10 mmoles of *(1)* or *(2)* under the conditions stated. The mercury was then syphoned off and the mixture was worked up by fractional distillation for distillable products and by crystallization from ethanol or acetonitrile for solid products. All the adducts were identified by C, H, N analyses and IR spectra, and most of them by hydrolysis with C_2H_5OH/H_2O (1:1) or by reaction with acyl chlorides.

Yields were generally very good. Polymerization and abstraction reactions competed, but with phenylacetylene only polymerization took place. Although only 1,2-addition normally occurred, with ethylenetetracarboxylic and 2-cyano-3-methylcrotonic ester we observed 1,4-addition to give the corresponding ketene acetals.

At least part of the additions occurs by way of radicals: ESR signals [3] were found during the four reactions with acetylenedicarboxylic and ethylenetetracarboxylic ester.

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[*] Dr. K. Kühlein, Prof. W. P. Neumann, and H. P. Becker
Institut für Organische Chemie der Universität
Ludwigstr. 21
63 Giessen (Germany)

[1] *K. Kühlein*, Diploma Thesis, Universität Giessen; cited in [2] and by *W. P. Neumann* and *K. Kühlein*, Liebigs Ann. Chem. *683*, 1 (1965).

[2] *N. S. Vyazankin, G. A. Razuvaev*, and *E. N. Gladisev*, Doklady Akad. Nauk SSSR *151*, 1326 (1963), encountered these compounds simultaneously and independently.

[3] We thank Prof. *A. Scharmann* and *G. Born* for these measurements.

[4] Prepared according to the equation:
$2\,(C_2H_5)_3GeH + Hg(C_2H_5)_2 \rightarrow [(C_2H_5)_3Ge]_2Hg + 2\,C_2H_6$
in absence of solvent and with exclusion of air at 20 °C, then at 120 °C until evolution of ethane is complete. The Ge–H band at 2006 cm^{-1} has then disappeared.

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Table 1. Addition of $(C_2H_5)_3Ge$ groups to multiple bonds; R = C_2H_5; X = $(C_2H_5)_3Ge$.

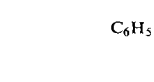
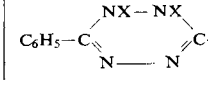
Reactant for *(1)*	Conditions (°C/min)	Product: Structure	Product: Properties	Yield (%)
ROOC–C≡C–COOR	110/120	ROOC–CX=CX–COOR	Colorless liquid, b.p. 129 °C/10^{-3} mm	78
HC≡C–$COOCH_3$	90/1500	H–CX=CX–$COOCH_3$	Colorless liquid, b.p. 120 °C/0.7 mm	55
$(ROOC)_2C$–$C(COOR)_2$	80/1800	$(ROOC)_2CX$–C(COOR)=C(OX)(OR)	Pale yellow oil	95
ROOC–N=N–COOR	0/15	ROOC–NX–NX–COOR	Colorless liquid b.p. 120 °C/10^{-4} mm	95
C_6H_5–N=N–C_6H_5	160/10	C_6H_5–NX–NX–C_6H_5	Colorless crystals m.p. 56 °C	85
	110/100		Red oil	80

Table 2. Addition of $(CH_3)_3Si$ groups to multiple bonds; R = C_2H_5; Y = $(CH_3)_3Si$.

Reactant for *(2)*	Conditions (°C/min)	Product: Structure	Product: Properties	Yield (%)
$(ROOC)_2C$=C$(COOR)_2$	20/240 [a]	$(ROOC)_2CY$–C(COOR)=C(OY)–OR	Yellow oil	95
$(CH_3)_2C$=C(CN)COOR	80/800	$(CH_3)_2CY$–C(CN)=C(OY)–OR	Yellow oil	70
ROOC–C≡C–COOR	20/5	ROOC–CY=CY–COOR	Colorless rhombs, m.p. 68 °C	60
H–C≡C–$COOCH_3$	80/5	H–CY=CY–$COOCH_3$	Colorless liquid, b.p. *ca.* 200 °C [c]	30
ROOC–N=N–COOR	–10/15 [b]	ROOC–NY–NY–COOR	Colorless liquid b.p. 58 °C/10^{-4} mm	95
C_6H_5–N=N–C_6H_5	160/10	C_6H_5–NY–NY–C_6H_5	Colorless needles, m.p. 108 °C	90

[a] In benzene. [b] In toluene. [c] Isolated by preparative gas chromatography.

Reaction of Phosphorylides with 2-Chlorovinyl Ketones [1]

By *Elisabeth Werner* and *E. Zbiral* [*]

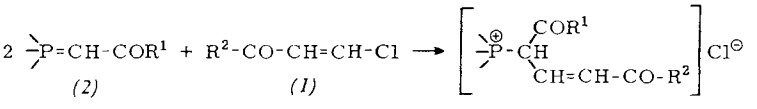
2-Chlorovinyl ketones *(1)* react readily with nucleophiles [2] thus:

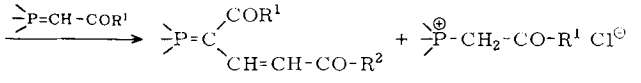
$$R\text{-}CO\text{-}CH{=}CH\text{-}Cl + B^{\ominus} \rightarrow RCOCH{=}CH\text{-}B + Cl^{\ominus}$$

(1)

Both stabilized phosphorylides *(2)* and alkylphosphorylides *(4)* can be alkylated by compounds of type *(1)*. The phosphonium salt formed as intermediate at once reacts further with a second molecule of the ylide used, undergoing transylidation [3].

The small yields from the ylides *(3d)* and *(3e)* (R^1 = alkyl group) are probably attributable to the *O*-alkylation [4] that predominates.





(3)

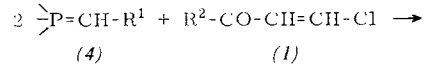
	R^1	R^2	Yield (%)	M.p. (°C)
(3a)	$-OC_2H_5$	$-CH_3$	49.4	172–175 [a]
(3b)	$-OC_2H_5$	$-CH_2CH_3$	81.4	170–171 [a]
(3c)	$-OC_2H_5$	$-CH(CH_3)_2$	90.0	138–140 [b]
(3d)	$-CH_3$	$-CH_3$	18.2	174–176 [a]
(3e)	$-CH_3$	$-CH(CH_3)_2$	20.7	146–148 [b]

[a] From ethyl acetate/cyclohexane (1:1).

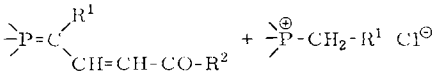
[b] From ether.

The compounds of type *(3)* are vinylogues of the diacylalkylidenephosphoranes prepared by *Horner* [5]. Whereas these no longer give salts, compounds *(3)* still dissolve in dilute HCl and can be precipitated therefrom. Hand in hand with this goes their ability to undergo a Wittig reaction with reactive aldehydes (*e.g.* phenylglyoxal).

Reaction of alkylphosphorylides *(4)* with 2-chlorovinyl ketones has been successful when $R^1 = C_6H_5\text{-}S-$, C_6H_5-, $C_6H_5\text{-}CH_2-$, and $CH_3CH{=}CH-$.



(4) *(1)*



(5)

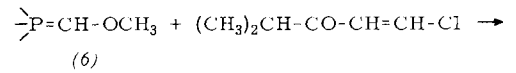
	R^1	R^2	Yield (%)	M.p. (°C) [a]
(5a)	$C_6H_5\text{-}S-$	CH_3CH_2-	25.8	188–189
(5b)	$C_6H_5\text{-}S-$	$(CH_3)_2CH-$	87.5	235–237
(5c)	$C_6H_5\text{-}S-$	C_6H_5-	66.3	218–220
(5d)	C_6H_5-	CH_3CH_2-	72.5	216–218
(5e)	C_6H_5-	$(CH_3)_2CH-$	87.0	227–229
(5f)	$C_6H_5CH_2-$	$(CH_3)_2CH-$	36.0	185–188
(5g)	$CH_3CH{=}CH-$	$(CH_3)_2CH-$	26.2	160–162 [b]

[a] All the compounds melt with decomposition and, except for *(5g)*, were recrystallized from acetonitrile.

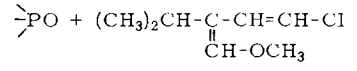
[b] Recrystallized from cyclohexane.

The reaction leading to *(5g)* with α-alkylation is remarkable. In such cases reaction with an acid chloride occurs with γ-alkylation [6].

(Methoxymethylene)triphenylphosphorane *(6)* and 2-chlorovinyl isopropyl ketone do not give a phosphorylide under these conditions, but instead a Wittig reaction occurs:



(6)



The structures of the compounds recorded were proved by elemental analyses and IR and NMR spectra.

Compounds (3a)–(3e)

To the ylide *(2)*, dissolved in anhydrous benzene, the 2-chlorovinylketone [0.5 mole for each mole of *(2)*] is added and refluxed for 5–10 hours. After cooling to room temperature the phosphonium salt is filtered off, the solution is washed well with water, dried over Na_2SO_4, and evaporated. After wetting with ether the ylides *(3)* usually crystallize on scratching.

Compounds (5a)–(5g)

The ylide is prepared by adding the corresponding volume of an etheral C_6H_5Li solution to a well stirred suspension of phosphonium salt $(C_6H_5)_3\overset{\oplus}{P}\text{–}CH_2R_1X^{\ominus}$ in anhydrous ether. After the addition of β-chlorovinylketone in ethereal solution stirring is continued for 10–15 minutes at room temperature. Then the two to threefold quantity of benzene is added and the mixture refluxed for one hour. After cooling to room temperature the solution is shaken with water and any undissolved residues are filtered off. The organic layer is dried over Na_2SO_4 and evaporated. The compounds *(5)* crystallize on wetting with ether.

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[*] Elisabeth Werner and Dr. E. Zbiral
Organisch-Chemisches Institut der Universität
Währingerstr. 38
A-1090 Wien (Austria)

[1] Part XVI of Reactions with Organophosphorus Compounds. – Part XV: *E. Zbiral* and *M. Rasberger*, Tetrahedron, in press.

[2] *N. K. Kochetkov, L. I. Kudryaskov*, and *B. P. Gottikh*, Tetrahedron *12*, 63 (1961); *N. K. Kochetkov*, Prakt. Chem. (Vienna) *12*, 336 (1961); *N. Sugiyama* and *G. Inoni*, Yuki Gosei Kagaku Kyokai Shi *19*, 373 (1961); Chem. Abstr. *55*, 17484 (1961).

[3] *H. J. Bestmann* and *B. Arnason*, Chem. Ber. *95*, 1513 (1962).

[4] *F. Ramirez* and *S. Dhersowitz*, J. org. Chemistry *22*, 41 (1957).

[5] *L. Horner* and *H. Oediger*, Chem. Ber. *91*, 473 (1958).

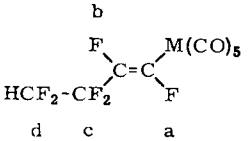
[6] *H. J. Bestmann* and *H. Schulz*, Liebigs Ann. Chem. *674*, 11 (1964); *E. Zbiral* and *L. Berner*, Tetrahedron, in press (Part XIV of this series).

Formation of Fluoroorganocarbonylmanganese and -rhenium Complexes from Hexafluoro-1,3-butadiene and Pentacarbonylmanganese and -rhenium Hydrides

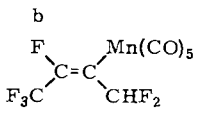
By *B. W. Tattershall, A. J. Rest, M. Green*, and *F. G. A. Stone*[*]

When tetrafluoroethylene reacts with carbonyl(transition metal) hydrides, the $F_2C{=}CF_2$ group is inserted into the metal-hydrogen bond forming, for example, $F_2HCCF_2Mn(CO)_5$[1], $(F_2HCCF_2)_2Fe(CO)_4$[2], and $F_2HCCF_2Co(CO)_4$[3].

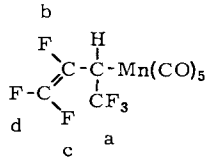
Treatment of hexafluoro-1,3-butadiene with pentacarbonylrhenium hydride at room temperature affords a volatile white crystalline complex *(1a)*[4] (yield 45%), the proposed structure being in accord with the infrared (ν(CO), 2142(s), 2067(m), 2038(vs), 2008(vs); ν(C=C–Re), 1638(m) cm^{-1}), ^{19}F-NMR (multiplets at 102.6(F_a), 118.7(F_c), 138.2(F_d), and 159(F_b) ppm, with relative intensity 1:2:2:1; $J_{a,b}$ = 129.5 and J_{d-H} = 53.4 Hz), and ^{1}H-NMR (τ = 4.05; J_{H-d} = 53.4 Hz) spectra.



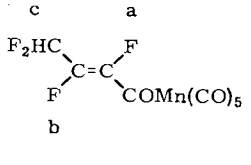
(1a), M = Re
(1b), M = Mn



(2)



(3)



(4)

In contrast, pentacarbonylmanganese hydride and hexafluoro-1,3-butadiene react rapidly at 0 °C to give several complexes with fluoroorganomanganese groups of a hitherto unknown type, as well as a mixture of *cis*- and *trans*-1,1,2,3,4,4-hexafluoro-2-butene. The nature of compounds *(1b)–(4)* was established by elemental analysis, mass spectrometry, and examination of their IR and NMR spectra: *(1b)*, yield 8%, ν(C=C–Mn) 1637(m) cm^{-1}; ^{19}F-NMR multiplets at 97.6(F_a), 118.6(F_c), 137.6(F_d), and 160.2(F_b) ppm, with relative intensity 1:2:2:1, J_{ab} = 126.5, J_{d-H} = 53.5 Hz; ^{1}H-NMR spectrum showed one band at τ = 4.06, J_{H-d} = 53.5 Hz.

(2), yield 15%, ν(C=C–Mn) 1648(sh), 1630(m) cm^{-1}; ^{19}F-NMR multiplets at 63.1(F_c), 81.4(F_b), and 93.5(F_a) ppm, with intensity 3:1:2, J_{a-H} = 60.0 Hz; ^{1}H-NMR showed a band at τ = 3.2, J_{H-a} = 60.0 Hz.

(3), yield 9%, ν(C=C–C–Mn) 1773(m) cm^{-1}; ^{19}F-NMR bands at 57.0(F_a), 107.1(F_d), 119.3(F_c), and 161.0(F_b) ppm, of intensity 3:1:1:1; ^{1}H-NMR showed a quartet split into a doublet of doublets at τ = 7.22.

(4), yield 13%, ν(C=C) 1674(m), ν(COMn) 1597(m) cm^{-1}; ^{19}F-NMR multiplets at 125.8(F_c), 144.5(F_a), and 170.9(F_b) ppm, with intensity 2:1:1, J_{ab} = 129.0, J_{cb} = 18.6, J_{c-H} = 51.8, and J_{b-H} = 14.6 Hz; ^{1}H-NMR spectrum showed one band at τ = 3.60, J_{H-c} = 51.8 and J_{H-b} = 14.6 Hz.

Complexes *(1a)* and *(1b)* correspond to a reaction involving 1,4-addition of the hydride to hexafluoro-1,3-butadiene, followed by a 1,3-fluorine shift:

$$F_2C{=}CF{-}CF{=}CF_2 + HMn(CO)_5 \rightarrow [F_2HC{-}CF{=}CF{-}CF_2{-}Mn(CO)_5] \rightarrow \textit{(1b)}$$
(5)

Evidence for the intermediacy of the insertion product *(5)* is provided by the isolation of 1,1,2,3,4,4-hexafluoro-2-butene, which could form by reaction of *(5)* with $HMn(CO)_5$[3]. Since the fluoroolefin is formed as a mixture of isomers, the 1,4-addition to give *(5)* cannot be stereospecific, and a cyclic concerted mechanism for the addition is unlikely. A two-stage process involving a resonance-stabilized allylic intermediate seems more probable.

Compound *(2)* appears to arise through 1,2-addition, followed by a 2,4-fluorine shift; while formation of *(3)* could involve 1,2-addition and then a hydride shift. It is suggested that the acyl complex *(4)* is produced by the capture by water of an allylic intermediate involved in the transformation of *(5)* to *(1b)*.

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[*] Dr. B. W. Tattershall, A. J. Rest, Dr. M. Green, and Prof. F. G. A. Stone
Department of Inorganic Chemistry,
The University of Bristol
Bristol 8 (England)

[1] *P. M. Treichel, E. Pitcher*, and *F. G. A. Stone*, Inorg. Chem. *1*, 511 (1962).

[2] *P. M. Treichel* and *F. G. A. Stone*, Abstracts 2nd International Symposium on Fluorine Chemistry, Estes Park, July 1962, p. 201; *M. R. Churchill*, Inorg. Chem. *6*, 185 (1967).

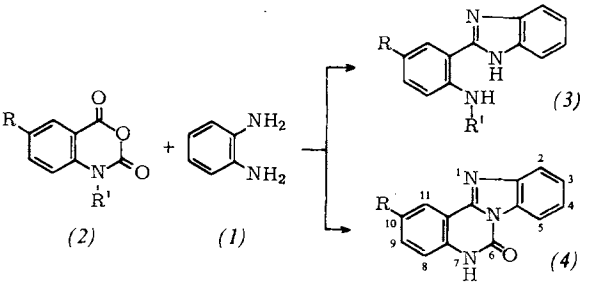
[3] *J. B. Wilford, A. Forster*, and *F. G. A. Stone*, J. chem. Soc. (London) *1965*, 6519.

[4] All the complexes prepared were separated by chromatography on a silica column, using pentane-CH_2Cl_2 as eluent. The complexes were purified by sublimation (subl. temp. 20 °C/0.001 mm).

Condensed Imidazoles from *o*-Diamines and Isatoic Anhydrides

By *E. C. Taylor* and *F. Yoneda*[*]

2-(*o*-Aminophenyl)benzimidazoles *(3)* and 6,7-dihydrobenzimidazo[1,2-*c*]quinazolin-6-ones *(4)* are formed when *o*-phenylenediamine *(1)* is heated with isatoic anhydrides *(2)* under gentle reflux for 20 minutes in sulfolane as solvent followed by cooling and dilution with water. *(3)* dissolves in boiling ethanol from which it is precipitated on dilution with water; it may be recrystallized from aqueous ethanol. *(4)* is purified by recrystallization from aqueous dimethylformamide.

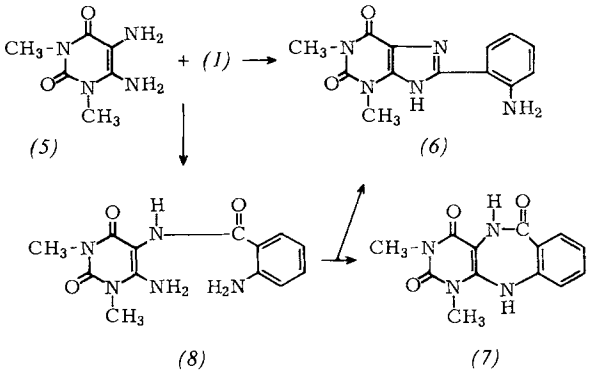


(2) *(1)* *(3)* *(4)*

	R	R'	*(3)* M.p. (°C)	*(3)* Yield (%)	*(4)* M.p. (°C)	*(4)* Yield (%)
a	H	H	213 [1]	68	334 [3]	20
b	Cl	H	244 [2]	56	>340	30
c	NO_2	H	295 (decomp.)	39	>350	57
d	H	CH_3	213	95	—	0
e	Cl	CH_3	175	90	—	0
f	NO_2	CH_3	315 (decomp.)	85	—	0
g	H	C_2H_5	124	85	—	0
h	H	$CH_2C_6H_5$	188	88	—	0

A remarkable solvent effect was found when *(1)* and *(2a)* were heated under gentle reflux for 30 minutes in dimethyl sulfoxide; the major product was benzimidazolone (69%), with only a minor amount (17%) of *(4a)* formed.

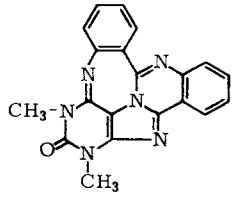
Reaction of 1,3-dimethyl-4,5-diaminouracil *(5)* with *(1)* in sulfolane under the conditions described above gave a mixture of 8-(*o*-aminophenyl)theophyllin *(6)* (m.p. > 320 °C) and 1,3-dimethyl-11*H*-pyrimido[4,5-*b*][1,4]benzodiazepine - 2,4,6-(1*H*, 3 *H*, 5 *H*)-trione *(7)* (m.p. 260 °C), which could be separated by fractional crystallization from dimethylformamide. The compounds were obtained in yields of 17 % and 16 % respectively and were purified by recrystallization from alcohol or dimethylformamide. Compound *(7)*, a 'homo-alloxazine' in which the central ring of alloxazine has been expanded to seven members, is the first example of this ring system.



(5) *(6)* *(8)* *(7)*

Fusion of *(1)* and *(5)* at 220 °C for 1 hour gave 4-amino-5-(*o*-aminobenzamido)-1,3-dimethyluracil *(8)* (m.p. 296 °C) which was purified by recrystallization from aqueous dimethylformamide. On boiling with $POCl_3$, *(8)* was converted into *(6)*, and into a mixture of *(6)* and *(7)* by heating in sulfolane.

The novel hexacyclic purine derivative *(9)* (m.p. 285 °C) was formed by heating either *(5)* or *(6)* with anthranilic acid in polyphosphoric acid at 250–280 °C for 5 hours, followed by addition of water (yield 25 %; purification by recrystallization from dioxane). The composition and structure of *(9)* was ascertained by elemental analysis, molecular weight determination (by mass spectrometry), and from IR (no N–H absorption) and NMR spectra. An analogous pentacyclic product is obtained from *o*-phenylenediamine and anthranilic acid in polyphosphoric acid [2].



(9)

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[*] Prof. E. C. Taylor and Dr. F. Yoneda
Department of Chemistry, Princeton University
Princeton, New Jersey (USA)

[1] *D. W. Hein, R. J. Alheim,* and *J. J. Leavitt,* J. Amer. chem. Soc. *79*, 427 (1957).

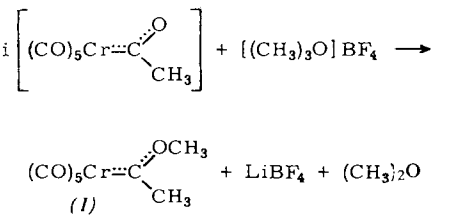
[2] *L. L. Zaika* and *M. M. Joullié,* J. heterocyclic Chem. *3*, 289 (1966).

[3] *S. von Niementowski,* Ber. dtsch. chem. Ges. *32*, 1478 (1898).

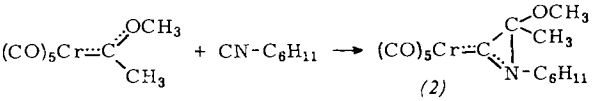
Addition of Isocyanides to Transition Metal Carbene Complexes

By *R. Aumann* and *E. O. Fischer* [*]

Methoxymethylcarbenepentacarbonylchromium(0) *(1)* can be readily obtained in good yields (>90 %) by the alkylation [1] of $Li[(CO)_5CrCOCH_3]$ [2] with $[(CH_3)_3O]BF_4$. It



reacts with isocyanides (at 0 °C in pentane) to form a new type of carbene complex *(2)*, in which the carbene carbon atom is incorporated in an aziridine system. The reaction proceeds by insertion of the isocyanide carbon atom into the original Cr-carbene bond.



Methoxymethylcarbenepentacarbonylchromium(0) (1):

A suspension of 10 g (0.045 mole) of dry, finely powdered $Cr(CO)_6$ in 500 ml of water-free ether is prepared in a 1 liter round bottom flask fitted with a side arm for nitrogen introduction. 90 ml of a 0.5 M ethereal $LiCH_3$ solution is added slowly to the suspension from a measuring pipette. During the addition, the mixture is stirred vigorously with a magnetic stirrer; an intense yellow coloration develops as the $Cr(CO)_6$ goes into solution. When all the $LiCH_3$ has been added, the ether is removed in a water-pump vacuum and the residue is dissolved in *ca.* 100 ml of water. 6.71 g (0.045 mole) $[(CH_3)_3O]BF_4$ is added in small portions to this solution whereupon the carbene complex immediately separates as an oil. Completion of reaction is indicated by acid reaction of the aqueous solution; oxonium salt is added until such an acid reaction is manifest. Since the complex itself is decomposed by acid it must be extracted with pentane (*ca.* 200 ml) immediately after the reaction has reached completion. The pentane solution is filtered (through a G4 sintered disk loaded with freshly ignited Na_2SO_4) and evaporated to one third of its original volume. On cooling *ca.* 9.8 g (87 %) of the complex crystallizes out as long yellow needles. The yield can be increased by evaporation of the mother liquor and sublimation of the residue. After one recrystallization from pentane, the complex has m.p. 34 °C.

(2) is formed as odorless, yellow crystals [m.p. 65.5–66.5 °C (decomp.)], which in air are rapidly converted into a green, resinous material. The mass spectrum [3] of *(2)* shows a molecular ion at $m/e = 359$ and $[(CO)_nCr\cdot Ligand]^+$ (n = 5,4...0) ions in accordance with the expected fragmentation pattern of a $(CO)_5Cr$ complex.

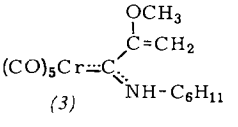
The following reactions have been carried out in order to establish the presence of an aziridine structure:

i) Reaction of *(2)* with benzoyl peroxide at 0 °C to give the compound *(3)* [yellow crystals, m.p. 99.5–100 °C].

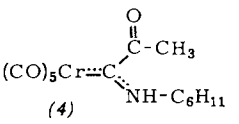
ii) Reaction of *(3)* with 2 N HCl in H_2O/THF at 20 °C to give *(4)* [yellow crystals, m.p. 114 °C (decomp.)].

iii) Compound *(4)* heated at 80–100 °C in a high vacuum to give *(5)* [colorless crystals, m.p. 72 °C].

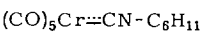
The compounds *(2)*, *(3)*, and *(4)*, which are obtained in almost quantitative yields, may be purified by recrystallization



(3)

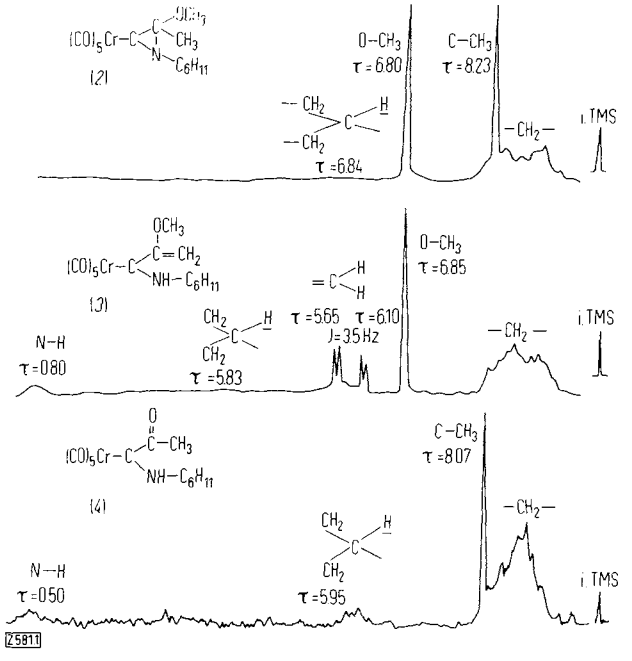


(4)

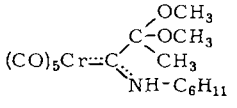


(5)

from pentane or hexane after removal of the reaction medium. The compounds have been characterized by elemental analysis, and by their IR, ^{1}H-NMR (10 % solution in C_6D_6, see figure), and mass spectra.



The formation of the stable aminodimethoxyketal carbene complex *(6)* [yellow crystals, m.p. 109.5–110 °C] when *(2)* is



(6)

allowed to react with CH_3OH at 20 °C is further evidence for the presence of an aziridine structure in *(2)*.

In the presence of aqueous acid, *(6)* is converted into *(4)*.

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[*] Dr. R. Aumann and Prof. E. O. Fischer
Anorganisch-Chemisches Laboratorium
Arcisstrasse 21
8 München 2 (Germany)

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[3] Studies carried out by *J. Müller*, Atlas CH4, 50 eV.

Thermophilic and Mesophilic Aminopeptidases from *Bacillus stearothermophilus* [1]

By *H. Zuber* and *G. Roncari* [*]

We have isolated from several strains of *Bacillus stearothermophilus* [2], three aminopeptidases that differ in molecular weight, thermal stability, and substrate specificity. Aminopeptidase I (AP I) is thermostable and is therefore designated a thermophilic enzyme. The aminopeptidases II and III (AP II and III) are mesophilic enzymes and thermolabile. All three enzymes are metal enzymes. In their native forms they probably occur as Co^{2+} or Mn^{2+} enzymes since, after inactivation by EDTA, they are best reactivated by Co^{2+} and Mn^{2+} ($Co^{2+} = Mn^{2+} \gg Mg^{2+} > Ni^{2+} > Cd^{2+}$). Ca^{2+}, Zn^{2+}, and Fe^{2+} do not activate but (in concentrations of 0.001 to 0.05 M) inhibit them. The pH optimum for all three enzymes is at pH = 7.5 to 9. The substrate specificity (Table 2) is, in part, very different from the specificity of leucinaminepeptidase (LAP) [3] from pig's kidneys.

Table 1. Properties of aminopeptidases I–III

	AP I	AP II	AP III
Molecular weight [a]	*ca.* 150000	*ca.* 70000	*ca.* 80000
Michaelis constant K_m (60 °C, Leu-Gly) (mmoles/l)	95	37	4
Activation energy [b] (kcal/mole)	16.3	16.3	—
Optimum temperature (°C)	90	60	60
Thermal stability [c] (% of initial activity after 3 min	—	64	81
18 min	120	35	54
120 min at 80 °C)	120	0	0

[a] Determined by gel filtration, Sephadex G-200, 0.05 M Tris-HCl buffer, pH = 7.2, 10^{-3} M Co^{2+}.

[b] Determined by hydrolysis of a 0.0075–0.06 M Leu-Gly solution (AP I and AP II), or of a 0.0002–0.002 M Leu-Gly solution (AP III) (0.05 M Tris-HCl buffer, pH = 7.2, 10^{-3} M Co^{2+}; incubation time 10 min at 20, 40, 60, 80, 90 °C).

[c] Determined by hydrolysis of a 0.06 M Leu-Gly solution, 0.05 M Tris-HCl buffer, pH = 7.2, 10^{-3} M Co^{2+}. Incubation time 10 min at 65 °C (AP I) or 37 °C (AP II and III).

AP I has a specific activity of 1000 units mg^{-1} min^{-1}, where the unit is defined as hydrolysis of 1 μmole of substrate per min. The molecular activity is 150000 mole·(mole of enzyme)$^{-1}$·min^{-1}. Both these activities were determined by hydrolysis of a 0.045 M solution of Gly-Leu-Tyr in 0.05 M Tris-HCl buffer at pH 7.2 and 65 °C with 10^{-3} M Co^{2+}.

Table 2. Substrate specificities (substrate concentrations: 0.045M, 65 °C, 0.05 M Tris-HCl buffer, pH = 7.2, + 10^{-3} M Co^{2+}). The figures (except those in column C_1) denote % hydrolysis in 5 min.

Peptide	AP I	C_1 [a]	AP II	AP III
Leu-Gly	16	30	1.6	1.6
Gly-Leu	0.8	1.4	0.1	0.09
Leu amide	5	8.8	9	1.2
Leu-Gly-Gly	30	50	25	80
Gly-Leu-Tyr	36	77	8	18
Pro-Tyr-Lys	3.2	5.6	2.7	25
Glu-Ala-Ala	5.5	9.8	1.2	1.7
Lys-Tyr-Glu	1.5	2.6	1.3	24

[a] $C_1 = k_1/E$; k_1 = rate constant for first-order reaction; E = protein concentration (mg of N per ml) on the basis of a 15 % nitrogen content in the protein.

AP I was purified by repeated chromatography in 0.05 M Tris-HCl buffer (10^{-3} M Co^{2+}) on Sephadex G-150 and DEAE-Sephadex A-50, and AP II and AP III by repeated chromatography on Sephadex G-100 and DEAE-Sephadex. AP I, AP II, and AP III are homogeneous on polyacrylamide electrophoresis [4] (pH = 8.9, 45 min). Preliminary experiments with the ultracentrifuge gave: for AP I, $S_{20} = 2.80 \times 10^{-13}$ and $D_{20} = 1.8 \times 10^{-7} \pm 0.16$ (symmetrical band). It follows that AP I is highly hydrated in solution or is a very extended molecule. AP I is stable in 8 M urea solution, but it is inactivated by reagents such as formic acid or LiBr that break hydrogen bridges and is thereby split into fragments (gel electrophoresis).

All three enzymes are found even at the beginning of the log phase of the growth curve of the bacteria, and both in the cells and in the culture medium. The yield of enzymes is maxi-

mal at the end of the log phase and in the stationary phase (24–30 h). The amounts of AP I, AP II, and AP III present in *Bacillus stearothermophilus* vary according to the strain. Obligatory thermophilic strains (temperature optimum 55 °C, no growth at 37 °C) produce much AP I and AP II and little AP III, whereas obligatory mesophilic strains (temperature optimum 37 °C, no growth at 55 °C) contain much AP III and very little AP I or AP II. Facultative strains (growth at 37 °C and 55 °C) may contain the three aminopeptidases in comparable amounts.

For preparation of the crude enzyme mixture the bacteria were opened up by ultrasonic vibrations or in a sand mill. Treatment with lysozyme liberated only AP II and AP III; AP I seems to be more firmly bound to the cell membranes. The aminopeptidases were obtained from the culture medium by adsorption on DEAE-Sephadex (pH = 7.2) and elution with 1 M NaCl solution (0.05 M Tris-HCl buffer, pH = 7.2, 10^{-3} M Co^{2+}).

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[*] Dr. H. Zuber and Dr. G. Roncari
Laboratorium für Molekularbiologie der
Eidgenössischen Technischen Hochschule
Universitätsstr. 6
CH-8006 Zürich (Switzerland)

[1] This work was supported by the Schweizerische Nationalfonds zur Förderung der wissenschaftlichen Forschung (Project No. 3426).

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Synthesis of Hydridopentacyanoiridate Complexes

By *K. Krogmann* and *W. Binder* [*]

Suggestions that complexes of the type $[MH(CN)_5]^{3-}$ (M = Co, Rh, Ir) exist in solution [1,2] have been questioned [3] since, hitherto, such compounds have not been successfully isolated. We have now been able to prepare iridium compounds of this type by reaction of bis(1,3-cyclohexadiene)-iridium chloride [4], $Ir(C_6H_8)_2Cl$, or bis(2,3-dimethylbutadiene)iridium chloride, $Ir(C_6H_{10})_2Cl$, with excess KCN in CH_3OH:

$$Ir(C_6H_8)_2Cl + 5\,KCN + CH_3OH \rightarrow K_3[IrH(CN)_5] + KCl + KOCH_3 + 2\,C_6H_8.$$

$K_3[IrH(CN)_5]$ is a white, crystalline, diamagnetic compound, which is unaffected by air; it is very soluble in water and moderately soluble in CH_3OH. It reduces two equivalents of iodine per mole Ir. Aqueous solutions are stable at room temperature for many hours, after which a grey-white polymer begins to deposit. The free acid, which may be prepared from the potassium salt by cation exchange, contains three strongly acidic protons, which can be titrated. It may be isolated as white $(H_3O)_3[IrH(CN)_5]$. Addition of $AgNO_3$ solution leads to the precipitation of white, insoluble $Ag_3[IrH(CN)_5]$, which turns dark at the surface on standing.

No deuterium exchange was observed in a solution of $K_3[IrH(CN)_5]$ in D_2O, even after 7 days at 20 °C.

IR-spectra of $K_3[IrH(CN)_5]$ (in KBr, nujol, and Hostaflon) show bands at 2110 cm^{-1} (vs) [shoulder at 2127 and at 2152 cm^{-1}], and 2043 cm^{-1} (m) as C–N– and Ir–H– stretching frequencies. Further bands occur at 810 (s, shoulder at 855), 533 (s), 513 (s), 454 (w), 404 (s), 386 (s), 333 (w), and 302 cm^{-1} (w) [5]. We assume ν(Ir–H) to be at 2043, δ(Ir–H) at 810 cm^{-1}.

The UV-spectrum of the aqueous solution of $K_3[IrH(CN)_5]$ has an absorption maximum at 470 nm (ε = 540) and a shoulder at 364 nm (ε = 36) [6]. In D_2O, there is a ^1H–NMR signal at δ = +1730 Hz (reference signal: HDO) or τ = 23.9 ppm [5], as expected [2]. All known data confirm C_{4v} symmetry for the complex.

Preparation: 3.25 g (50.0 mmole) of KCN is dissolved in 200 ml of water-free CH_3OH and then 1.94 g (5.00 mmole) of $Ir(C_6H_8)_2Cl$ or 1.96 g of $Ir(C_6H_{10})_2Cl$ is added. The yellow color of the solution disappears within minutes. Olefin, together with CH_3OH, is driven off from the solution by distillation. Methanol must be added to the solution during the distillation until all the liberated olefin has been removed. Within 3 h the desired complex separates from the solution as a white, finely crystalline mass, which can be dried under vacuum (yield 85 %).

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[*] Priv.-Doz. Dr. K. Krogmann and Dipl.-Chem. W. Binder
Laboratorium für anorganische Chemie der
Technischen Hochschule
Schellingstr. 26
7 Stuttgart-N (Germany)

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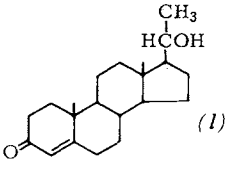
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[5] Thanks are due to Prof. *G. Laukien* (Karlsruhe) and Mr. *T. Keller* for recording the NMR spectrum.

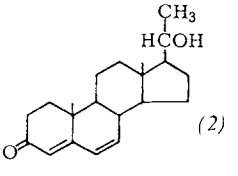
Identification of the Subsidiary Steroids from the Prothoracic Protective Gland System of *Dytiscus marginalis* [1,2]

By *H. Schildknecht* and *D. Hotz* [*]

The methanol-soluble part of the secretion from the prothoracic protective glands of *Dytiscus marginalis* contains cortexone as main component [3]. When this steroid is isolated as previously described [4], it contains as impurities substances whose molecular weights are shown by their mass spectra to be 316 and 314. If, however, the gland secretion is worked up by thin-layer chromatography [silica gel G and cyclohexane/ethyl acetate (1:1)], these subsidiary products are found to be enriched together in the zone immediately above that of cortexone. By repeated chromatography [5] this mixture can be separated into two components with absorption maxima at 283 and 240 nm.



(1)



(2)

Help with identification of these compounds was obtained from the circular dichroism of the less polar compound whose absorption maximum is at 240 nm. The position and fine structure of the maximum at 331 nm indicated a 3-oxo-Δ4-steroid [6], and indeed we found in the mass spectrum a peak at *m/e* = 124 characteristic of such a steroid [7]. Comparison with the mass spectrum of a steroid that we had isolated from the prothoracic protective glands of the water beetle *Acilius sulcatus* [5] enabled the *Dytiscus* steroid of *m/e* 316 to be identified as 20α-hydroxy-4-pregnen-3-one *(1)*.

Our assumption that, as with *Acilius sulcatus* and *Cybister lateralimarginalis* [8], the second subsidiary steroid would be the corresponding 6,7-dehydro compound was confirmed by

IR spectroscopy. However, this 20α-hydroxy-4,6-pregnadien-3-one (cybisterone) occurs in vanishingly small amounts compared with *(1)*.

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[*] Prof. H. Schildknecht and Dipl.-Chem. D. Hotz
Organisch-Chemisches Institut der Universität
Tiergartenstrasse
69 Heidelberg (Germany)

[1] Part 29 of Protective Substances of Arthropods. – Part 28: *H. Schildknecht, H. Winkler, D. Kraus,* and *U. Maschwitz,* Z. Naturforsch., in press.

[2] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie. We thank Dr. *Wiechert* (Schering, Berlin) for samples.

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Preparation of *N*-(Dichloromethylene)-chlorosulfonamide and -fluorosulfonamide [1]

By *H. W. Roesky* and *U. Biermann* [*]

Chlorosulfonyl isocyanate *(1)* [2] reacts with phosphorus pentachloride *(2)* to give *N*-(dichloromethylene)chlorosulfonamide *(3)*.

$$\underset{(1)}{ClSO_2\text{-}N{=}C{=}O} + \underset{(2)}{PCl_5} \longrightarrow \underset{(3)}{ClSO_2\text{-}N{=}C(Cl)Cl} + \underset{(4)}{POCl_3}$$

0.1 mole each of *(1)* and *(2)* are heated together in a sealed, thick-walled glass tube for 1.5 h at 210 °C. The tubes may be opened at room temperature without cooling. *(1)* and *(4)* are distilled off at atmospheric pressure, and *(3)* is then distilled off in a water-pump vacuum (b.p. 71–72 °C/15–16 mm, 32–33 °C/0.2 mm; yield 10 %). At this stage, the product *(3)* contains $(CNCl)_3$ as impurity; it is obtained pure by repeated distillation.

The mass spectrum contains, besides the molecular ion at *m/e* 195, peaks for the following fragments: SO_2NCCl_2 (160), SO_2Cl (99), $NCCl_2$ (96), SO_2 (64), NCCl (61), SO (48), and CCl (47). The IR spectrum (capillary film) in the NaCl and KBr regions contains bands at 1608, 1570, 1402, 1180, 940, 790, 627, 593, 550, and 530 cm^{-1}. These are provisionally assigned as follows: ν(C=N) 1608 and 1570 (because of Fermi splitting) ν_{as}(SO) 1402, ν_s(SO) 1180, ν_{as}(CCl) 940, ν_s(CCl) 790, ν(S–N) 627, ν(S–Cl) 593, and deformation vibrations. The compound *(3)* reacts with antimony trifluoride to afford *N*-(dichloromethylene)fluorosulfonamide *(5)*.

$$\underset{(3)}{} + SbF_3 \longrightarrow \underset{(5)}{FSO_2\text{-}N{=}C(Cl)Cl}$$

0.3 mole of *(3)* is heated with an excess of SbF_3 ($SbCl_5$ as catalyst) for 2 h at 60 °C and for a further 2 h at 85 °C. The mixture is then distilled in an oil-pump vacuum. The product *(5)* is collected in a cold trap (liquid nitrogen) and then refractionated. Crude yield, 0.2 mole; pure yield, 0.05 mole (b.p. 114–115 °C). Compound *(5)* can also be obtained from fluorosulfonyl isocyanate and phosphorus pentachloride in a sealed tube, the yield being 5 %.

The IR spectrum of *(5)* contains bands at 1615, 1440, 1220, 950, 850, 798, 628, 570, and 500 cm^{-1}. Provisional assignments are: ν(C=N) 1615, ν_{as}(SO) 1440, ν_s(SO) 1220, ν_{as}(C–Cl) 950, ν(SF) 850, ν_s(C–Cl) 798, ν(SN) 628, and deformation vibrations. The ^{19}F-NMR spectrum contains a signal at $\delta = -54.2$ ppm referred to CCl_3F as external standard. The mass spectrum shows, besides the molecular ion at *m/e* = 179, fragments FSO_2NCCl (144), SO_2F (83), SF (51), and SO (48).

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[*] Dr. H. W. Roesky and Dipl.-Chem. U. Biermann
Anorganisch-Chemisches Institut der Universität
Hospitalstr. 8/9
34 Göttingen (Germany)

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Adsorption of Nitrogen on Iron

By *R. Brill, E.-L. Richter,* and *E. Ruch* [*]

In connection with investigations on the catalysis of NH_3 synthesis by iron, experiments on the adsorption of nitrogen on iron tips were performed by means of the field electron microscope. Fig. 1a shows the emission picture of the clean tip prepared by field evaporation in presence of hydrogen. The crystal is oriented with the axis of the tip perpendicular to 110. Fig. 1b shows the effect of physical adsorption of N_2 at the temperature of liquid nitrogen. The pattern shown in Fig. 1c was obtained after the tip with physically adsorbed N_2 had been heated, without field, for 3 seconds to a temperature of about 400 °C. It can easily be seen that the main change takes place at the 111 faces. Here the work function is remarkably large. (Some change also occurs at the 100 poles and in a circular zone around them. This circular zone probably represents a series of steps.)

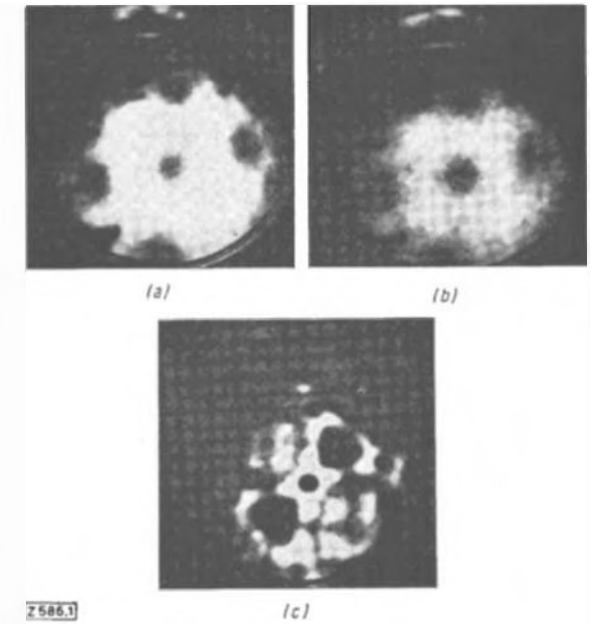


Fig. 1. Field electron microscope patterns. (a) A clean iron tip (longitudinal axis of iron tip perpendicular to the 110 face), (b) the same tip after adsorption of N_2 at 76 °K, and (c) after adsorption of N_2 and subsequent heating at *ca.* 400 °C for about 3 sec.

From these experimental results the following conclusions may be drawn:

1. N_2 is preferentially chemisorbed at the 111 face of iron.

2. The work function is increased by the adsorption of N_2.

3. The adsorption of N_2 diminishes the surface energy of the 111 face; consequently, this non-equilibrium face grows.

These facts can be understood on the basis of a theoretical model[1] which describes the possibility of binding the nitrogen molecule. According to this model the partner should be able to accept the four π electrons of an N_2 molecule without completely destroying the bonds they form between the nitrogen atoms. For this reason the partner should have empty orbitals of low energy that are transformed according to $e^{i\varphi}$ and $e^{-i\varphi}$ with regard to an at least threefold symmetry-axis. These orbitals should overlap with the π orbitals of the nitrogen molecule when oriented along this axis, and there should be no considerable repulsion between other electrons of the binding partners.

In an iron crystal, all iron atoms are surrounded by eight nearest neighbors at the corners of a cube; the 111 surface therefore appears to be a suitable binding partner for nitrogen molecules having their molecular axes perpendicular to this surface. As the iron atoms of the 111 plane occupy lattice points of a two-dimensional hexagonal lattice and the distance between these surface atoms is $2\sqrt{2}/3$ times the nearest-neighbor distance within the crystal, the iron atoms on the surface surround cavities of trigonal symmetry. It can be assumed that the surface atoms provide unoccupied atomic orbitals which can combine to give π orbitals with regard to the trigonal cavity axis. Thus the adsorption of nitrogen molecules at the cavities of the 111 surface can be explained. Since the assumed binding weakes the N_2 π bonds of the nitrogen molecules this may well represent the initiating step in the catalysis of the ammonia synthesis.

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[*] Prof. R. Brill and E. L. Richter
Fritz-Haber-Institut der Max-Planck-Gesellschaft
Faradayweg 4–6
1 Berlin 33 (Dahlem) (Germany)
Prof. E. Ruch
Institut für Quantenchemie der Freien Universität
Holbeinstr. 48
1 Berlin 45 (Germany)

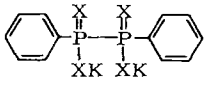
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Dipotassium Diphenylhypophosphonate and Diphenyltetrathiohypophosphonate

By *E. Fluck* and *H. Binder*[*]

Hypophosphonic and tetrathiohypophosphonic acid and their derivatives were hitherto unknown.

We have now prepared the potassium salts of diphenylhypophosphonic acid *(1)* and diphenyltetrathiohypophosphonic acid *(2)* by reduction of phenylphosphonic anhydride *(3)* and phenyldithiophosphonic anhydride *(4)*, respectively, with elemental potassium.



(1) X = O
(2) X = S

Phenylphosphonic anhydride (14.0 g, 0.05 mole) is added to a solution of potassium (3.9 g, 0.1 g-atom) in 100 ml liquid ammonia, whereupon the blue color rapidly disappears. After removal of the solvent, the salt *(1)* can be extracted from the residue with 80 % ethanol. On concentration of the solution, *(1)* is precipitated as colorless needles that are readily soluble in water (yield 47.5 %). The ^{31}P-NMR spectrum contains one singlet, which proves the equivalence of the two phosphorus atoms. The chemical shift is $\delta_P = -5.2$ ppm (referred to 85 % aqueous H_3PO_4).

Reduction of phenyldithiophosphonic anhydride[1] is effected by adding it to a solution of potassium in the tris(dimethylamide) of phosphoric acid, *e.g.* 17.2 g (0.05 mole) of the anhydride to a solution of 3.9 g (0.1 g-atom) of potassium in 50 ml of $OP[N(CH_3)_3]_2$. Heat is evolved and within about 30 min the initially blue solution becomes colorless. After the amide has been distilled off in a vacuum a pale yellow product is found which can be recrystallized from 80 % ethanol. Yield 35 %. The chemical shift of the singlet in the ^{31}P-NMR spectrum occurs at $\delta_P = -95.2$ ppm.

The free acids can be obtained from the potassium salts by adding dilute HNO_3 to their aqueous solutions[2].

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[*] Prof. E. Fluck and Dr. H. Binder
Anorganisch-Chemisches Institut der Universität
Tiergartenstrasse 4
69 Heidelberg 1 (Germany)

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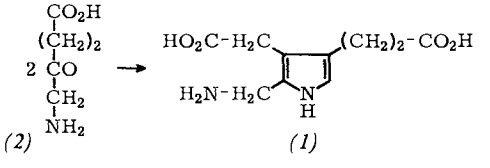
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Preparation of Porphobilinogen from 5-Aminolevulic Acid by means of *Propionibacterium shermanii*

By *G. Bezold*, *G. Müller*, and *O. Müller*[*]

Porphobilinogen *(1)* can be prepared by chemical methods only with difficulty[1]. It is isolated from the urine of patients suffering from acute porphyria or from the urine of rabbits that have been treated with Sedormid or other compounds that induce porphyria[1]. A further method of obtaining porphobilinogen consists in enzymic treatment of 5-aminolevulic acid *(2)* with 5-aminolevulic acid dehydratase[1,2].

We have found that porphobilinogen *(1)* can be obtained from 5-aminolevulic acid *(2)* by fermentation with *Propionibacterium shermanii*. Porphobilinogen is isolated from the culture medium. Resting cells also yield porphobilinogen, and this has the advantage that the difficult isolation from the culture medium is not needed. The bacteria can be used for several batches; the yield is decreased slightly but only on the third incubation.



(2) *(1)*

When *P. shermanii* acts on 5-aminolevulic acid, products other than porphobilinogen are also found in the medium. We are studying whether these further compounds[3] are intermediates in the formation of porphyrin or in the biosynthesis of the corrin ring.

Experimental

A cobalt-free batch (4 liters) of *P. shermanii* is grown for three days under conditions described previously[4]. The moist bacterial mass (*ca.* 100 g) obtained on centrifugation is washed with tris[(hydroxymethyl)amino]methane/HCl buffer (pH = 8.2)[5] and suspended in 1500 ml of this buffer. A solution of 5-aminolevulic acid hydrochloride (820 mg) in water (100 ml), whose pH has been adjusted to 7 by NaOH, is added and the mixture is incubated for 1 h at 70 °C with stirring and passage of nitrogen. The solution is freed from bacteria by

centrifugation, adjusted to pH = 7.2 by dilute hydrochloric acid and placed on a column (10 cm in length, 4.5 cm in diameter) of DEAE-cellulose (DEAE-Sephadex A-25) whose chloride form has been washed with tris[(hydroxymethyl)-amino]methane/HCl buffer (pH = 7.2) until the eluate has pH = 7.2. The column is eluted with buffer until no more porphobilinogen is removed from it. The eluates are evaporated in a vacuum to *ca.* 1800 ml, then adjusted to pH = 4 by dilute hydrochloric acid and treated with 20 % mercury(II) acetate solution. The resulting precipitate is centrifuged off, washed with 1 % mercury(II) acetate solution, and suspended in *ca.* 3 ml. of water. H_2S is passed into the suspension to decompose the mercury compound. Then the precipitate is centrifuged off, nitrogen is passed into the liquid to remove H_2S, and the pH of the liquid is adjusted to pH = 4 by dilute hydrochloric acid. This precipitates crude porphobilinogen[6] which is centrifuged off after having been kept for 12 h in a refrigerator. Just sufficient 0.5 N ammonia is added to the centrifuge tube to dissolve the porphobilinogen, undissolved material is centrifuged off, the pH is adjusted carefully to 4 by glacial acetic acid for precipitation of the porphobilinogen, and the whole is left overnight in a refrigerator. The crystals are filtered off under suction and washed with ice-cold dilute acetic acid (pH = 4) and immediately thereafter with a little cold acetone. Drying in a vacuum desiccator gives 73 mg (12 %) of porphobilinogen.

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[*] Dipl.-Chem. G. Bezold, Dr. G. Müller, and Dr. O. Müller
Isotopenlaboratorium der Abteilung für Chemie, Geologie und Biologie der Universität
Azenbergstrasse 14–16
7 Stuttgart (Germany)

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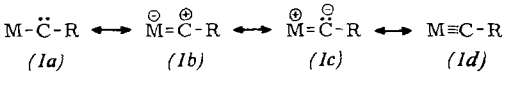
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Triphenylstannyl- and Trimethylsilyl-ethoxycarbonylcarbene from Ethyl Diazo-(triphenylstannyl)- and -(trimethylsilyl)-acetate

By *U. Schöllkopf* and *N. Rieber*[*]

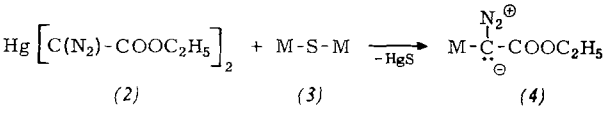
Unusual properties are to be expected for metalated carbenes because the empty or filled electron orbitals of the metal may interact with those of the carbene-carbon atom, giving the mesomeric limiting structures *(1a)* to *(1d)*. We have obtained



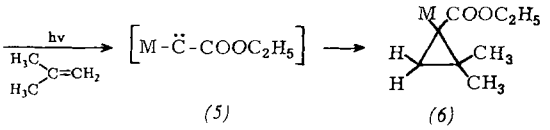
(1a) *(1b)* *(1c)* *(1d)*

M=Metal

the first metalated carbenes, namely, triphenylstannyl- and trimethylsilyl-ethoxycarbonylcarbene *(5)*, by photolysing ethyl diazo-(triphenylstannyl)- [$\nu(N_2)$ = 2080 cm^{-1}, $\nu(CO)$ = 1670 cm^{-1}] and -(trimethylsilyl)-acetate [$\nu(N_2)$ = 2090 cm^{-1}, $\nu(CO)$ = 1685 cm^{-1}] in isobutene (0.03 M or 0.3 M, respectively) until the solutions were decolorized[1]. This affords ethyl 2,2-dimethyl-1-(triphenylstannyl)cyclopropanecarboxylate *(6a)* (yield 35 %) and the corresponding trimethylsilyl ester *(6b)* (yield 49 %), respectively, [$\nu(CO)$ = 1710 cm^{-1} for *(6a)*, 1715 cm^{-1} for *(6b)*; NMR, AB spectrum of the cyclopropyl protons, τ = 8.7 (CCl_4), J_{AB} = 4.5 Hz for *(6a)*, τ = 9.0 (C_6D_6), J_{AB} = 4 Hz for *(6b)*]. The starting materials *(4a)* and *(4b)* were obtained (in yields of 80 and 95 %, respectively) by treating diethyl mercuribis(diazoacetate) *(2)*[2] in boiling benzene for 5 and 3 h, respectively, with rather more than one equivalent of bis(triphenylstannyl) or bis(trimethylsilyl) sulfide *(3)*. After filtration, the benzene solutions were evaporated (aspirator vacuum) in a rotary evaporator.



(2) *(3)* *(4)*



(5) *(6)*

(a), M = $Sn(C_6H_5)_3$
(b), M = $Si(CH_3)_3$

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[*] Prof. U. Schöllkopf and Dr. N. Rieber
Organisch-Chemisches Institut der Universität
Windausweg 2
34 Göttingen (Germany)

[1] Conditions: Hanovia lamp 450 W, Pyrex filter, −7 °C.

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Sulfur and Selenium Adsorbate on Platinum Electrodes in Acid and Alkaline Electrolytes

By *H. Binder, A. Köhling*, and *G. Sandstede*[*]

Since the properties of catalysts are modified by adsorbates, it is of interest to find out the conditions under which adsorbed substances exist on the surface of catalysts. We have studied the adsorption of sulfur and of selenium on platinum by the

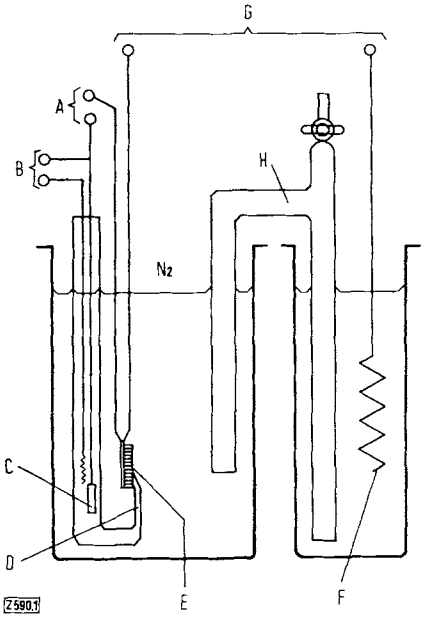


Fig. 1. Half-cell for potentiodynamic current density measurements. A: continuously increasing, or decreasing, reference voltage; B: electrolytic H_2-production for the H_2-reference electrode; C: H_2-reference electrode; D: capillary; E: measuring electrode; F: counter electrode; G: anodic or cathodic current flow caused by change of reference voltage.

triangular voltage sweep method. A continuously increasing voltage (against a reversible hydrogen reference electrode in the same electrolyte) was applied to a porous platinum electrode [1] (Raney platinum) in a half cell arrangement (Fig. 1).

The voltage was allowed to attain a prefixed value (*ca.* 1300mV) and was then continuously decreased. The resulting anodic or cathodic current flow was recorded as a function of the reference voltage (Fig. 2).

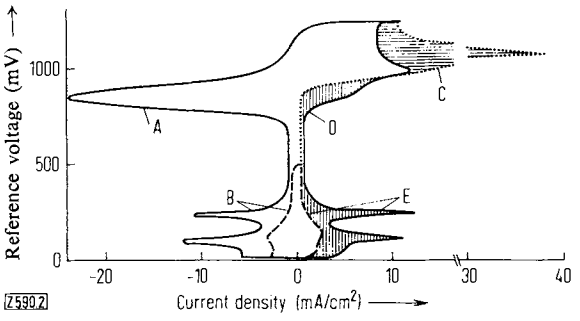


Fig. 2. Periodic current-voltage curve of a platinum electrode with (and without) selenium adsorbate, and potentiodynamic curve of the oxidation of selenium adsorbate.

——— without selenium adsorbate; with selenium adsorbate; ····· oxidation of the selenium adsorbate; electrolyte: 3 N H_2SO_4; 90 °C. Rate of change of reference voltage 40 mV/min.

A: Cathodic reduction of O-adsorbate; B: cathodic reduction (discharging) of H^+ ions during formation of H-adsorbate; C: anodic oxidation of Se-adsorbate; D: anodic oxidation of H_2O during formation of O-adsorbate; E: anodic oxidation of H-adsorbate.

In many acidic and alkaline electrolytes a monatomic hydrogen adsorbate, which is formed reversibly on the platinum surface, is present at 0 mV; at *ca.* 1300 mV a monatomic oxygen adsorbate is present. In acid electrolytes, oxygen adsorbate formation, which is caused by electron transfer from adsorbed water, begins at 800 mV. In alkaline electrolytes, oxygen adsorbate formation caused by electron transfer from adsorbed hydroxide ions begins at 550 mV. Reduction of oxygen adsorbate starts at a lower reference voltage than that at which it is formed.

Sulfur as well as selenium can be adsorbed on the platinum surface to form a complete monolayer, thus preventing hydrogen adsorption on the covered atoms. It is possible to determine the degree of coverage by comparing the quantities of charge (the area under the curves in the range 0 to 500 mV) necessary for the deposition or removal of hydrogen adsorbate layer with, and without, sulfur or selenium adsorbate (Fig. 2).

Sulfur is adsorbed when the electrode is placed in sulfur vapor, sulfur solution, carbon disulfide, hydrogen sulfide gas or sodium sulfide solution. It can also be deposited by cathodic reduction of sulfuric acid, sulfurous acid, or sulfite solution. Selenium can be adsorbed from a solution in concentrated sulfuric acid after slight dilution. Other elements may be deposited by similar methods.

The adsorbate layers may be oxidized anodically (Fig. 2). For a complete oxidation of sulfur it is necessary to keep the potential of the electrode at a value above 1200 mV for approximately one hour (selenium: several hours). The quantity of charge required for a complete oxidation of the sulfur or selenium adsorbate is approximately four times that necessary for oxidizing the displaced hydrogen. We conclude that on each surface platinum atom a sulfur or selenium atom is adsorbed which can be oxidized to SO_2 or SeO_2 respectively.

At 70 °C the sulfur adsorbate is stable up to a potential of about 650 mV [2]. This value surpasses the standard potential of oxidation of sulfur, in acid, by 200 mV. In potassium hydroxide solution oxidation sets in at about 450 mV (sulfur is not thermodynamically stable in alkaline media). Selenium is not oxidized below 900 mV in sulfuric acid (Fig. 2) (standard oxidation potential 740 mV). The simplest way of obtaining different coverages is the partial oxidation of a complete layer. It has recently been observed that adsorbates are not only responsible for inhibition of but also for acceleration of various reactions; the shift reaction and the decomposition as well as the anodic oxidation of carbon monoxide or formic acid at a platinum electrode, which are considerably accelerated by a partial coverage of the electrode surface with sulfur or selenium [2], may be cited as examples.

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[*] Dr. H. Binder, A. Köhling, and Dr. G. Sandstede
Battelle-Institut e.V.
Postfach 1337
6 Frankfurt/Main (Germany)

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CONFERENCE REPORTS

Use of Viridic Acid as Coloring Matter for Foodstuffs

By *R. Burkhardt* [*]

One of the means by which chlorogenic acid can be detected on chromatograms is by its reaction with ammonia or ammonium carbonate. This reaction leads to the formation of viridic acid, which is an unstable green compound.

More than 100 years ago a housewife unknowingly used the formation of a stabilized viridic acid to color cakes. A crude green coffee bean was left overnight in egg white that had been separated from the yolk. Chlorogenic acid extracted from the coffee bean reacted with the egg white which provided the amino groups needed for the reaction, the optimal pH, and an oxidizing enzyme, and at the same time acted as protective colloid. Pure chlorogenic acid behaves in the same way; the resulting stabilized viridic acid, is firmly bound to the albumin and cannot be separated from it without destruction.

At present chlorophyll is the only natural coloring matter allowed to be added to foodstuffs. It is now proposed that the brilliant grass-green viridic acid compound should be used; this dye is unobjectionable and is not a foreign substance since (i) it contains the digestible egg white and (ii) chlorogenic acid is a substance that occurs in many vegetable foodstuffs.

Lecture at Weinheim on April 28th, 1967 [VB 80 IE]
German version: Angew. Chem. *79*, 872 (1967)

[*] Dr. R. Burkhardt
Brentano-Strasse 4
6222 Geisenheim (Germany)

Tin Content of Condensed Milk

By *W. Wodsak* [*]

Condensed milk is stored almost exclusively in tin-plate cans. The tin content of condensed milk samples that were not older than four weeks was at most 40 ppm and rose

only inappreciably during a further five months. In storage experiments lasting more than 2 years the tin content rose to 160 ppm in exceptional cases. It was higher, on the average, in condensed milk with 10% fat content than in that with 7.5%.

There have been no reports of poisoning by the tin present in condensed milk. Nevertheless the manufacturer should be instructed to state the date of filling on the cans so that it is possible to use only tins of recent date for feeding babies.

Lecture at Weinheim on April 28th, 1967 [VB 81 IE]
German version: Angew. Chem. 79, 872 (1967)

[*] Dr. W. Wodsak
Foßsölen 6
2 Hamburg-Volksdorf (Germany)

Recovery, in Aqueous Solution, of Nuclear Fuels of High Plutonium Content

By *F. Baumgärtner* [*]

In the future, fuel elements of high plutonium content will accumulate, especially as a result of the use of fast breeder reactors. The presence of such large amounts of plutonium will make chemical reprocessing of these fuel elements difficult in many respects. In the simultaneous extraction of uranium and plutonium the uranium strongly represses the extraction of plutonium, and critical concentrations of plutonium can result in the aqueous phase. In reductive separation of plutonium and uranium, decontamination of the uranium is made difficult by the presence of large quantities of plutonium; part of the plutonium becomes irreversibly bound in the organic phase owing to radiolysis of the organic extracting medium.

Measurements of the rate of material transfer for plutonium and uranium indicated the possibility of a rapid extraction procedure and this has been developed by means of a centrifugal separator, by use of which up to 120 kg of nuclear fuel can be worked up safely per hour. At the same time disturbance of the extraction by radiolysis is reduced to *ca.* 1/20. More than 99% separation of plutonium from uranium is possible when U(IV) is used as reducing agent.

Lecture at Hannover (Germany) on June 15th, 1967 [VB 85 IE]
German version: Angew. Chem. 79, 872 (1967)

[*] Prof. Dr. F. Baumgärtner
Kernforschungszentrum
Postfach 947
75 Karlsruhe (Germany)

The Fundamental Photographic Process in Silver Halide Crystals

By *W. F. Berg* [*]

The latent image state of silver halide crystals increases the rate of reduction of the silver halides to metallic silver in the developer. We are therefore dealing with a catalyst.

In analogy with visible photolysis of silver halides it is assumed that the latent image state involves accumulation of electrons and silver atoms, about whose degree of aggregation there is still speculation. Absorption of only four quanta suffices to produce this state.

The simplest interpretation is to consider formation of the latent image as the formation of a new solid phase. The most important features of this view are:

a) The latent image state is formed independently in individual microcrystals of an emulsion.

b) Its formation is a process involving several steps – several quanta are necessary.

c) Its formation involves a reverse process: regression.

d) The latent image is formed on the surface and in the interior of the crystals.

e) Crystallization nuclei, formed by chemical treatment or preillumination, play an important role.

f) Competition between nuclei of different effectivity is important. Often several nuclei occur in any one microcrystal; these then compete with one another for latent-image substance.

These simple concepts are sufficient to account for the majority of photographic effects, such as reciprocity failure and its temperature sensitivity.

Gurney and *Mott* assumed that absorption of light liberates mobile photoelectrons, which in some cases are captured. This leads to an electric field, which attracts the mobile silver ions in interstitial positions (Frenkel defects). An aggregate of silver atoms is formed in this way. The essential principle of the *Gurney-Mott* theory is the interplay of photelectrons and mobile silver ions.

Mitchell emphasized the role of structural defects and defect electrons. A requirement of this theory is that electrons and defect electrons must remain separated; *Mitchell* achieves this by the postulate of electric charge transfer at the centers where the charge carriers are captured. On capture of defect electrons, interstitial silver ions are produced that take part in forming the image. The natural sites for capture of electrons are apparently the crystal defects and the foreign nuclei adsorbed on them (*Mitchell*); the sites of capture of the defect electrons are point defects (*Malinowski*), which stabilize the defect electrons by charge transfer (*e.g.* $Cu^{+} \rightarrow Cu^{2+}$). Thus silver halide crystals containing suitable impurities would have an in-built mechanism for separation of electrons and defect electrons.

The essential constituents of our interpretation of the formation of the latent image are thus:

1. Formation of a new solid phase.

2. The *Gurney-Mott* principle: formation of this phase by movement of electrons and silver ions.

3. The *Mitchell* principle: separation of electrons from defect electrons and their stabilization by charge transfer.

4. Separation of these charge carriers by capture on centers of different kinds – electrons on crystal defects, and defect electrons an point defects amenable to charge transfer.

Lecture at Berlin (Germany) on May 26th, 1967 [VB 87 IE]
German version: Angew. Chem. 79, 871 (1967)

[*] Prof. Dr. W. F. Berg
Eidgenössische Technische Hochschule,
Photographisches Institut
Clausiusstr. 25
CH-8006 Zürich (Switzerland)

Surface Diffusion and Relaxation Times of Adsorbed Molecules

By *R. Haul* [*]

Information about the mobility of adsorbed molecules on the surface of solids has been obtained by three methods of investigation.

a) At low surface coverage (Θ = 0.1 to 0.001 of a monomolecular layer), determination of residence times from the transport process on molecular streaming of adsorbed gas through a single capillary. Examples: Ar, Kr, Xe on Pyrex glass [1].

b) At high surface coverage (Θ = 0.1 to 1.5), determination of surface diffusion coefficients D_S from measurements of the adsorption velocity in a large number of pores (Aerosil disk) by means of a vacuum sorption balance. Examples: Ar, N_2, and organic molecules. For benzene and cyclohexane between 15 and 55 °C the D_S values are of the same order as the diffusion coefficients in liquids (10^{-5} cm²/sec). At all temperatures there is a distinct maximum at about half a monomolecular layer. Examples, at 52 °C: benzene at Θ = 0.4, $D_S = 2.0\times10^{-5}$ cm²/sec; cyclohexane at Θ = 0.3, $D_S = 2.1\times10^{-5}$ cm²/sec. This is explained by the fact that the activation energy for surface diffusion at first diminishes rapidly (from 70 % of the adsorption energy at $\Theta \approx 0.1$ to about 40 % at Θ 0.5) and that D_S increases correspondingly (filling of energy holes). As the coverage increases further the probability of place exchange of the adsorbed molecules decreases and D_S becomes correspondingly lower.

c) Determination of relaxation times from measurements with a nuclear resonance impulse spectrometer on the same samples as were used for measurement of Ds. The spin-spin relaxation times for benzene in the temperature range studied lies between that of the liquid (T_2 about 50 sec) and of the solid state (T_2 about 10 μs); for benzene adsorbed on Aerosil (Θ = 0.68) at −60 °C, T_2 = 10 ms; at +100 °C, T_2 = 80 ms.

Lecture at Hamburg (Germany) on May 25th, 1967 [VB 90 IE]
German version: Angew. Chem. 79, 908 (1967)

[*] Prof. Dr. R. Haul
Institut für Physikalische Chemie und Elektrochemie
der Technischen Hochschule
Callinstr. 46
3 Hannover (Germany)

[1] *R. Haul* and *B. Gottwald*, Surface Science *4*, 321, 334 (1966).

Structure, Preparation, and Properties of Cyclopolyphosphines

By *L. Maier* [*]

Although many cyclopolyphosphines containing aliphatic substituents have been prepared during recent years, among those with aromatic substituents only the phenyl derivative has been closely characterized [1]. Phenylcyclopolyphosphine, $(C_6H_5P)_x$, occurs in various forms, with melting points (A) 150 °C, (B) 190 °C, (C) 252–256 °C, and (D) 262–285 °C. It has been shown by X-ray structure analysis that form A is pentaphenylcyclopentaphosphine, in which the phosphorus atoms form an equilateral pentagon with approximate m symmetry. Form B occurs in at least four crystal modifications, all having the structure of hexaphenylcyclohexaphosphine with the phosphorus atoms forming a six-membered ring in the chair conformation. Forms C and D give the same Debye diagram and are highly crystalline [2], but their structures are not known.

Depending on the reaction conditions, treatment of $ClC_6H_4PCl_2$ with $ClC_6H_4PH_2$ gives three (chlorophenyl)-cyclopolyphosphines of formula $(ClC_6H_4P)_x$ with melting points (A, from ether) 191–193 °C, (B, from benzene) 194–198 °C, and (C, no solvent) 161–165 °C. Determination of the molecular weights in exaltone (cryoscopic) and benzene (osmometric) shows that the phosphorus rings are five-membered in form (A), six-membered in form (B), and four-membered in form (C).

So far, two forms of the *o*-tolyl compounds $(o\text{-}CH_3C_6H_4P)_x$ have been isolated, the melting points being (A) 290–299 °C and (C) 198–202 °C. Determination of the molecular weight in $CHBr_3$ indicates a five-membered phosphorus ring for form (A). Form (C) crystallizes in the tetragonal system, probably of space group $J\bar{4}$ with parameters $a = b = 12.89$, $c = 7.60$ Å; there are eight $o\text{-}CH_3C_6H_4P$ units in the unit cell. Although the possibility that C is monomeric or dimeric cannot yet be excluded, it is very probable that this form contains a four-membered phosphorus ring.

Lecture at Würzburg on July 7th, 1967 [VB 93 IE]
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[*] Dr. L. Maier
Monsanto Research SA
Binzstr. 39
CH-8045 Zürich (Switzerland)

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Experiments on the Scattering of Molecular Beams for the Study of Reactions of Potassium with Methyl Iodide, Hydrogen Bromide, and Bromine

By *J. P. Toennies* [*]

Theoretical and experimental developments have led to marked advances in the study of gas-phase reactions during the last few years. Particular interest attaches to work on the determination of reactive collision cross-sections (σ) by means of scattering experiments with crossed molecular beams. Reactive collision cross-sections are important for the theory of chemical reactions because they are dependent on the interaction potential $V(R)$ between all the atoms taking part in the reaction and are thus the only quantities that afford direct information about this potential. The relation between the potential and the cross-section is derived by classical calculations of trajectories. The cross-sections obtained from experiments on the scattering of molecular beams have made it possible, for the first time, to study the connection between the interaction potential and the reaction constants.

For experimental reasons, the scattering of molecular beams can at the present time only be used for study of those reactions involving at least one alkali atom (M). The exothermic reaction

$$K + CH_3I \rightarrow KI + CH_3 \qquad (\Delta E = -22 \text{ kcal/mole})$$

has been studied by the molecular beam method and has also been very recently subjected to intensive theoretical investigation by trajectory methods.

The angular distribution of the KI formed indicates that the reaction occurs mainly during the central collision in which the K atom is reflected backwards with capture of the I atom. The collision process can thus be described by the following diagram:

K	→	←	ICH_3	Before
KI	←	→	CH_3	After

The backward scattering observed indicates a short reaction time ($\tau < 10^{-12}$ sec), so that the reaction does not proceed by way of an activated complex as postulated by the Eyring theory. The velocity of the KI shows that most of the reaction energy is used for internal activation of the KI molecule. Similar results have been obtained for the reaction between K and HBr.

Bunker and *Karplus* and co-workers have carried out extensive trajectory calculations for the K + CH_3I reaction. They calculated reactive cross-sections for five potential models, of which one was shown to be satisfactory by comparing the experimental cross-section with the corresponding theoretical values; with this model the whole of the reaction energy becomes free when the distance between K and the I of CH_3I amounts to about 4 Å. In this way the first determination of the interaction potential for a reaction was made.

The potential model agrees well with the view that one electron

$K + ICH_3 \rightarrow K^{\oplus} + I^{\ominus}CH_3 \rightarrow KI + CH_3$

jumps from the potassium atom to the CH_3I. The strong attraction between the resulting ions explains why the reaction energy is liberated before the products are formed.

The electron-jump mechanism, which is also known for reactions in the liquid phase, was first used by *M. Polanyi* as early as the 1930's to explain the high velocities of reactions of the type $M + X_2$ observed in sodium flames. The results of molecular beam studies of this type of reaction agree well with the cross-section found by *Polanyi*. Molecular beam measurements also show that the products of this reaction are scattered forwards, as is to be expected from the large cross-section.

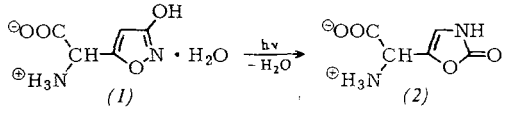
K	$\rightarrow$	$\leftarrow$	Br_2	Before
Br	$\leftarrow$	$\rightarrow$	KBr	After

Lecture at Kiel on May 11th, 1967 [VB 94 IE]
German version: Angew. Chem. 79. 907 (1967)

[*] Doz. Dr. J. P. Toennies
Physikalisches Institut der Universität
Nussallee 12
53 Bonn (Germany)

SELECTED ABSTRACTS

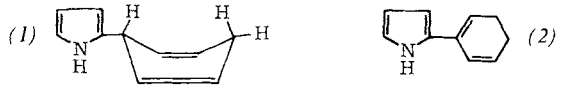
The formation of 2-oxazolones by photorearrangement of 3-hydroxyisoxazoles has been observed by *H. Göth, A. R. Gagneux, C. H. Eugster*, and *H. Schmid*. UV irradiation of aqueous solutions of ibotenic acid *(1)* from toadstools leads in 35% yield to muscazone *(2)*, an α-amino acid that has been



(1) *(2)*

isolated from *Amanita muscaria*. Similarly, UV irradiation of muscimol (5-aminomethyl-3-hydroxyisoxazolone), another active principle from *Amanita* leads to 5-aminomethyl-2-oxazolone (15%), together with 3-hydroxy-5-hydroxymethylisoxazole. 3-Hydroxyisoxazoles, *e.g.* 3-hydroxy-5-methylisoxazole, can be obtained from ethyl 3,3-bis(methoxy)butyrate by conversion into the hydroxamic acid and ring closure by heating under vacuum or with HCl gas in anhydrous methanol or glacial acetic acid. / Helv. chim. Acta *50*, 137 (1967) / –Ma. [Rd 653 IE]

A 1,4-photoaddition of pyrrole to benzene was observed by *M. Bellas, D. Bryce-Smith*, and *A. Gilbert*. UV irradiation of solutions of pyrrole in benzene at 25 °C under nitrogen led to a mixture of 1:1 adducts, about 95% of which consisted of a colorless compound having the constitution *(1)*, m.p. 15 °C. The compound is practically non-basic, and is not attacked by dilute mineral acids. On catalytic hydrogenation it gives 2-cyclohexylpyrrole and a trace of 2-phenylpyrrole. *(1)* is



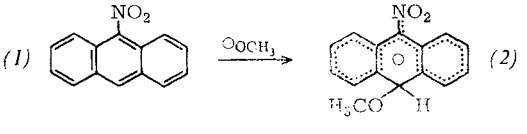
(1) *(2)*

rearranged by potassium t-butoxide into an unstable diene, probably *(2)*. The assumed constitution *(1)* is in agreement with the UV and NMR spectra. / Chem. Commun. *1967*, 263 / –Ma. [Rd 685 IE]

The Protein Sequenator described by *P. Edman* and *G. Begg* is an instrument for automatic amino-acid sequence analysis. It was used to automate the "Edman degradation", *i.e.* the reaction of the N-terminal amino acid of a peptide chain with phenyl isothiocyanate and conversion of the adduct into the peptide chain having one amino acid less and the 2-anilinothiazolin-5-one derivative of the amino acid removed. This is delivered to a fraction collector, converted outside the Sequenator into the 3-phenyl-2-thiohydantoin, and identified by thin-layer chromatography. One reaction cycle, *i.e.* the removal of one amino-acid residue from a peptide chain, involves 30 operations and takes 93.6 min. The average yield per cycle has so far been 98.5%; this permits about 100 cycles, and hence the sequence analysis of a protein consisting of 100 amino acid units. The reaction vessel, which is maintained at 50 °C thermostatically, consists of a glass beaker rotating at a constant speed of 1425 r.p.m., in which the reaction solution covers the wall in the form of a film. With this arrangement, the necessary technical operations such as dissolution, evaporation, vacuum drying, and extraction can be carried out in such a way that the protein always remains in the reaction vessel.

The Sequenator was used for the sequence analysis of humpback-whale apomyoglobin. 5.0 mg of protein were sufficient. The analysis was allowed to proceed for 60 cycles, and it was found that within this sequence of 60 amino acids, six were interchanged in relation to the sequence in sperm-whale myoglobin. / Europ. J. Biochem. *1*, 80 (1967) / –Hö. [Rd 683 IE]

A Meisenheimer complex *(2)* **containing only one nitro group** has been detected by *R. Foster, C. A. Fyfe, P. H. Emslie*, and *M. I. Foreman* by NMR spectroscopy. The addition of sodium methoxide to 9-nitroanthracene *(1)* in dimethyl sulfoxide yields a deep red solution (λ_{max} = 505 nm), and a band appears in the NMR spectrum at –4.96 ppm, whereas the absorption of the hydrogen in position 10 of *(1)* is situated at –8.92 ppm.

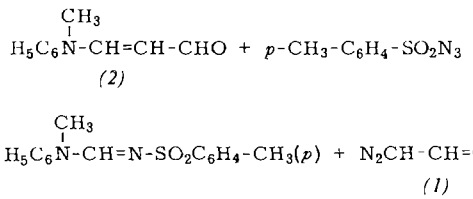


(1) *(2)*

The absorption of the protons in positions 1 and 8 is shifted from –8.2 ppm to –8.8 ppm, and the multiplet due to the remaining hydrogens is shifted from –7.75 to –7.16 ppm. Meisenheimer compounds from dinitrophenyl ether and methoxide and from trinitroaromatic compounds and acetonate (color carriers of the Janovski reaction) exhibit similar NMR-spectroscopic behavior. / Tetrahedron *23*, 227 (1967) / –Bu. [Rd 667 IE]

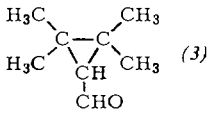
Diazoacetaldehyde *(1)* was synthesized by *Z. Arnold* by heating β-*N*-methylanilinoacrolein *(2)* with excess *p*-toluenesulfonyl azide at 70–80 °C under vacuum, whereupon diazoacetaldehyde *(1)* distilled off [pure *(1)* detonates violently when overheated!] (yield approx. 70%). *(1)* can be purified by vacuum distillation (bath temp. < 50 °C) or by extraction from aqueous solution with methylene chloride; it is a yellow liquid having b.p. 40 °C/10 mm, and is stable at

−70 °C. Decomposition of *(1)* in tetramethylethylene in the presence of copper acetylacetonate gives tetramethylcyclopropanecarbaldehyde *(3)* (yield 25 %); it is assumed that formylcarbene occurs as an intermediate.



(2)

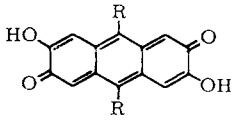
(1)



(3)

/ Chem. Commun. *1967*, 299 / −Ma. [Rd 699 IE]

Derivatives of amphi-anthraquinone, a new quinone system, have been synthesized by *P. Boldt*. 3,7-Dihydroxy-2,6-anthraquinone *(1)*, which is obtained from 2,3,6,7-tetrahydroxyanthracene by dehydrogenation with 2,3-dichloro-5,6-dicyanobenzoquinone, is a pale yellow, very unstable compound.



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

If positions 9 and 10 are screened by methyl groups, the stable, orange 3,7-dihydroxy-9,10-dimethyl-2,6-anthraquinone *(2)* is obtained. / Chem. Ber. *100*, 1270 (1967) / −Ma. [Rd 684 IE]

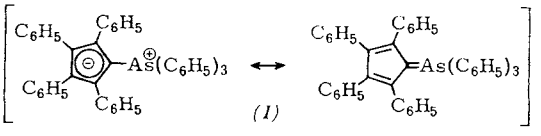
Metal carbonyls, such as $Fe(CO)_4 \cdot C_6H_5CN$, $Fe(CO)_5$, $Fe_2(CO)_9$, $W(CO)_6$, and $Mo(CO)_6$, catalyse (at concentrations of about 1 wt.-%) the conversion of isocyanates into carbodiimides. Thus bis(*o*-tolyl)carbodiimide was obtained in yields of 82.3 to 85.6 % when *o*-tolyl isocyanate was refluxed in the presence of such catalysts.

The reaction proceeds as follows:

$$M{=}C{=}O + RNCO \rightarrow M{=}C{=}NR + CO_2$$
$$M{=}C{=}NR + RNCO \rightarrow RN{=}C{=}NR + M{=}C{=}O$$

/ Tetrahedron Letters *1967*, 1731 / −Ma. [Rd 698 IE]

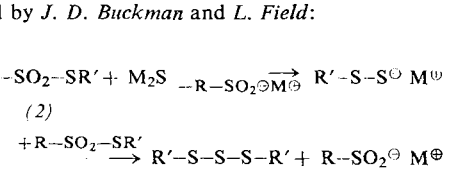
An arsene ylide has been obtained for the first time by *D. Lloyd* and *M. I. C. Singer* from a carbene and an arsine. When diazotetraphenylcyclopentadiene is heated in triphenylarsine, tetraphenylcyclopentadienylidene triphenylarsorane is formed *(1)* [m.p. 228–230 °C (decomp.), golden-yellow crystals (from nitromethane)]. This synthesis provides a new route to the formation of a C–As bond. *(1)* dissolves in perchloric acid to form triphenyl(tetraphenylcyclopentadienyl)arsonium



(1)

perchlorate. This compound and *(1)* are stable in air. *(1)* reacts only with difficulty with benzaldehyde to form 1,2,3,4,6-pentaphenylfulvene. / Chem. and Ind. *1967*, 510 / −Ma. [Rd 701 IE]

A new route to symmetrical trisulfides *(1)* *via* thiosulfonates has been found by *J. D. Buckman* and *L. Field*:



(2)

(1)

(a), R=R′=*p*-CH_3–C_6H_4; *(b)* R=*p*-CH_3–C_6H_4, R′=$C(CH_3)_3$ M=K or Na

In this way it is possible to obtain symmetrical trisulfides with a primary or tertiary alkyl group, or with an aryl group, in yields of 82–95 % and in a very pure state. The reaction of *(2a)* with potassium sulfide in methanol for 30 min at room temperature gives di-*p*-tolyl trisulfide *(1a)* (m.p. 81–82 °C) in 90 % yield. On the other hand, the reaction of t-butyl *p*-toluenethiosulfonate *(2b)* is better carried out in an ether-water mixture, since *(1b)* (b.p. 108–110 °C/20 mm Hg) is otherwise contaminated with tetrasulfide. / J. org. Chemistry *32*, 454 (1967) / −WG. [Rd 707 IE]

Thermodynamic data on the "mutarotation" of fructose, *i.e.* on the reaction

$$\beta\text{-fructopyranose } (F_6) \underset{k-}{\overset{k+}{\rightleftharpoons}} \beta\text{-fructofuranose } (F_5)$$

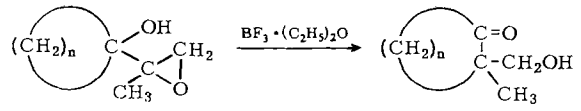
were determined by *F. Grønlund* and *B. Andersen* from the following information: initial concentrations of fructose, specific rotations α_F of the pure forms F_6 and F_5 (α_{F5} determined by *B. Andersen* and *H. Degn*, Acta chem. scand. *16*, 215 (1962) by enzymatic hydrolysis of cane sugar), time-dependence of the instantaneous rotation and its ultimate equilibrium value α_∞, and temperature-dependence of the

T (°C)	k_+ (min^{-1})	k_- (min^{-1})	$K = k_-/k_+$
25.00	0.0609	0.128	0.476
20.00	0.0370	0.0870	0.426
10.50	0.0136	0.0398	0.343

rate constants and equilibrium constants. E_A+($F_6 \rightarrow F_5$) = 17.2 kcal mole^{-1}; E_A-($F_5 \rightarrow F_6$) = 13.4 kcal mole^{-1}; ΔH^0 = 3.80 kcal mole^{-1}. / Acta chem. scand. *20*, 2663 (1966) / −Jg. [Rd 695 IE]

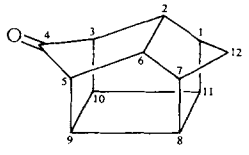
The reaction of monosaccharides with thiocyanic acid was studied by *J. C. Jochims*, *A. Seeliger*, and *G. Taigel*. D-Glucose, D-xylose, D-galactose, L-arabinose, and D-ribose react with HSCN in acidic solution to give 5-substituted 2-thioxo-6-hydroxyhexahydro-*cis*-furo[2,3-*d*]oxazoles *(1)*. D-Lyxose gives a pyranose. Fructose gave a mixture from which two compounds were isolated as the main products. A peracetylated thiourethane was obtained from D-mannose on warming with alcohol and acetylation. Compounds *(1)* cannot have more than one *endo* substituent for steric reasons. Consequently, mannose, gulose, and lyxose do not form hexahydro-*cis*-furo[2,3-*d*]oxazoles. / Chem. Ber. *100*, 845 (1967) / −Ma. [Rd 687 IE]

A ring expansion in 1-(isopropenyl) cycloalkanol epoxides *(1)* has been reported by *C. J. Cheer* and *C. R. Johnson*. Epoxides *(1)* are obtained from the olefin by oxidation with *m*-chloroperbenzoic acid in chloroform. The rearrangement to form the cyclic ketone *(2)* is effected in methylene chloride at



$-5\,^{\circ}C$ with boron trifluoride/ether as catalyst, or in boiling benzene with acid-washed aluminum (Merck). When BF_3/ether is used as catalyst, the yield of *(2)* falls from 63 % ($n = 3$) to 49 % ($n = 4$), and thence to 15 % ($n = 5$). / J. org. Chemistry *31*, 428 (1967) / –WG. [Rd 704 IE]

The "birdcage ketone" *(1)* (hexacyclo[5.4.1.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}] dodecan-4-one) and some of its derivatives have been prepared by *R. J. Stedman* and *L. S. Miller*. The synthesis of *(1)* from 1,2,3,4,7,7-hexachloronorbornadiene and the ethylene ketal of tetrachlorocyclopentadienone or the last-named compound and vinyl chloride takes place in four or six steps respectively, *via* stereoselective Diels-Alder reactions, which are followed by photochemical processes.



(1)

The structure of *(1)*, m.p. 180–182 °C, is shown *inter alia* by IR, NMR, and mass spectra. / J. org. Chemistry *32*, 35 (1967) / –WG. [Rd 670 IE]

Oleic acid is the precursor of naturally occurring acetylenes in *Tricholoma grammopodium* cultures, as was indicated by radiochemical investigations carried out by *J. D. Bu'Lock* and *G. N. Smith*. All the radioactive products occurring in the following scheme could be chromatographically separated (as the methyl esters) and detected 7 days after the cultures had been fed with [10–^{14}C]-oleic acid *(1)*.

$CH_3-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-CH_2-{}^{14}CH{=}CH-(CH_2)_7-COOH$

$\downarrow -2\,H$ *(1)*

$CH_3-CH_2-CH_2-CH_2-CH_2-CH{=}CH-CH_2-{}^{14}CH{=}CH-(CH_2)_7-COOH$

$\downarrow -2\,H$

$CH_3-CH_2-CH_2-CH_2-CH_2-C{\equiv}C-CH_2-{}^{14}CH{=}CH-(CH_2)_7-COOH$

$\downarrow -2\,H$

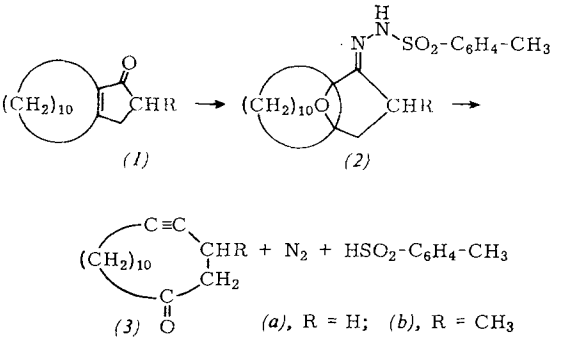
$CH_3-CH_2-CH_2-CH{=}CH-C{\equiv}C-CH_2-{}^{14}CH{=}CH-(CH_2)_7-COOH$

$\downarrow$

$CH_3-C{\equiv}C-C{\equiv}C-C{\equiv}C-CH{=}{}^{14}CH-CH_2OH$

These experiments provide the first experimental proof of the biogenetic path postulated some ten years ago for the dehydrogenation of fatty acids to form acetylenes; however, the detailed mechanism of the formation of the triple bond is still unknown. / J. chem. Soc. (London) C *1967*, 332 / –Bu. [Rd 671 IE]

A novel fragmentation of cyclic α,β-unsaturated carbonyl systems has been discovered by *A. Eschenmoser*, *D. Felix*, and *G. Ohloff*. The bicyclic ketone *(1a)* or *(1b)* is first epoxidized and then converted into the α,β-epoxy *p*-toluenesulfonylhydrazones *(2a)* or *(2b)*, which are stirred for 20 hours with two equivalents of sodium methoxide in dimethyl sulfoxide. As expected, this yields 4-cyclopentadecyn-1-one *(3a)* (m.p.



(a), R = H; *(b)*, R = CH_3

40 °C, 60–65 % yield) or *(3b)*. The structure of *(3a)* is evidenced, *inter alia*, by the formation of exaltone on catalytic hydrogenation; the structure of *(3b)* is established by hydrogenation to form racemic muscone. / Helv. chim. Acta *50*, 708 (1967) / –WG. [Rd 706 IE]

Trichlorovinylamines *(3)* are obtained, together with cyclopropane derivatives, on reaction of allylamines *(1)* with phenyltrichloromethylmercury, as was found by *W. E. Parham* and *J. R. Potoski*. The following reaction probably takes place:

$R_2N-CH_2-CH{=}C(CH_3)_2 + C_6H_5-Hg-CCl_3 \rightarrow$

(1)

$R_2\overset{\oplus}{N}-CH_2-CH{=}C(CH_3)_2$
$H_5C_6-\overset{\ominus}{Hg}-CCl_3 \rightarrow$

$R_2N-CCl_2-Hg-C_6H_5 + ClCH_2-CH{=}C(CH_3)_2$

(2)

$\downarrow$

$R_2N-\ddot{C}-Cl + C_6H_5HgCl$

$\downarrow +CCl_2$

$(C_6H_5HgCCl_3) \rightarrow R_2N-C{=}C(Cl)-Cl$ (Cl)

(3)

Other reaction products detected are isoprene, chloroform, and adducts of dichlorocarbene with isoprene and with *(2)*. As the basicity of the amine *(1)* increases, the yield of cyclopropane decreases, and the quantity of vinylamine *(3)* and chloroform increases. The reaction can proceed in this manner only if the allyl chain contains at least four carbon atoms. / J. org. Chemistry *32*, 278 (1967) / –WG. [Rd 705 IE]

Syntheses and rearrangements of hydrazonic acid azides have been reported by *A. F. Hegarty*, *J. B. Aylward*, and *F. L. Scott*. The hydrazonoyl bromides *(1)* not only react with

$R-C(Br){=}N-NHAr \rightarrow R-C(N_3){=}N-NHAr \rightarrow$

(1) *(2)*

$[R-N{=}C{=}N-NHAr] \rightarrow R-NH-C(=O)-NH-NHAr$

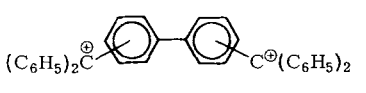
(3) *(4)*

R = C_6H_5, *p*-Cl–C_6H_2, *p*-$(CH_3)_3CH-C_6H_4$, *p*-$CH_3-C_6H_4$, *p*-Br–C_6H_4

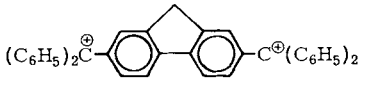
Ar = *o*-Br–C_6H_4, *p*-$NO_2-C_6H_4$, *o*,*p*-$Br_2-C_6H_3$

H_2NNH_2 and HNO_2 to give tetrazoles, but also react readily and uniformly with the equivalent quantity of NaN_3 in a dioxane/water mixture (4:1) at 25 °C to give hydrazonic acid azides *(2)*. The isomeric tetrazoles cannot be obtained from *(2)* either by heating or by the action of alkali or excess NaN_3, whereas imidic acid azides undergo this reaction readily. The hydrazonic acid azides *(2)* rearrange in trifluoroacetic acid or acetic acid/sulfuric acid to give semicarbazides. There is considerable evidence to suggest that this rearrangement takes place *via* an *N*-aminocarbodiimide *(3)*. The retention of optically active residues R shows that the residue R is never free during the course of the rearrangement. / Tetrahedron Letters *1967*, 1259 / –Jg. [Rd 696 IE]

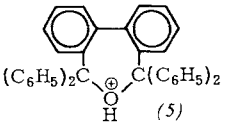
Dicarbenium ions of the biphenyl series, *(1)* to *(4)*, in aqueous H_2SO_4 following the synthesis of the corresponding dicarbinols have been studied by *H. Hart, Th. Sulzberg, R. H. Schwendeman*, and *R. H. Young*. (For data in the longest wavelength absorption and $pK_{R^{++}}$ values, see Table). The experimental longest wavelength absorption maxima μ_{max} are linearly related to the calculated (MO method; ω technique) Δm values (= energy difference between the highest occupied and lowest unoccupied MO's). Data for the tetraphenylxylyl dications were also plotted. It must be concluded that the central biphenyl grouping in *(2)* is twisted through > 20°; the extremely low $pK_{R^{++}}$ value of *(3)* is due to the formation of the stable 2,7-dihydrooxepinium ion.



(1), p,p'
(2), m,m'
(3), o,o'



(4)



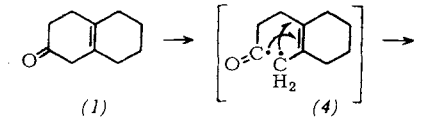
(5)

	λ_{max}	ε_{max}	$pK_{R^{++}}$ [*]
(1)	530	90000	– 8.2
(2)	430	67500	– 8.4
(3)	428	35500	–15.0
(4)	568	152000	
$(C_6H_5)_3C^{\oplus}$	432	37500	– 7.4

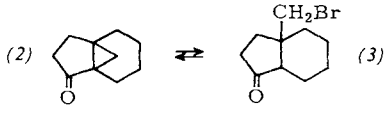
[*] For the definition and determination of $pK_{R^{++}}$ see J. Amer. chem. Soc. *85*, 1800 (1965).

/ Tetrahedron Letters *1967*, 1337 / –Jg. [Rd 697 IE]

A new photochemical rearrangement of β,γ-unsaturated cyclic ketones is described by *J. R. Williams* and *H. Ziffer*. Irradiation of 1,2,3,4,5,6,7,8-octahydronaphthalen-2-one *(1)* (high-pressure mercury lamp, N_2, t-butanol) gave the bicyclic ketone *(2)* (60% yield), which could be converted in good yield into *(3)* by treatment with HBr in glacial acetic acid.



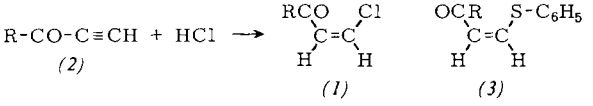
(1) *(4)*



(2) *(3)*

Reaction with alkali leads to reformation of *(2)*. The reaction may proceed *via (4)*. 17β-Hydroxyester-5(10)-en-3-one undergoes the same rearrangement. / Chem. Commun. *1967*, 194 / – Ma. [Rd 650 IE]

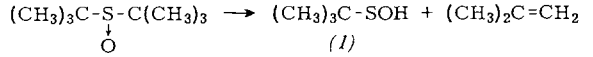
***cis*-(2-Chlorovinyl) ketones** *(1)*, unlike the *trans* compounds, have hitherto remained unknown. According to *D. Landini* and *F. Montanari*, they can be obtained by the addition of the stoichiometric quantitiy of HCl to ethynyl ketones *(2)* in dry chloroform at –40 °C in the presence of CuCl. The reaction is complete in 6–24 hours, and its course can be followed by IR spectroscopy. A small excess of acid or the use of high reaction temperatures leads to *cis* → *trans* isomerization. The ketones *(1)* can be converted into *cis*-phenylthiovinyl ketones *(3)* by reaction with thiophenolate ions in acetone/



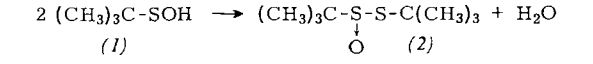
(2) *(1)* *(3)*

water at 0 °C. The *trans*-sulfides are thermodynamically less stable than the *cis*-compounds, and can be converted into the latter by base catalysis. / Chem. Commun. *1967*, 180 / –Ma. [Rd 651 IE]

The existence of t-butylsulfenic acid *(1)*, the first aliphatic sulfenic acid, has been demonstrated by *J. Reid Shelton* and *E. Davis*. *(1)* is formed on partial thermolysis (80 °C) of di-t-butyl sulfoxide in various solvents. The final product is the thiosulfinate *(2)*. *(1)* was detected by NMR and IR spectroscopy and by its addition reaction with electrophilic olefins.



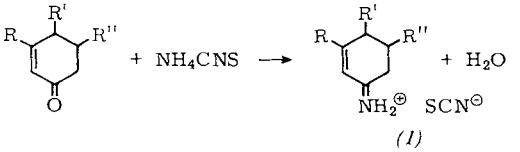
(1)



(1) *(2)*

Addition to ethyl acrylate gave ethyl β-t-butylsulfinylpropionate, while addition to methyl propiolate (with loss of isobutylene) led to bis(*trans*-methoxycarbonylvinyl) sulfoxide (diadduct) *(3)*. / J. Amer. chem. Soc. *89*, 718 (1967) / –Ma. [Rd 652 IE]

A new condensation reaction of α,β-unsaturated cyclic ketones with ammonium thiocyanate has been described by *G. Kabas*. Condensation of 3-substituted 2-cyclohexen-1-ones with NH_4CNS in a non-polar solvent with azeotropic removal of water, *e.g.* in boiling toluene, leads, *via* a heterogeneous reaction, to iminium thiocyanates *(1)*. Salts such as NaCl, Na_2SO_4, and Na phosphates increase the yield, probably by stabilization of *(1)*. The orange-yellow compounds are very readily soluble in polar solvents; the solutions can be kept for several days, but are hydrolysed by $NaHCO_3$, with reformation of the ketone. Examples: isophorone → 3,5,5-trimethyl-2-cyclohexene-1-iminium thiocyanate, 85% yield



(1)

3-phenyl-2-cyclohexen-1-one → 3-phenyl-2-cyclohexene-1-iminium thiocyanate, 81.5%. / J. org. Chemistry *32*, 218 (1967) / –Ma. [Rd 647 IE]

The polymerization of 4-azido-1-butyne by inner 1,3-dipolar addition to form a polyethylenetriazole *(1)* is described by *K. E. Johnson, J. A. Lovinger, C. O. Parker,* and *M. G. Baldwin.* 4-Azido-1-butyne could be prepared from 3-butynyl *p*-toluenesulfonate and NaN_3 in sulfolane/water (69% yield), and could be polymerized by bulk polymerization or precipitation polymerization from boiling benzene. The product



(1)

does not exhibit thermal decomposition below 320 °C. *(1)* contains a mixture of 1,4- and 1,5-substituted triazole rings. / Polymer Letters 4*B*, 977 (1966) / –Ma. [Rd 648 IE]

The arylation of aromatic and heterocyclic compounds by nitro compounds at high temperatures is described by *E. K. Fields* and *S. Meyerson.* The components are made to react for 2–30 sec in a continuous flow reactor packed with quartz pieces. Nitrobenzene/benzene (molar ratio 1:5) at 600 °C in a current of N_2 gives a mixture of 62% of biphenyl and 13.9% of terphenyl (total yield 85 mole-%). The phenylation of pyridine with nitrobenzene at 600 °C leads to a mixture of the 2-, 3-, and 4-isomers (63·6:26.3:10.1) in 72% yield. Thiophene/nitrobenzene gives a mixture of 2- and 3-phenylthiophene (75:25) in a yield of 60 mole-%. 3-Nitrobiphenyl and *m*-terphenyl (7:1) are obtained in 40% yield from *m*-dinitrobenzene and benzene at 450 °C. Arylations have also been carried out with trinitrobenzene, 1-nitronaphthalene, *m*-nitrobenzotrifluoride, and methyl *p*-nitrobenzoate. The reaction proceeds *via* free radicals. / J. Amer. chem. Soc. *89*, 724 (1967) / –Ma. [Rd 649 IE]

BOOK REVIEWS

Radioaktive Isotope in der organischen Chemie und Biochemie (Radioactive Isotopes in Organic Chemistry and Biochemistry). By *H.-R. Schütte.* Verlag Chemie. GmbH., Weinheim/Bergstr. 1966. 1st Edit., xi, 689 pages, (of which 417 pages form the tabular part), numerous figures and tables. DM 78.–.

This is an excellent book for the chemist, biologist, or physician who is using radioactive isotopes in practice, as well as for the advanced student who wishes to familiarize himself with the principles of the use of isotope techniques in organic chemistry and biochemistry. The author presents a very readily understandable introduction to this field, while the well-chosen examples of applications, the numerous references, and the comprehensive tables make the book a useful reference work.

Starting with a detailed chapter on the monitoring techniques of radioactive preparations, autoradiographic detection processes, and a short section on radiation protection and the equipment of isotope laboratories, two long chapters follow which deal with the preparation of labeled compounds and their many uses. Numerous examples of the use of labeled reagents in analysis, degradation methods for the determination of the activity distribution in labeled compounds, the investigation of reaction mechanisms, and in particular the successful use of radionuclides for the elucidation of biochemical processes are described concisely and clearly.

The second part of the work consists of several tables listing more than two thousand organic compounds labeled with radioactive carbon, phosphorus, sulfur, iodine, bromine, or chlorine, and whose preparations have already been described in the literature. The comprehensive list of references, which covers the literature up to the end of 1965, is an excellent source list for anyone who wishes to learn about the synthesis or use of labeled compounds. Though a somewhat more complete index would have been desirable, the book can be warmly recommended to all those who intend to use radioactive isotopes in organic chemistry and biochemistry.

A. Schwarz [NB 605 IE]

Fluorimetrie. Eine Anleitung zur Ausführung von quantitativen fluorimetrischen und spektrofluorimetrischen Messungen (Fluorimetry. An introduction to quantitative fluorimetric and spectrofluorimetric measurements). By *J. Eisenbrand.* Wissenschaftliche Verlagsgesellschaft mbH, Stuttgart 1966. 1st Edit., vii, 153 pp., 81 figures, linen DM 44.–.

Fluorescence methods have been in use for some time for the qualitative and quantitative analysis of many substances that either fluoresce themselves or can be converted by specific reactions into substances that fluoresce. They are particularly suitable for the analysis of small quantities of material, where they are inferior only to the much more costly radiochemical methods.

The present monograph deals with the methods and applications of such fluorescence measurements for analytical purposes. In addition to earlier instruments, a selection of commercial photoelectric fluorescence spectrometers is described, including a recent development in which the excitation is carried out with selected parts of the xenon continuum. The decrease in excitation intensity in comparison with excitation with mercury radiation is unimportant, owing to the sensitivity of modern radiation detectors, and is more than compensated for by the greater freedom of choice of the excitation conditions

As examples of the application of the methods, detailed analytical procedures, largely developed and proved in the author's laboratory, are given for various inorganic and organic substances. The groups of substances discussed include porphyrins, vitamins, optical brighteners, and scintillators. These more specialized methods are accompanied by general hints on the development of procedures. A short bibliography includes other monographs on fluorescence. However, this list does not contain the book on fluorescence analysis published a few years ago by *Udenfriend*, which is included only among the journal references.

The present monograph should be useful to anyone who uses fluorescence methods as analytical aids and prefers to use procedures that have already been developed.

Th. Förster [NB 589 IE]

Quantitative Bestimmung organischer funktioneller Gruppen (Quantitative determination of organic functional groups). By *R. Kaiser.* Volume 4 of the series "Methoden der Analyse der Chemie" (Analytical methods in chemistry). Akademische Verlagsgesellschaft. Frankfurt am Main 1966. 1st Edit., x, 445 pp., 33 figures, 11 tables, DM 58.–.

The classical methods of determining functional groups in organic compounds and their mixtures are today supplemented and frequently replaced by physical methods; satisfactory summaries of each approach are available. Undoubtedly a combination of the two routes will be needed to provide the optimum solution to analytical problems, some of which, in fact, can be solved only by such means. Supported by the

extensive experience of a large analytical laboratory, *R. Kaiser* gives an excellent survey of the quantitative determination of all important functional groups; both the above categories are considered in terms of their present development.

Following a survey of conventional systems, *Kaiser* proposes a new uniform system built up on "functional numbers". A functional number is defined as the numerical value of the concentration by weight of the key atom that is being determined in the form of the functional group. These data are explicit and facilitate establishment of the compositions of mixtures. Control methods and error determination are treated in detail, and equal care is devoted to the optimization of analytical procedures. Sampling errors are assigned their critical role: "90 % of all analytical errors are sampling errors". The combination of group determination with chromatographic methods of separation concludes the first part; the author's great experience in this field becomes obvious in this section.

In the second part the most frequently encountered functional groups are dealt with individually. In every case the qualitative detection (mostly in the UV, IR, and NMR spectrum) and the analytical behavior are given first and at least one proved standard method is described in detail together with an indication of its range of application and the most frequently encountered interference. The third part gives a survey of additional methods, mainly in the form of tables and references.

The presentation is clear and easy to understand. A lively style matches the book's good external appearance. The work should soon become an indispensable aid, both for the research chemist and for his colleagues in the control laboratory.

G. Hesse [NB 632 IE]

Handbuch der physiologisch- und pathologisch-chemischen Analyse, für Ärzte, Biologen und Chemiker (Handbook of Physiological and Pathological Chemical Analysis for Physicians, Biologists, and Chemists). By *Hoppe-Seyler/Thierfelder*, edited by *K. Lang* and *E. Lehnartz* with the assistance of *O. Hoffmann-Ostenhof* and *G. Siebert*. Vol. 6: Enzymes, Part B. Springer-Verlag, Berlin-Heidelberg-New York 1966. 10th Edit., xvi, 1282 pages, bound DM 424.– (subscription DM 339.20).

Appearing eighteen months after the publication of Part 6 A [*], the present Part 6 B contains the conclusion of the article on oxidoreductases, the contribution headed transferases and the beginning of the contribution on hydrolases. The assignment of the enzymes to these groups is somewhat confusing, since all the coenzyme A dependent enzymes are included under oxidoreductases, though only about 20% of the 50 or so enzymes discussed belong to this group; the others are hydrolases, transferases, lyases, isomerases, or ligases. A similar situation is found for the folic acid dependent enzymes and for the "phosphate-transferring enzymes", which is the description used for the pyrophosphorylases. As in the first Part, some of the topics receive a treatment such as might be expected in a monograph: coenzyme A enzymes (*O. Wieland*), transaminases (*Trautschold* and *Werle*), ribonucleases (*Siebert*), glycosidases (*Wallenfels* and *Diekmann*) and the "phosphate-transferring enzymes" (*Rohdewald*). In addition to analytical procedures, these chapters contain considerable additional information that cannot be found elsewhere in such a compact form. Other enzymes are dealt with more briefly with the main emphasis on the methods.

It is regrettable that in some cases the literature is covered only up to 1961 or 1962. It is to be hoped that the final Part, with the index for all three volumes will be published soon, so that greater use may be made of this work than is possible at present. The print and presentation are excellent.

H. Sund [NB 599 IE]

[*] Cf. Angew. Chem. *78*, 215 (1966); Angew. Chem. internat. Edit. *5*, 262 (1967).

Chemisch-physikalische Vitamin-Bestimmungsmethoden (Physicochemical methods for the determination of vitamins). By *G. Gstirner*. Ferdinand Enke Verlag, Stuttgart 1965. 5th revised Edit., xii, 426 pages, 26 figures, 20 tables, plastic DM 58.–; paper DM 53.50.

The present 5th edition of this well known work [*] has been thoroughly revised. It now includes methods for the elimination of interfering accessory compounds in order to increase the specificity and sensitivity of the processes. New entries include methods for the determination of vitamin B_{12} (cyanocobalamin), panthenol, and (valuable, though disputed from the strictly vitamin point of view) choline and rutin. New methods are also described for pyridoxine, *p*-aminobenzoic acid, and folic acid. The polarographic determination of some vitamins is also discussed for the first time.

Theoretical discussions are deliberately kept brief, without detriment to the book. This leaves room for detailed descriptions of the processes, generally in the words of the original publication. The selection seems rather narrow in places, but this is counterbalanced by the range of possible applications described. They relate to the testing and determination not only of pure vitamins, but also of natural products of all kinds, foods, fodder and pharmaceutical preparations (tablets, juices, solutions for injection, multivitamin preparations). Physiological-chemical methods for animal organs, tissues, urine, and blood, as well as clinical-chemical methods, are also included. The grouping of the procedures is simple and clear, and the critical evaluation of the various determination methods is particularly welcome.

The print, composition, and presentation leave nothing to be desired. The present edition, to an even greater extent than the earlier editions, will be a useful source of advice to those interested in the field and also to the food chemist.

J. Schormüller [NB 613 IE]

[*] Cf. Angew. Chem. *63*, 541 (1951).

Chemie-Lexikon (Encyclopedia of Chemistry). By *H. Römpp*, edited by *E. Ühlein* (4 Volumes). Franckh'sche Verlagshandlung, Kosmos-Verlag, Stuttgart 1966. Sixth Edit., 7408 columns of text, 452 columns of tables, and an English-language index. DM 390.–.

When *Hermann Römpp* died in 1964 many asked whether, and how, "Römpp" would live on. The new sixth edition of this chemical encyclopedia answers the question. Much of the manuscript of this edition is *Hermann Römpp*'s, completed by the new editor, Dr. *Erhard Ühlein*.

For the first time the encyclopedia comprises 4 volumes, with about 3900 pages containing 37,500 entries (over 25 % more than the fifth edition which was published in 1962). Entries such as "Antimatter," "Catenane", "Electrophoretic Coating", "Ionic Propellants", "Laser Crystals", "Desalination of Sea-water", "Rocket Fuels" and "Tranquilizers" are included, to name only a few that demonstrate the topicality of the work. The 37,500 entries hide nearly 49,000 literature references, 29,500 source references, 13,500 tradenames, and 1150 biographical sketches. It is difficult to think of a problem that is not answered in "Römpp".

A 182-page English index of the entries is a novelty. It is placed at the end of the fourth volume and not only facilitates the use of the encyclopedia by English-speaking readers, but extends the scope of the work to that of an English-German chemical dictionary. To help the German-speaking reader to find the English equivalent of an entry this is given at the end of each description. There is no doubt that this extension was an excellent idea.

It is unnecessary to recommend "Rompp". Without exaggeration it may be stated that the work never leaves its user in the lurch. Its information is reliable, well balanced, and despite its brevity sufficiently detailed to provide more than just preliminary data. Further details are easily ob-

tained with the aid of the cited literature. "Römpp" does not just have a place in every library – it is a miniature library in its own right.

H. Grünewald [NB 646 IE]

Technisches Taschenwörterbuch (Pocket Technical Dictionary), English-German, German-English. By *H. G. Freeman.* Max Hueber Verlag, Munich 1965. 285/297 pp., soft cover, DM 9.80 each volume.

When one reads in the foreword to a dictionary that "Nearly every engineer needs – rightly and properly – to consult a technical dictionary from time to time. Such dictionaries .... should not confront the user with a crossword puzzle in every 7 out of 8 renderings", then one is dealing either with a very good dictionary, or else with a very self-confident author. After looking through these two volumes, the reviewer has gained the impression that the latter alternative is the more likely. Or is it not, perhaps, a "crossword puzzle" to find – without any distinction being drawn – "waste, refuse; decrease, drop" for "Abfall", or "outlet, discharge; outflow; expiration" for "Ablauf"? The engineer seeking to satisfy his "right and proper" needs will be disappointed, for a list of such puzzles would run right through the alphabet.

A good solution has been found to the problem of composite words: to avoid long lists of similarly formed words, the author in each case quotes only the first part of such words, illustrating its use with a few examples. This enables both volumes to remain compact at no cost to the information contained.

It is difficult to discern precisely for whom the dictionary is intended. The vocabulary extends to practically all branches of industrial technology (the list of subjects covered by the dictionary contains over 90 entries). Translations of some 13000 terms are given, so that there is some justification for the claim made in the foreword, that the user will seldom be at a loss. However, even the author should not believe that the user will *never* be at a loss, although he offers this as a modest alternative to "seldom".

H. Grünewald [NB 582 IE]

Rodd's Chemistry of Carbon Compounds. Edited by *S. Coffey.* Vol. 1. Part D: Dihydric Alcohols, Their Oxidation Products and Derivatives. Elsevier Publishing Company, Amsterdam-London-New York 1965. 2nd Edit., xvi, 418 pages, 32 tables, bound Dfl. 65.–, subscription Dfl. 55.–.

The fourth part of the seven-part first volume of the 2nd edition of Rodd (the 1st Edition [*] had only two parts) has now been published, shortly after the appearance of the earlier parts. Six well-arranged chapters deal with the preparation, properties, and reactions of acyclic compounds containing two functional groups (on different carbon atoms). Six authors discuss the following classes of compounds: glycols and glycol ethers, their sulfur analogues, nitro- and amino-alcohols, diamines (*E. S. Waight*); hydroxyaldehydes and -ketones and dicarbonyl compounds (*E. S. Waight*); monohydroxymonocarboxylic acids and their derivatives (*D. St. C. Black, G. M. Blackburn, G. A. R. Johnston*); amino acids and their derivatives, peptides, hydrazo and azo acids (*I. E. Davies*); keto acids (*D. St. C Black, G. M. Blackburn, G. A. R. Johnston*); dicarboxylid acids and their derivatives (*J. Oldham*).

The chapters on keto acids, dicarboxylic acids, and amino acids are much larger than in the first edition owing to the rapid expansion of these fields. The arrangement of individual sections is on a mechanistic basis, *e.g.* the description of diazo esters as nucleophilic and electrophilic reagents and as carbene generators, or according to preparation, *e.g.* in the preparation of peptides (by amino or carboxyl activation or by dehydrating agents). This gives a very clear presentation of the extensive material covered. The consistent application should be encouraged whenever possible in subsequent volumes. This volume with numerous references, which also include early publications as well as reviews (mostly up to 1963), is a valuable source of information which no organic chemistry laboratory should lack. Print and presentation are excellent.

K. Hafner [NB 609 IE]

[*] Cf. Angew. Chem. *78*, 397, 398 (1966); Angew. Chem. internat. Edit. *5*, 433, 434 (1966).

The Acridines. Their Preparation, Physical, Chemical, and Biological Properties, and Uses. By *A. Albert.* Edward Arnold (Publishers) Ltd., London 1966. 2nd Edit., xii, 604 pages, numerous figures and tables, 168 s.

Because of the inclusion of many new results in the acridine field, the 2nd edition of this book is almost twice as large as the first edition (1951). The grouping of the material is the same as in the previous edition, the preparation, the physical, chemical, and biological properties, and the many uses of the acridines being discussed in five sections. It should be mentioned that the C atoms and the N atoms of the acridine ring are numbered in accordance with the IUPAC recommendations, with the result that earlier confusion with regard to the positions of substituents has now been eliminated.

The first eight chapters deal from the practical angle with the methods of synthesis known up to September 1965. The most successful of these methods are naturally discussed at greatest length, and an added note gives advice about the most suitable methods for individual cases, fine purification, and the manipulation of the acridines. The next few chapters are devoted to special properties, such as surface activity, dipole moments, association and ionization, redox potentials, and absorption, fluorescence, and phosphorescence spectra. The relationship between the electron distribution and the physical and chemical properties of the compounds are discussed, and reference is made to the possibility of prediction of the properties of as yet unknown acridines.

The largest section deals with the chemical properties of acridine as well as of fused-ring and substituted acridines. Special attention is given to the amino-substituted acridines, with are used as medications and dyes A new feature of this section is a short chapter on the photochemistry of the acridines, which has recently been intensively studied. The photoproducts lead over to the acridanes, which are also discussed, together with the hydroacridines, acridones, thioacridones, and selenoacridones.

Like the first edition, the present edition contains an up-to-date comparison of physical, chemical, and biological properties. In addition to the use of the acridines in clinical medicine, the topics discussed include the interaction of these substances with nucleic acids and the relationship between their physical and chemical properties and their bactericidal, carcinogenic, and anticarcinogenic effects.

The final part of the book deals with the use of acridines as pigments and dyes, corrosion inhibitors, biochemical reagents, fuel cells, and microscopic and photographic reagents. Numerous figures and tables make the book very readable, and a great deal of information is presented in this way.

The fact that the present-day production of acridine-based medications amounts to more than 500 tons per year testifies to the considerable extension of the chemistry of acridine and its derivatives. This is particularly clear from the new edition of the book, which has not only organic chemists, but also physical chemists as well as physicians and biologists as potential readers. The book is strongly recommended to anyone who wishes a survey of the present situation in this field.

V. Zanker [NB 612 IE]

Organic Stereochemistry. By *G. Hallas*, McGraw-Hill Publishing Company Ltd., London-New York-Toronto-Sydney 1965. 1st Edit., xi, 244 pages, numerous figures, paper 28s.

The author intends this book as an introduction to static stereochemistry for students. A short historical introduction is followed by a discussion first of the optical isomers resulting from the presence of an asymmetric C atom, and then of other types of optical isomers. A special chapter is devoted to the definition and determination of relative and absolute configuration. This is followed by sections on "geometrical isomers" and methods for the determination of their configuration, and on the stereochemistry of cyclic compounds, allenes, and systems containing nitrogen. The monograph closes with a short collection of problems.

The subject matter is presented in a pleasing and readily understandable form, and the examples are drawn both from "classical" and from modern stereochemistry. Comprehension is greatly assisted by clear tables and short legends to each of the very numerous reaction schemes. The original literature is not cited, but a list of important monographs and reviews is given at the end of each chapter. References to reaction mechanisms are confined to the most important. The dynamic aspects of organic stereochemistry are almost completely ignored. The problems for practice vary considerably in difficulty, and suffer from frequent repetition, since they are taken from the courses of several universities.

There are very few printing errors (*e.g.* Fig. 5.10 is identical with Fig. 5.9). All the steric formulae are neat and correct. Despite the fact that it is confined to static problems, this book provides an excellent introduction to the principles of stereochemistry, and can be recommended to all those who wish to obtain a short review of this subject.

G. Snatzke [NB 604 IE]

Nonclassical Ions. By *P. D. Bartlett*. W. A. Benjamin, New York-Amsterdam 1965. 1st. Edit. xiv, 559 pp., many illustrations. $ 12.00.

Few questions of organic chemistry have given rise to so much discussion and so many well thought out experiments as the question concerning the existence of nonclassical ions. Developments have now reached a stage at which it is possible for only a small circle to follow competently a discussion or even to make contributions to this field. For these reasons the appearance of a book about nonclassical ions is more than well timed.

The present work consists of a collection of 75 publications concerning nonclassical ions. The publications, which are arranged in chronological order, are each introduced by a commentary dealing with the significance of the subject matter with respect to the existence of nonclassical ions. Each publication is reproduced complete (including the experimental part).

Thus instead of a review, or a justification of a particular viewpoint, the author offers the reader an opportunity to form his own opinion as to this controversy, which is now almost 30 years old. It is the declared purpose of the book to present 'how we know what we know, and why we hold our present opinions' in this special field. The author leaves it to the reader to examine the validity of the interpretation. However, the reviewer doubts whether research students, for whom this book is primarily intended, are capable of such critical reading.

The overall picture of a logical and consistent development, which is presented to the reader is an adequate justification of the choice of publications made. The book begins with the work carried out by *Roberts* and *Kimball* on bromonium ions (1937) and is concluded by the NMR investigations conducted by *Saunders*, *Schleyer*, and *Olah* (1964). A number of later publications (up to August 1965) is cited, without commentary, in the appendix.

Although the author does not conceal his own ideas regarding the more controversial points when he deals with them in the various commentaries, the final evaluation of the results is, however, left to the reader. The commentaries will thus scarcely help the biased reader to lose his prejudices, or the non-critical reader to form his own opinion. In spite of this fact, the value of the book lies in the commentaries, which occupy *ca.* 50 pages, and by virtue of which the book becomes more than a collection of reprints. Questions are posed and relationships are demonstrated which go beyond the bounds of the individual publications and render "Nonclassical Ions" stimulating reading material.

The value of the book is further enhanced by a complete author index. It is, however, regrettable that some of the publications have been reduced in size to such a degree that they are difficult to read. *W. R. Roth* [NB 622 IE]

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Nitrenes and the Decomposition of Carbonylazides

BY W. LWOWSKI[*]

Gratefully dedicated to Professor Karl Freudenberg

The decomposition of organic carbonylazides can lead to the formation of nitrenes. Ethoxycarbonylnitrene is formed in the photolytic and thermal decomposition of ethyl azidoformate and by α-elimination from N-(p-nitrobenzenesulfonyloxy)urethan. Both of the possible electronic states of this nitrene take part in intermolecular reactions. Pure singlet nitrene is formed by α-elimination from the urethan and on thermal decomposition of ethyl azidoformate, but changes so rapidly into the triplet form that the reactions of both forms are observed. Singlet ethoxycarbonylnitrene undergoes selective and stereospecific insertion into C–H bonds and adds stereospecifically to olefins. Triplet ethoxycarbonylnitrene, however, does not undergo insertion into C–H bonds, and adds to olefins with complete loss of the geometric configuration. By following quantitatively the stereospecificity of the addition reaction and by selective interception of the triplet and singlet forms of the nitrene, it can be shown that the photolysis of ethyl azidoformate leads directly to nitrene of which one third is in the triplet state. In the decomposition of aryl- and alkylcarbonylazides (acid azides), the removal of nitrogen is accompanied by a synchronous rearrangement to isocyanates (Curtius rearrangement). In this system, nitrenes are obtained only by photolysis. They add to double bonds and undergo very selective insertion into C–H bonds, but do not rearrange at a measurable rate to isocyanates. The photolytic Curtius rearrangement is also a concerted reaction.

1. Introduction

Interest in the study of electron-deficient, uncharged intermediates has increased greatly in the past 15 years. A great deal of work is being carried out in particular on the carbenes, but their nitrogen analogues have also attracted increasing attention. These compounds contain a nitrogen atom having only six electrons in its valence shell. Two of these electrons form the bond with the single ligand, while the other four can be arranged in two ways, *i.e.* as two pairs of electrons on a nitrogen atom with a low-energy empty orbital (singlet nitrene) or as one electron pair plus two electrons with parallel spins (triplet nitrene). In the triplet state, one of the three low-energy orbitals that are not used for bonding is occupied by a pair of electrons, and the other two contain one electron each.

The terms "singlet" and "triplet" are borrowed from spectroscopy, but the two electronic states must not be confused with the spectroscopic states. The very short-lived spectroscopic states have the geometric configuration of the ground state (Franck-Condon principle). The long-lived states of *e.g.* the nitrenes or carbenes, on the other hand, assume the energetically most favorable conformation, which can differ very appreciably from that of the ground state. States separated from the ground state by forbidden transitions can be sufficiently long-lived to enter into intermolecular reactions before crossing to the electronic ground state.

In the study of the mechanisms of potential nitrene reactions, therefore, one is concerned, not only with the questions of whether a nitrene is in fact present and how it behaves chemically, but also with the

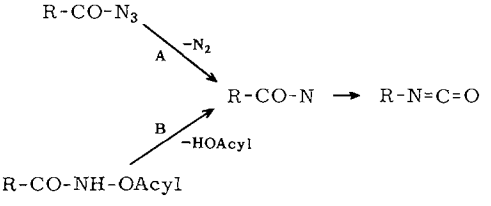
[*] Prof. W. Lwowski
New Mexico State University, Research Center
Las Cruces, N.M. 88001 (U.S.A.)

question of the electronic state of the reacting nitrene. It is possible (and does in fact happen; see below) that two different electronic states of a nitrene enter into intermolecular reactions, in which they behave quite differently.

Unfortunately, there is as yet no agreement on nomenclature. Molecules R–N are described as azenes, azylenes, imenes, imines, imidogen derivatives, and nitrenes [1,2]. These names are all open to objections [1,2]. The name "nitrene" is used in the present article because of the analogy with "carbene".

It is not intended to present a survey of the entire nitrene field, which has been the subject of recent reviews [1–3]. Instead, the present article will deal with some aspects of the chemistry of the carbonylnitrenes, R–CO–N, connected with our investigations on the decomposition of carbonylazides.

The carbonylazides (acid azides) were discovered by *Curtius* [4,5], who also observed their rearrangement [6] to isocyanates on thermal decomposition. As early as 1896, *Stieglitz* [7] explained the Curtius rearrangement (path A) as involving a nitrene intermediate, similar to *Tiemann*'s formulation [8] of the Lossen rearrangement (path B).



Curtius later coined the term "rigid azides" [9] for azides that do not rearrange, but form "short-lived intermediates R–N<", which react intermolecularly. Thus *Curtius* wrote that sulfonylazides form the residues Ar–SO_2–N<, which exhibit "unmistakable analogies" to the residues R–CH<, which are nowadays known as carbenes [10]. Though *Stieglitz*'s views on the mechanism of the Curtius rearrangement appear to be incorrect (Section 6), it is obvious that *Tiemann*, *Stieglitz*, and *Curtius* had a clear conception of carbenes and nitrenes as early as seventy years ago. They simply lacked the means of proving conclusively the existence of these species. Moreover, at that time there was no theoretical foundation for an understanding of the reactivity of the nitrenes.

The first nitrene whose existence was verified by physical methods was NH. This nitrene can be prepared by the decomposition of hydrazoic acid, and can be detected spectroscopically in the gas phase. Some of its reactions have been elucidated (for reviews see [2,11]).

[1] See *L. Horner* and *A. Christmann*, Angew. Chem. *75*, 707 (1963); Angew. Chem. internat. Edit. *2*, 599 (1963).

[2] See *R. A. Abramovitch* and *B. A. Davis*, Chem. Rev. *64*, 149 (1964).

[3] *W. Kirmse*, Angew. Chem. *71*, 537 (1959).

[4] *T. Curtius*, Ber. dtsch. chem. Ges. *23*, 3023 (1890).

[5] Cf. *A. Darapsky*, J. prakt. Chem. *125*, 1 (1930).

[6] *T. Curtius*, Ber. dtsch. chem. Ges. *27*, 778 (1894).

[7] *J. Stieglitz*, Amer. chem. J. *18*, 751 (1896).

[8] *F. Tiemann*, Ber. dtsch. chem. Ges. *24*, 4162 (1891).

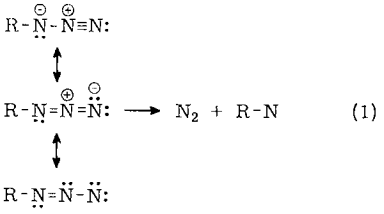
[9] *T. Curtius* and *F. Schmidt*, Ber. dtsch. chem. Ges. *55*, 1571 (1922).

[10] *T. Curtius*, Z. angew. Chem. *26*, III, 134 (1913).

[11] *P. A. S. Smith*: Open Chain Nitrogen Compounds. Benjamin, New York 1965, Vol. 1, p. 4.

2. Reactions of Nitrenes and Azides

The assumption that the first step in the decomposition of an azide is the removal of nitrogen appears satisfactory, since the great heat of formation of the nitrogen molecule and its suitability as a leaving group (*e.g.* in the decomposition of the diazonium salts) are well known.



(1)

However, this does not mean that the activation energy for the process (1) must necessarily be low and that the nitrene hypothesis may be accepted without question for all azide decompositions. In fact, for all the azide decompositions that can be explained on the basis of nitrenes, it is also possible to offer other reasonable mechanisms. This can be illustrated by nitrene and azide mechanisms for the formation of rearrangement, addition, and insertion products (see eq. (2)–(7) on facing page).

In fact, the heat-induced Curtius rearrangement appears to proceed *via* an azide mechanism (eq. (3)) and not *via* a nitrene (eq. (2)) (see Section 6). With reference to the formation of aziridines from olefins and decomposing azides (eq. (4), (5)), it has been known for a long time that triazolines can be prepared by addition of azides, and that they can decompose to form nitrogen and aziridines [12].

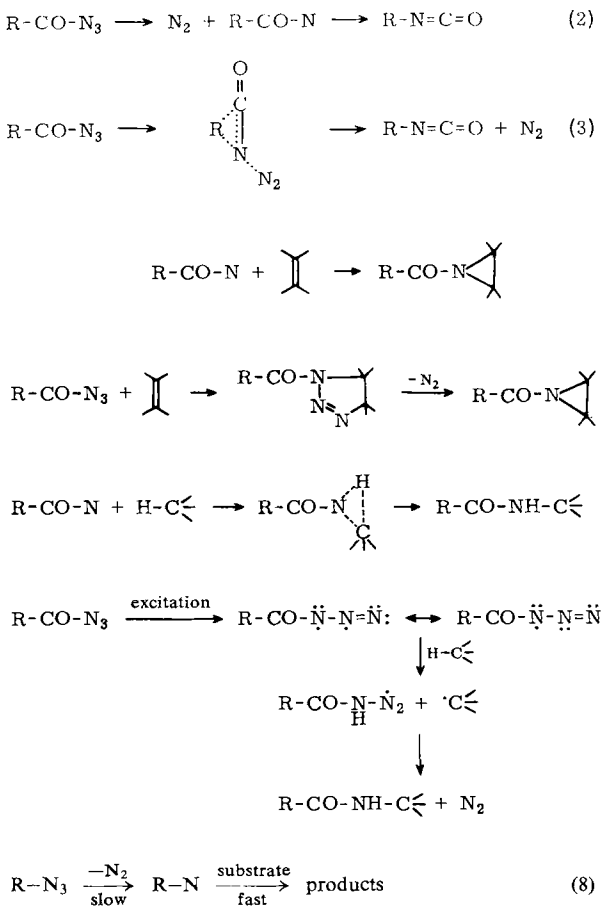
The nitrene mechanism (6) seems particularly attractive for insertion reactions; however, evidence favoring the azide mechanism (7) can also be produced. Thus one would expect that a radical pair such as that in (7) can dissociate, the nitrogen radical then yielding nitrogen and R–CO–NH_2 by abstraction of another H atom. Amide (or amine in the case of alkylazides R′–N_3) is in fact always found as a by-product.

Similar arguments can also be advanced in every other case for the distinction between azide and nitrene mechanisms, *i.e.* the reaction mechanism cannot be deduced entirely from the nature of the products.

Kinetic measurements provide further evidence concening the thermal decomposition of azides. It may be assumed that the reactions of a nitrene will be faster than its formation (see eq. (8)).

The solvent used as the substrate participates only indirectly (by solvation) in the formation of the nitrene, and should have only a relatively small in-

[12] *L. Woff*, Liebigs Ann. Chem. *394*, 30, 68 (1912); *K. Alder* and *G. Stein*, *ibid. 485*, 211 (1931); *R. Huisgen*, Angew. Chem. *72*, 370 (1960); *G. Szeimies* and *R. Huisgen*, Chem. Ber. *99*, 491 (1966); Shinogi and Co., Netherlands Pat. Appl. 6514295 May 6, 1966; Chem. Abstr. *65*, 16941a (1966). For a review, see *R. Huisgen*, *G. Grashey*, and *J. Sauer* in *S. Patai*: The Chemistry of Alkenes. Interscience, New York 1964, p. 835ff.



(2)

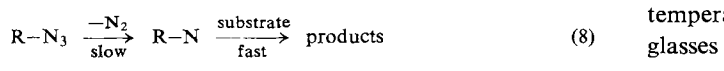
(3)

(4)

(5)

(6)

(7)



(8)

fluence on the rate or temperature of the decomposition of the azide. However, the solvent (substrate) is involved in an azide reaction, and its chemical nature must have a decisive influence on the rate of the reaction.

Waters and *Walker*[13] observed two types of kinetic behavior in the thermal decomposition of some aryl- and alkylazides in various solvents. In one group of solvents the rate of decomposition (at 132 °C) is independent of the nature of the solvent (mineral oil, tetrachloroethylene, *etc.*); the authors conclude that the reaction proceeds by a nitrene mechanism in these solvents. In other solvents (benzene, indene, styrene) the rate of decomposition (again at 132 °C) is higher, and is determined by the solvent, indicating that an azide mechanism is involved. For example, the ratio of the rates of decomposition of phenylazide in mineral oil and in indene is 1:225. Indene evidently reacts directly with the azide. *D. S. Breslow*[14] studied the thermolysis of a number of azidoformates in aliphatic and aromatic solvents as well as in ketones and alcohols. The very slight differences in the rate of decomposition indicate a nitrene mechanism.

Strictly speaking, the procedure described shows only that the solvent is not involved in the rate-determining step. It tells us nothing about the nature of the intermediate, which could be a valence tautomer of the azide or of the nitrene rather than a nitrene. Unfortunately, the procedure cannot be applied to photolytic decompositions, in which the rate of decomposition of the azide is determined by the light flux and the quantum yield.

The existence of a number of nitrenes has been demonstrated by physical methods. The triplet state of the simplest member of the series, NH, can be identified by its optical absorption spectrum[2], and the disappearance of NH in mixtures with ethylene has been followed spectroscopically[15]. Most of the available data relate to triplet nitrenes at very low temperatures, particularly ESR measurements in glasses between 4 and 80 °K[16].

Though measurements of this type show the existence of nitrenes under the conditions in question, they do not answer questions about the chemical properties of nitrenes, and tell us nothing about the mechanisms by which azides decompose at room temperature and in liquid solutions. Moreover, the measurements provide information only about the electronic ground state of the nitrenes observed. It is quite possible, however, that a nitrene is formed in a higher electronic state, *e.g.* the lowest singlet, and enters into chemical reactions in this state before it has a chance to cross to the electronic ground state. It will be shown in Section 4.1 that this is in fact what happens to ethoxycarbonylnitrene.

3. Ethoxycarbonylnitrene

The photolytic[17,18] or thermal[18,19] decomposition of ethyl azidoformate[20] in various solvents yields products whose formation can be explained by the

[13] *P. Walker* and *W. A. Waters*, J. chem. Soc. (London) *1962*, 1632.

[14] *T. J. Prosser, A. F. Marcantonio, C. A. Genge*, and *D. S. Breslow*, Tetrahedron Letters *1964*, 2483.

[15] *D. W. Cornell, R. S. Berry*, and *W. Lwowski*, J. Amer. chem. Soc. *88*, 544 (1966).

[16] *G.Smolinsky, E.Wasserman*, and *W.A.Yager*, J. Amer.chem. Soc. *84*, 3220 (1962); *G.Smolinsky, L.C.Snyder*, and *E.Wasserman* Rev. mod. Physics *35*,576 (1963); *E.Wasserman, L.C.Snyder*, and *W. A.Yager*, J. chem. Physics *41*, 1763 (1964); *E.Wasserman, G.Smolinsky*, and *W.A.Yager*, J.Amer.chem.Soc. *86*, 3166 (1964); *R. M. Moriarty, M. Rahman*, and *G.J.King*, *ibid. 88*, 842 (1966); For UV-spectra, see: *A. Reiser, H. Wagner*, and *G. Bowes*, Tetrahedron Letters *1966*, 2635; *A. Reiser, G. Bowes*, and *R. J. Horne*, Trans. Faraday Soc. *62*, 3162 (1966).

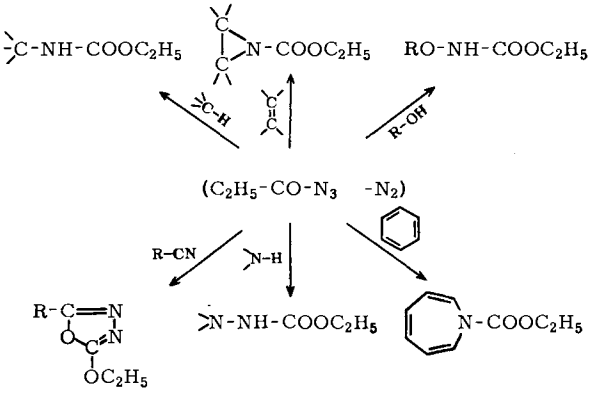
[17] *W. Lwowski* and *T.W. Mattingly, jr.*, Tetrahedron Letters *1962*, 277.

[18] *W. Lwowski* and *T. W. Mattingly, jr.*, J. Amer. chem. Soc. *87*, 1947 (1965).

[19] *R.J.Cotter* and *W.F.Beach*, J. org. Chemistry *29*, 751 (1964).

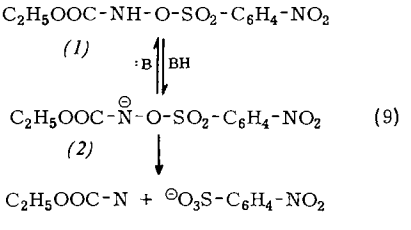
[20] *M. O. Forster* and *H. E. Fierz*, J. chem. Soc. (London) *93*, 81 (1908).

assumption of a nitrene intermediate, RO–CO–N, or by azide mechanisms. A number of reactions of this type are shown in Scheme 1.



Scheme 1. Decomposition of ethyl azidoformate in hydrocarbons [17, 18, 21–23, 27], olefins [17, 18], alcohols]24, 25], benzene [21, 26, 28], amines [26, 29], and nitriles [30, 31].

To settle the question of the existence of ethoxycarbonylnitrene as an intermediate in the reactions in Scheme 1, we prepared the nitrene by an independent route [21, 32]. *N*-(*p*-Nitrobenzenesulfonyloxy)urethan *(1)* can be converted even by weak bases into its anion *(2)*, which splits off a *p*-nitrobenzenesulfonate ion in a first-order reaction. The half-life of the reaction (in dichloromethane at room temperature) is about 7 seconds [33]. The other fragment formed is ethoxycarbonylnitrene. In the presence of the solvents indicated in Scheme 1, the same products are formed as from ethyl azidoformate.



(9)

[21] *W. Lwowski, T. J. Maricich,* and *T. W. Mattingly, jr.*, J. Amer. chem. Soc. *85*, 1200 (1963).

[22] *W. Lwowski* and *T. J. Maricich*, J. Amer. chem. Soc. *86*, 3164 (1964).

[23] *M. F. Sloan, T. J. Prosser, N. R. Newburg,* and *D. S. Breslow*, Tetrahedron Letters *1964*, 2945.

[24] *R. Puttner* and *K. Hafner*, Tetrahedron Letters *1964*, 3119.

[25] *W. Lwowski, R. DeMauriac, T. W. Mattingly, jr.*, and *E. Scheiffele*, Tetrahedron Letters *1964*, 3285.

[26] *K. Hafner* and *C. König*, Angew. Chem. *75*, 89 (1963); Angew. Chem. internat. Edit. *2*, 96 (1963); *K. Hafner, D. Zinser,* and *K. L. Moritz*, Tetrahedron Letters *1964*, 1733.

[27] *H. Nozaki, S. Fujita, H. Takaya,* and *R. Noyori*, Tetrahedron *23*, 45 (1967).

[28] *W. Lwowski* and *R. Johnson*, Tetrahedron Letters *1967*, 891.

[29] *W. Lwowski* and *L. Selman*, Abstracts 150th Meeting Amer. Chem. Soc., Sept. 1965, Abstract S 25.

[30] *W. Lwowski, A. Hartenstein, C. DeVita,* and *R. L. Smick*, Tetrahedron Letters *1964*, 2497.

[31] *R. Huisgen* and *H. Blaschke*, Liebigs Ann. Chem. *586*, 145 (1965).

[32] *W. Lwowski* and *T. J. Maricich*, J. Amer. chem. Soc. *87*, 3630 (1965).

[33] *W. Lwowski* and *T. J. Maricich*, unpublished.

The following quantitative comparison of the C–H insertion products confirms our belief in a common intermediate in the decomposition of *(2)* and of ethyl azidoformate.

Insertion into the C–H bonds of 2-methylbutane gives four isomeric products *(3)–(6)*. Division of the ratios of the quantities (determined by gas chromatography) by the number of hydrogen atoms of each type gives the relative reactivities, which are shown in Table 1. The two methyl groups on C-2 in 2-methylbutane have the same reactivity. Despite somewhat different reaction conditions, the figures differ only slightly. We regard this as confirmation of a common reactive intermediate, which must be ethoxycarbonylnitrene.

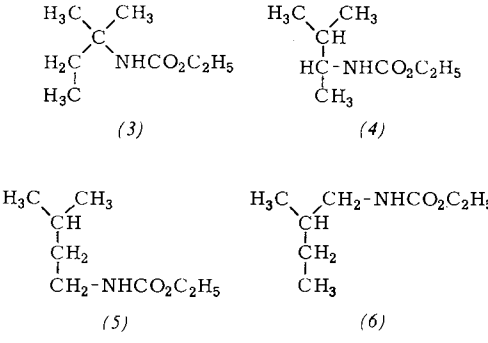


Table 1 also contains data on the thermolysis of ethyl azidoformate in 2-methylbutane, which were determined independently by *D. S. Breslow* [23], and which agree well with our results. The differences in the numerical values for nitrenes prepared by different methods are probably due to the fact that the very different leaving groups (N_2 and $^{\ominus}O_3S–C_6H_4–NO_2$) in the photolysis and in the α-elimination are still located in the neighborhood of the nitrene. The difference in the values for the photolysis and the thermolysis of the azidoformate is probably due mainly to the difference in the reaction temperatures (30 °C and 100 °C respectively).

Table 1. Relative reactivities of ethoxycarbonylnitrene with tertiary (3°), secondary (2°), and primary (1°) C–H bonds.

Hydrocarbon and solvent	Nitrene source: Azide photolysis 3°:2°:1°	Azide thermolysis 3°:2°:1°	α-Elimination 3°:2°:1°
100% 2-Methylbutane	37 9 1	30 [23] 10 [23] 1	27 11 1
38 mole-% 2-Methylbutane in dichloromethane	36 10 1	— — —	25 8 1
100% 3-Methylhexane [34]	16 5.3 1	17 6 1	— — —
27 mole-% 3-Methylhexane in dichloromethane [34]	14 5.2 1	18 6.6 1	13.5 4.7 1

Similarly, good agreement was found in the mixtures obtained with cyclohexene [18, 21, 32] and with nitriles [30]. Such a marked agreement cannot be coincidence, and it must therefore be accepted as certain that the decomposition of ethyl azidoformate and α-elimination reactions of *(1)* proceed *via* a common intermediate.

[34] *W. Lwowski* and *J. M. Simson*, unpublished; *J. M. Simson*, Dissertation, Yale University 1967.

4. Singlet and Triplet Ethoxycarbonylnitrene

4.1. Addition to C=C Double Bonds

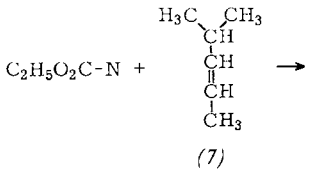
Following the detection of ethoxycarbonylnitrene as a reactant, there arose the question of its electronic state at the moment of reaction. *Wasserman* [35] recently showed by spin-resonance measurements at the temperature of liquid helium that the ground state of ethoxycarbonylnitrene is the triplet. However, it may be assumed that the nitrene is formed in the singlet state, particularly in α-elimination from *(1)* and in the thermolysis of azides. Spontaneous spin reversal is practically unknown in reactions of this type, though it is not impossible on the grounds of any natural law. Nothing is known about the lifetime of the nitrene in the singlet state, except that it is quite capable of entering into intermolecular reactions in solution (see below).

Attempts to determine the spin state of ethoxycarbonylnitrene spectroscopically and at the same time to follow its reactions in the gaseous state by flash photolysis have so far been unsuccessful [36]. In the absence of a reaction partner, the nitrene (presumably as the triplet) decomposed, with a life time of between 3×10^{-7} and 10^{-5} sec, to alkoxy and isocyanate radicals.

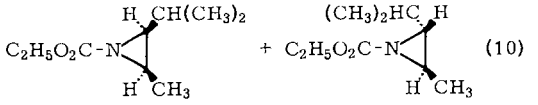
The problem was finally solved by a method developed by *Skell* for carbenes [37], which proved very successful [38] in spite of many critical arguments, though theoretical details still remain to be clarified [39].

Skell has postulated that singlet carbenes add to C=C double bonds in a single step, and hence stereospecifically. Triplet carbenes, on the other hand, should first react with the olefin to form an open-chain diradical, the ring closure of which proceeds more slowly than rotation about the former C=C double bond. This free rotation leads to the establishment of an equilibrium between conformers, and finally to the formation of a mixture of geometrically isomeric cyclopropanes. In the extreme case, the composition of this mixture depends only on the position of the equilibrium between the conformers, and not on the nature (*cis* or *trans*) of the starting olefin. Scheme 2 shows the application of *Skell*'s method to nitrenes.

We had observed that the addition of ethoxycarbonylnitrene to *cis*- and *trans*-4-methyl-2-pentene is only partly stereospecific. Both ethyl *cis*- and *trans*-2-isopropyl-3-methylaziridine-1-carboxylate are formed in both cases. The main product is the aziridine whose configuration corresponds to that of the olefin used. If the nitrene is prepared by α-elimination in dichloromethane solution containing 33 mole-% of *cis*-olefin *(7)*, the total aziridine yield [based on *(1)*] is 57 %, of

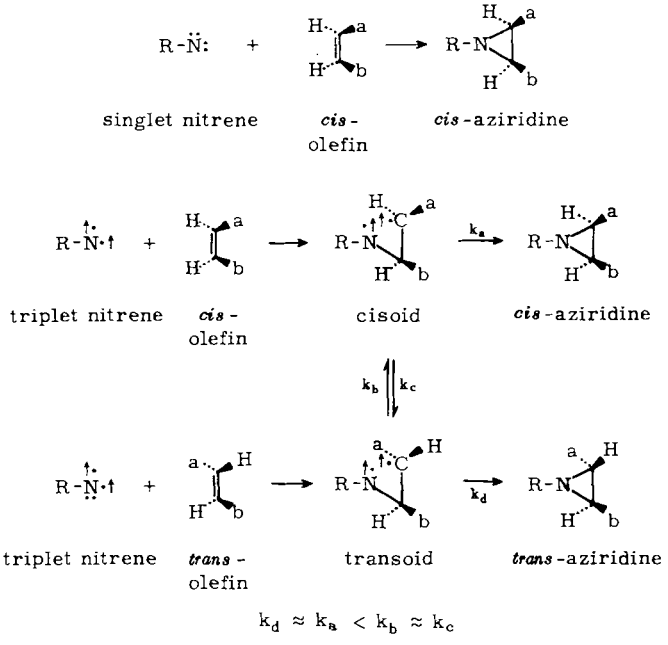


(7)



(8), cis *(9), trans*

which 92 % is *(8)* and 8 % is *(9)*. *Hafner* [40] found a similar situation in the photolysis of methyl azidoformate in *cis*- and *trans*-2-butene. If it is assumed that all the nitrene is formed in the singlet state and that *Skell*'s method is applicable, the formation of



$k_d \approx k_a < k_b \approx k_c$

Scheme 2. Application of *Skell*'s method to the addition of singlet and triplet nitrenes to *cis*- and *trans*-olefins.

products resulting from nonstereospecific reactions can be explained by the additional assumption that part of the singlet nitrene changes into triplet nitrene before adding to the olefin. This (hypothetical) transition should be a first-order reaction and the addition to the olefin a second-order reaction; this hypothesis can be checked by the use of different olefin concentrations. The lower the olefin concentration, the greater should be the quantity of nonstereospecifically formed aziridine. This is the case, as can be seen from Table 2 [41].

The values can be quantitatively explained by a simple kinetic model, which is shown in Scheme 3. According to this model the precursor P [ethyl azidoformate or *(1)*] forms only singlet nitrene, which then enters into competing reactions leading either to triplet nitrene

[35] *E. Wasserman* (Bell Laboratories), personal communication.

[36] *D. W. Cornell, R. S. Berry*, and *W. Lwowski*, J. Amer. chem. Soc. *87*, 3626 (1965).

[37] *P. S. Skell* and *R. C. Woodworth*, J. Amer. chem. Soc. *78*, 4496 (1956); *R. C. Woodworth* and *P. S. Skell*, *ibid. 81*, 3383 (1959).

[38] See *P. P. Gaspar* and *G. S. Hammond* in *W. Kirmse*: Carbene Chemistry. Academic Press, New York 1964, p. 259 ff.

[39] *R. Hoffmann*, Trans. New York Acad. Sci., Ser. II, *28*, 475 (1966).

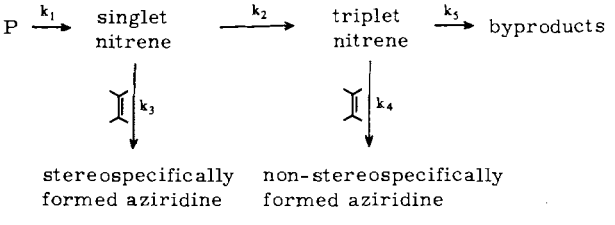
[40] *K. Hafner, W. Kaiser*, and *R. Puttner*, Tetrahedron Letters *1964*, 3953.

[41] *W. Lwowski* and *J. S. McConaghy*, J. Amer. chem. Soc. *87*, 5490 (1965).

Table 2. Stereospecificity of the addition of ethoxycarbonylnitrene to *cis*- and *trans*-4-methyl-2-pentene in dichloromethane.

Olefin concentration (mole-%)	Total yield of aziridines (%)	*trans*-Aziridine from *cis*-olefin (% in mixture)	*cis*-Aziridine from *trans*-olefin (% in mixture)
Nitrene produced by α-elimination			
33	57	7.8	2.6
10	50	17.5	—
5		26	8.0
3.3	38	34	—
2.5		37.5	—
1.5	24	43	12.3
Nitrene produced by thermolysis of azide			
100	67	14	
33		18	
10	78	33	
5		41	
3.3	60	46	
1.5		51	
1.0		54	
Nitrene produced by photolysis of azide			
100	70	26	6.4
33		28.5	
10	58	35	
5	43		
2.5		50	
1.5	55	54.5	14.7

(unimolecular) or to stereospecific combination with the olefin and formation of aziridine (bimolecular). The triplet nitrene adds on nonstereospecifically to the olefin or is consumed in side reactions. Since all the triplet nitrene is formed from the singlet nitrene, side reactions of the singlet nitrene do not affect the distribution between the paths k_3 and k_4.



Scheme 3. Possible reactions between nitrene and olefin.

The stereospecific path (k_3) leads to the formation of *(8)* from *cis-(7)* and *(9)* from *trans-(7)*. In the reaction of the triplet nitrene (k_4), the same mixture of *(8)* and *(9)* is formed both from *cis*- and from *trans-(7)*. The composition of the mixture of aziridines depends only on the position of the equilibrium between the conformers of the open-chain diradical intermediate (cf. Scheme 2). In our case the mixture consists of 80 % of *trans*-aziridine *(9)* and 20 % of *cis*-aziridine *(8)* [42]. If it is assumed that k_1 is much smaller than k_3, and that k_2 and k_3 are of a similar order of magnitude, a steady state assumption for the concentration of the triplet nitrene leads to the following relationship (eq. (11)) [42].

$$T/S = k_2\,(k_3\,[\text{olefin}] + k_5/k_4)^{-1} \qquad (11)$$

where T is the yield of aziridine mixture (80 % *trans* + 20 % *cis*) formed by nonstereospecific reaction; S is the yield of stereospecifically formed aziridine; for k_2, k_3, k_4, and k_5 see Scheme 3.

[42] *J. S. McConaghy* and *W. Lwowski*, J. Amer. chem. Soc. *89*, 2357 (1967).

Figure 1 shows the results of the experiments with the nitrenes produced by α-elimination. As required by Scheme 3, a straight line is obtained if k_5/k_4 is taken to be 0.015. The slope of the line is 0.036 ± 0.004. This indicates that the addition of the singlet nitrene to 4-methyl-2-pentene is about 30 times as fast as the singlet-triplet transition, *i.e.* $k_3/k_2 = 30$. (Note however that k_3 is a second-order rate constant, whereas k_2 is a first-order constant.)

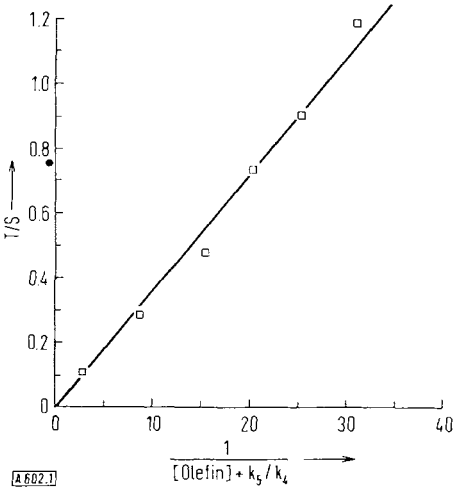


Fig. 1. Experimental results of the addition of the ethoxycarbonylnitrene obtained by α-elimination to the 4-methyl-2-pentenes. For explanations see eq. (11).

The thermolysis of ethyl azidoformate in dichloromethane solutions of *cis*- and *trans*-4-methyl-2-pentene gives similar results. Corresponding to the higher temperature, k_2/k_3 is greater, *i.e.* 0.08 instead of 0.036. The straight line for the data obtained in the thermolysis of azide, like the line in Figure 1, passes through the origin. This means that both the α-elimination and the thermal decomposition of ethyl azidoformate [43] yield only singlet nitrene, and that the triplet nitrene is formed from singlet nitrene.

The photolysis of ethyl azidoformate with light of wavelength 2537 Å [43], on the other hand, leads directly to a mixture of about $^1/_3$ triplet and $^2/_3$ singlet nitrene. A plot similar to that in Figure 1 gives a straight line that does not pass through the origin, but intersects the ordinate at $T/S = 0.44$. This corresponds to a triplet component of 0.44/1.44 = 30.5 % in the nitrene formed. At 12 °C, the slope of the line is 0.035. The mathematical evaluation of the photolytic reactions is basically the same as for the thermal reaction and for the α-elimination, but owing to the complete absorption of light it is necessary to use expressions other than k_1, and the fact that triplet nitrene is formed directly requires that a steady state condition also be applied to the singlet nitrene concentration.

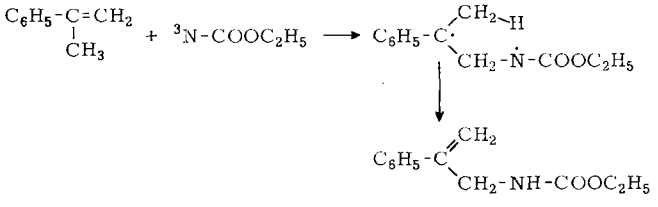
The quantitative agreement of the experimental data with the requirements of Scheme 3 does not in itself conclusively prove the correctness of our assumptions concerning the electronic states of the nitrenes and the mechanisms of their reactions. Other reaction mechanisms could fit in with the same kinetic laws, and intermediates other than singlet and triplet nitrene could add stereospecifically or non-stereospecifically to olefins. However, our ideas are supported by independent observations:

Both the triplet nitrene and the singlet nitrene can be intercepted by reactions in which only one of the two types of nitrene takes part. *Skell* assumes a diradical

[43] *J. S. McConaghy* and *W. Lwowski*, J. Amer. chem. Soc. *89*, 4450 (1967).

intermediate for the triplet reaction in his scheme for carbenes, which has been applied here to nitrenes (Scheme 2). The rate of formation of this intermediate should be greater for more strongly stabilized radicals, since this stabilization should already be reflected in the transition state leading to the diradical.

The triplet nitrene can be intercepted with α-methylstyrene. The reaction of a solution containing 3.3 mole-% of *cis*-4-methyl-2-pentene in dichloromethane [production of nitrene by α-elimination from *(1)*] gives absolute yields of 25 % of ethyl *cis*-2-isopropyl-3-methylaziridine-1-carboxylate and 13 % of the *trans* isomer. When 3.3 mole-% of α-methylstyrene is added to the reaction mixture, only a trace of the *trans*-substituted aziridine is formed, while the yield of *cis*-aziridine falls to 16 %. The reaction is thus almost completely stereospecific. When 1.5 mole-% each of *cis*-4-methyl-2-pentene and α-methylstyrene are used, the aziridine mixture obtained contains only 2.1 % of the *trans* compound, as opposed to 43 % of the *trans* compound in the absence of the triplet interceptor. It can be calculated from these results that triplet ethoxycarbonylnitrene reacts 86 times as rapidly with α-methylstyrene as with *cis*-4-methyl-2-pentene. The nature of the reaction product supports the assumption of a diradical intermediate[42]; thus α-methylstyrene gives, not an aziridine, but ethyl *N*-(2-phenyl-2-propenyl)carbamate *(10)*.



(10)

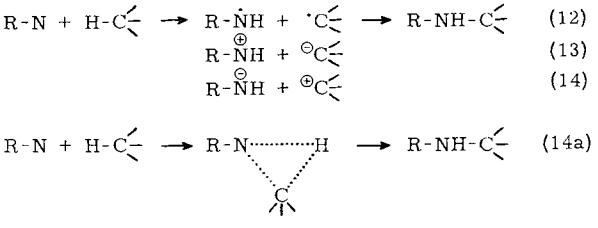
Singlet ethoxycarbonylnitrene can also be selectively intercepted. It undergoes very rapid insertion into C–H bonds, a reaction that has not so far been observed with triplet ethoxycarbonylnitrene[44]. If ethoxycarbonylnitrene produced by photolysis is allowed to react with cyclohexene (0.2 and 100 mole-% in dichloromethane), the ratio of the yield of aziridine to the yield of insertion products (insertion into the 4-position and the more active 3-position of cyclohexene) is 58:1 and 5:1 respectively[45]. The failure of triplet ethoxycarbonylnitrene to undergo insertion into C–H bonds is also confirmed by the experiments with 3-methylhexane (see Section 4.2).

When ethyl azidoformate is photolysed in cyclohexane, a large part of the singlet nitrene is intercepted as cyclohexylurethan. The directly formed triplet nitrene remains, and can add nonstereospecifically to added *cis*-4-methyl-2-pentene At an olefin concentration of 5 %, this gives a 33 % yield of an aziridine mixture consisting of 54.5 % of *trans*-substituted and 44.5 % of *cis*-substituted aziridine. On the other hand, if the nitrene is formed by α-elimination (again in 5 % *cis*-olefin + 95 % cyclohexane), the total yield of aziridines is 15 %, of which 30 % are *trans* compound and 70 % *cis*. With dichloromethane as the solvent, a 43 % yield of an aziridine mixture containing 26 % of *trans* compound would be expected. Cyclohexane evidently intercepts only the singlet nitrene; the triplet nitrene produced by photolysis remains and leads to the formation of a large quantity of *trans*-aziridine and to higher yields. It is possible to calculate from these data the proportion of triplet nitrene formed directly during photolysis. The calculation gives a result of 31 %, which agrees almost exactly with the value (30.5 %) obtained from the experiments in olefin-dichloromethane solutions.

The mechanism of the direct photochemical formation of triplet nitrene has not yet been elucidated. However, experiments on the acetophenone sensitized decomposition of ethyl azidoformate indicate that the triplet azide is not the precursor of the triplet nitrene[18].

4.2. Insertion into C—H Bonds

The insertion of nitrenes into C–H bonds may in principle proceed in one or two steps. In one-step processes, the atoms involved may assume electric charges in the transition state (eq. (13), (14)), or they may remain entirely or substantially uncharged (eq. (12), eq. (14a), cf. eq. (6)).



In a two-step reaction, insertion on asymmetric carbon atoms should lead to at least partial loss of optical activity.

Smolinsky[46] found that in intramolecular insertions with formation of five-membered rings (2-ethyl-2-methylindoline and 4-ethyl-4-methyloxazolidin-2-one), the optical activity is at least partly retained. It was later shown[47] that 4-ethyl-4-methyloxazolidin-2-one is formed with almost complete retention of configuration. We[48] have studied an intermolecular insertion reaction because various substrate concentrations can be used in such a system, and it is therefore possible to search for insertion reactions of triplet nitrene. As was mentioned in Section 3, ethoxycarbonylnitrene and 3-methylhexane react to form all the possible insertion products. Starting with optically active 3-methylhexane, we separated the ethyl *N*-(1-ethyl-1-methylbutyl)carbamate *(11)* by gas chromatography, and found that this product is formed

[44] However, triplet cyanonitrene reacts with C–H bonds: *A. G. Anastassiou*, J. Amer. chem. Soc. *88*, 2322 (1966).

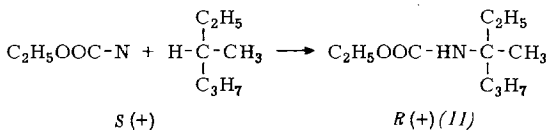
[45] *W. Lwowski* and *F. P. Woerner*, J. Amer. chem. Soc. *87*, 5491 (1965).

[46] *G. Smolinsky* and *B. I. Feuer*, J. Amer. chem. Soc. *86*, 3085 (1964).

[47] *S. I. Yamada*, *S. Terashima*, and *K. Achiwa*, Chem. pharmac. Bull. (Tokyo) *13*, 751 (1965).

[48] *W. Lwowski* and *J. Simson*, Abstracts, 153th Meeting Amer. chem. Soc., April 1967, Report O 163; *J. Simson*, Dissertation, Yale University 1967.

with complete retention of configuration. The absolute configurations of the starting material [49] and of the product [48] are known.



S(+) *R*(+)(*11*)

The optical purity of *(11)* is independent of the experimental conditions, as can be seen from Table 3.

Table 3. Stereospecificity of the insertion of ethoxycarbonylnitrene into the tertiary C–H bond of 3-methylhexane.

Method of nitrene production	3-Methylhexane in CH_2Cl_2 (mole-%)	Observed rotation value *(11)* (°)	Retention of configuration (%)
α-elimination	1.2	+ 1.67	98 ± 7
azide thermolysis	100	+ 1.69	99 ± 5
azide photolysis	1.2	+ 1.74	102 ± 3
azide photolysis	26.8	+ 1.71	100 ± 6
azide photolysis	100	+ 1.67	97 ± 5

Since the proportion of triplet nitrene must be very much higher at low substrate concentrations (1.2 mole-%) than in pure substrate, whereas the rotation value remains unchanged, it must be concluded that the triplet nitrene either inserts with retention of configuration or does not take part in the reaction at all. Since the yield of insertion product decreases very rapidly with decreasing substrate concentration, we feel (taking earlier results [45] into account) that triplet nitrene does not take part in the reaction [44].

It may therefore be concluded that the insertion of ethoxycarbonylnitrene into the C–H bonds of simple hydrocarbons is a one-step process. However, the one-step singlet mechanism need not apply to all C–H bonds. It is known [2] that nitrenes can remove hydrogen atoms from other molecules. If this led to the formation of a radical pair with a low activation energy of combination, a two-step insertion mechanism such as that found for cyanonitrenes [44] could occur [27].

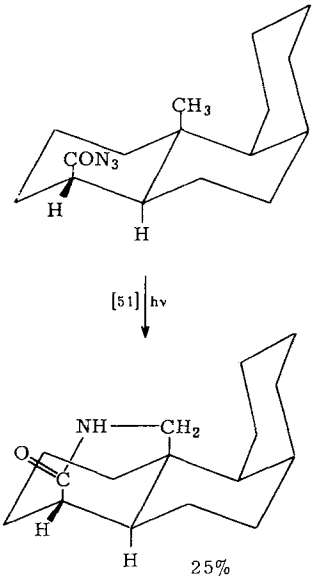
The nature and size of the charge distribution in the transition state of a one-step insertion are not fully known. The marked preference for tertiary rather than secondary and primary C–H bonds (Table 1) is compatible both with a positive charge and with "radical character" of the carbon atom involved. In experiments with norbornane, whose C-1 and C-4 atoms accept positive charges only with difficulty, smooth insertion into these positions has been observed. The average reactivity of all the other C–H bonds in norbornane (per C–H bond) is only about 1.7 times as great as that of the C–H bonds on C-1 and C-4 [50]. Thus these carbon atoms do not assume a strong positive charge.

[49] *K. Freudenberg* and *W. Hohmann*, Liebigs Ann. Chem. *584*, 54 (1954).

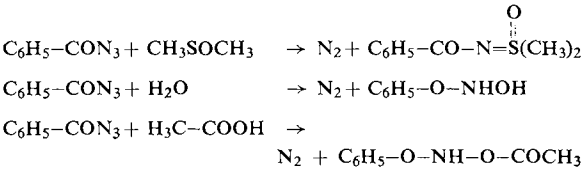
[50] *W. Lwowski* and *J. Reed*, unpublished.

5. Other Carbonylnitrenes

Ethoxycarbonylnitrene can be prepared particularly easily and in various ways, since the starting materials exhibit only a small tendency to undergo the Curtius or Lossen rearrangements [25]. Alkyl- and arylcarbonyl azides rearrange readily to isocyanates. Nitrenes are formed from these azides only on photolysis, and not on thermal decomposition (see below). *Edwards* [51] first observed intramolecular insertion into C–H bonds in his work on atisine and in the decomposition of acid azides [51,52]. These cyclizations are valuable in preparative work [53,54].



On photolysis of benzoyl azide in dimethyl sulfoxide, dioxane/water, or acetic acid, *Horner* [55,56] found products that can be attributed to intermolecular reactions of benzoylnitrene:



Products resulting from further reaction of phenyl isocyanate were also formed.

When acetyl azide was photolysed in benzonitrile and in phenylacetylene, *Huisgen* [57] obtained 2-methyl-5-phenyl-1,3,4-oxadiazole and 2-methyl-5-phenyl-1,3-oxazole respectively, *i.e.* the formal products of 1,3-cycloaddition of acetylnitrene to the triple bonds of the solvents.

[51] *J. ApSimon* and *O. E. Edwards*, Proc. chem. Soc. (London) *1961*, 461; Canad. J. Chem. *40*, 896 (1962).

[52] See reference [2], pages 171 and 172.

[53] *W. L. Meyer* and *A. S. Levinson*, Proc. chem. Soc. (London) *1963*, 15; J. org. Chemistry *28*, 2859 (1963).

[54] *R. F. C. Brown*, Austral. J. Chem. *17*, 47 (1964).

[55] *L. Horner* and *A. Christmann*, Chem. Ber. *96*, 388 (1963).

[56] *L. Horner*, *G. Bauer*, and *J. Dörges*, Chem. Ber. *98*, 2631 (1965).

[57] *R. Huisgen* and *J.-P. Anselme*, Chem. Ber. *98*, 2998 (1965).

While trying to find a model system for the study of the mechanism of the photolytic Curtius rearrangement [58], we observed the cyclizations of photolytically produced (with light of wavelength 2537 Å) alkylcarbonylnitrenes indicated in Table 4. In agreement with *Edwards'* results [51,52], δ-lactams are formed in preference to γ-lactams [59].

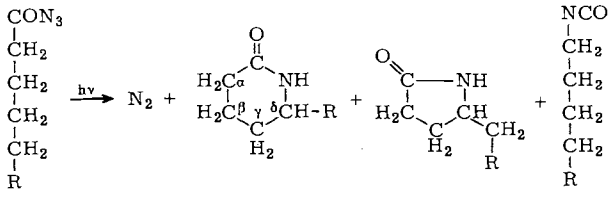


Table 4. Photolysis of n-alkanecarboxylic azides in dichloromethane and cyclohexane.

Starting material $R-CON_3$ where R =	Photolysis in dichloromethane: Yield of intramolecularly formed products	Photolysis in cyclohexane: Yield of intramolecularly formed products	Yield of *N*-cyclohexyl-n-alkanecarboxamide
C_3H_7	3.5 % 2-Pyrrolidinone	1 % 2-Pyrrolidinone	8.1 %
C_4H_9	23.5 % 5-Methyl-2-pyrrolidinone	7.8 % 5-Methyl-2-pyrrolidinone	4.7 %
C_5H_{11}	Total 33.5 %: 10.8 % 5-Ethyl-2-pyrrolidinone 22.7 % 6-Methyl-2-piperidinone	Total 15.8: 5.1 % γ-Lactam 11.5 % δ-Lactam	1.9 %
C_7H_{15}	Total 32.0 %: 11 % 5-Butyl-2-pyrrolidinone 21 % 6-Propyl-2-piperidinone	Total 16.0: 5.5 % γ-Lactam 11.5 % δ-Lactam	1.4 %

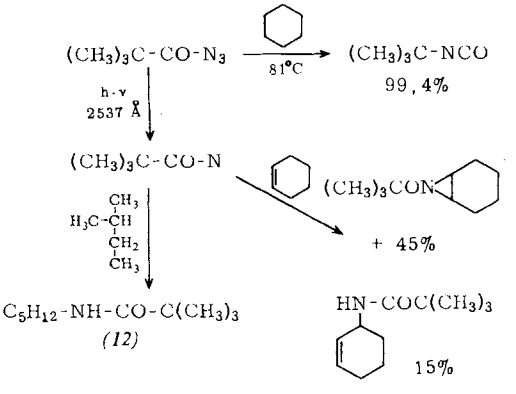
The preferential formation of the six-membered lactams agrees with the assumed three-membered ring transition state in insertions into C–H bonds (eq. (6)). The transition state for the formation of the δ-lactam would be a six-membered ring with a fused three-membered ring. The assumption of a linear transition state for the insertion (–N.....H.....C–) requires a distorted seven-membered ring with three atoms arranged in a line for the formation of the δ-lactam; this is probably a much less favorable arrangement.

6. Pivaloylnitrene and the Mechanism of the Curtius Rearrangement

Edwards [52], *Horner* [56], *Huisgen* [57], and we [60] observed that (unrearranged) nitrene products are obtained only on photolysis, and not on thermolysis, of alkane- and arenecarboxylic azides. No nitrene products can be found on thermolysis, in spite of careful searches, whereas they are often formed in large quantities on photolysis. This shows that no nitrenes are formed during the thermal Curtius rearrangement; the reaction evidently proceeds in a single step with simultaneous removal of the nitrogen and migration of the alkyl or aryl group. Thus the Stieglitz formulation *(2)* [7] is invalid at least for the thermal rearrangement, and it must be assumed that the reaction proceeds as indicated in eq. (3). In the photolytic reaction, on the other hand, it seemed a reasonable assumption that the first step is the formation of a carbonylnitrene R–CO–N, which partly rearranges into isocyanate and partly forms nitrene products R–CO–NXY resulting from intramolecular and intermolecular reaction.

On photolysis of pivaloyl azide, pivaloylnitrene is formed in a yield of at least 47 %. The nitrene adds to the double bond of cyclohexene and undergoes insertion into C–H bonds [59,60]. Four isomers of *(12)* are obtained from 2-methylbutane in an overall yield of 25 %.

The photolysis of pivaloyl azide in cyclohexane gives *N*-cyclohexylpivalamide in 20 % yield, and 0.5 % of pivalamide. The quantity of gas evolved is always greater than would correspond to the theoretical yield of nitrogen. Analysis showed that isobutylene is also formed. (The isobutylene was determined as its mercuric nitrate complex [61].) For example, photolysis in



neopentane gives a 13 % yield of isobutylene. Thus if the pivaloylnitrene is not intercepted in some other way, it appears to decompose into isobutylene and isocyanic acid. The isocyanic acid, together with part of the isobutylene, forms a polymeric oil, whose IR spectrum shows C–H absorption (at 2994 cm^{-1}) as well as O–H or N–H (broad, about 3290 cm^{-1}) and carbonyl absorptions (broad, about 1686 cm^{-1}). Including the oil and t-butyl isocyanate, the total yields were always greater than 90 %, based on the pivaloyl azide used [59].

The selectivity of the insertion of pivaloylnitrene into C–H bonds is greater than that of ethoxycarbonylnitrene, and is 160:9:1 for the tertiary, secondary, and primary C–H bonds in 2-methylbutane [60].

[58] *L. Horner, E. Spietschka,* and *A. Gross,* Liebigs Ann. Chem. *573,* 17 (1951).

[59] *S. Linke* and *W. Lwowski,* unpublished.

[60] *W. Lwowski* and *G.T.Tisue,* J. Amer. chem. Soc. *87,* 4022 (1965).

[61] *G. Denigès,* C. R. hebd. Séances Acad. Sci. *126,* 1043 (1898); *C.D. Hurd* and *A.R. Goldsby,* J. Amer. chem. Soc. *56,* 1815 (1934); *C. E. Starr* and *T. Lane,* Analytic. Chem. *21,* 572 (1949).

The yield of t-butyl isocyanate (on photolysis with light of wavelength 2537 Å at −10 °C) is always 39–42 %. This provides a clue to the mechanism of the rearrangement.

If pivaloylnitrene were the precursor of the isocyanate, the quantity of isocyanate obtained should decrease with increasing ability of the solvent to intercept nitrenes. In neopentane (which contains only unreactive primary C–H bonds), only 0.2 % of *N*-neopentylpivalamide is obtained, together with 0.7 % of pivalamide, 40 % of t-butyl isocyanate, 13.5 % of isobutylene, and polymeric oil. In cyclopentane, which contains the much more reactive secondary C–H bonds, 13 % of insertion product, 41 % of isocyanate, and 0.5 % of pivalamide are obtained, together with isobutylene and polymer. In cyclohexene, in which the addition and insertion products are formed in a total yield of 47 %, the isocyanate is formed in 41 % yield. Thus the isocyanate cannot have been formed from the nitrene, but must be formed directly from excited pivaloyl azide. The photolytic Curtius rearrangement is therefore also a concerted reaction.

It is interesting to note that pivaloylnitrene does not rearrange into isocyanate. On paper, there appears to be nothing to prevent such a rearrangement, and it might be assumed that such a reactive intermediate would react intramolecularly much more readily than intermolecularly. Nevertheless, the life of pivaloylnitrene must be appreciable (extending over many collisions), since it would otherwise be impossible to explain its high selectivity coupled with relatively good yields (*e.g.* in insertion into C–H bonds).

Our understanding of the finer details of the chemical behavior of nitrenes (and of electron-deficient intermediates in general) is still incomplete. Further theoretical and experimental effort will be necessary before it will be possible to make reliable predictions about the behavior of such intermediates.

I am very grateful to my co-workers for their untiring efforts and for the numerous contributions they have made to the planning of new experiments. Our work would not have been possible without the generous financial support of the National Institutes of Health and the National Science Foundation (U.S.A.).

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Syntheses with Ketones, Sulfur, and Ammonia or Amines at Room Temperature [***]

BY F. ASINGER AND H. OFFERMANNS [*]

A large number of preparatively interesting compounds have become readily available by the simultaneous action of sulfur and ammonia or amines on ketones. Direct syntheses of Δ^3-thiazolines, Δ^3-imidazoline-5-thiones, 5,6-dihydro-4H-1,4-thiazines, and the 1,2,3,4,5,6-hexathiocane system from ketones, sulfur, and ammonia or amines, and further possibilities for the synthesis of these heterocyclic systems have been proposed. Other heterocycles containing N or N and S (thiazoles, thiophenes, thiazolidines, tetrahydrothiazolo[2,3-c]-1,4-thiazines, thiomorpholines, 4-amino-2H-imidazoles, etc.) are readily obtainable by further reactions of these compounds. Hydrolysis of the Δ^3-thiazolines yields α-mercapto ketones, which are the starting materials for other syntheses. Most of the syntheses described proceed at room temperature and at normal pressure.

1. Introduction
2. Δ^3-Thiazolines (Action of Sulfur and Ammonia on Ketones)
2.1. Syntheses
2.2. Properties and Reactions
3. Syntheses with α-Mercapto Ketones
4. 5,6-Dihydro-4*H*-1,4-thiazines, 5,6,8,8a-Tetrahydrothiazolo[2,3-*c*]-1,4-thiazines, and Thiomorpholines (Action of Sulfur and Ethylenimine on Ketones)
5. Δ^3-Imidazoline-5-thiones (Action of Sulfur and Ammonia on Methyl Ketones).
5.1. Syntheses
5.2. Reactions
6. 8-Alkylamino-8-aryl-1,2,3,4,5,6-hexathiocane-7-thione (Action of Sulfur and Primary Amines on Methyl Aryl Ketones)

1. Introduction

Elementary sulfur, or even sulfur in the polysulfide form, is often used instead of oxygen for dehydrogenations (abstraction of hydrogen with formation of hydrogen sulfide) or oxidations (introduction of mercapto, thioxo, or dithio acid functions, or subsequently of carbonyl or carboxyl groups) of organic compounds [1,2].

The action of sulfur alone or sulfur in the presence of basic additives (alkalis, amines) at high temperatures on organic compounds such as paraffins, cycloparaffins, olefins, alkylaromatic compounds, nitrated aromatic compounds, aryl alkyl ketones, *etc.* has been extensively studied [1,2] and is of industrial interest in many cases, *e.g.* for the preparation of carbon disulfide, thiophenes, dicarboxylic acids (terephthalic acid), *p*-aminobenzaldehyde, and sulfur dyes, as well as in vulcanization. On the other hand, no investigations on the reactions of organic compounds with elementary sulfur under mild conditions were reported for a long time.

In 1956, one of the present authors [3] discovered a novel synthesis in which Δ^3-thiazolines are formed by the action of elementary sulfur and gaseous ammonia on ketones at room temperature and at normal pressure.

In this synthesis, an intermediate α-mercapto ketone formed by a thiolation instantaneously and irreversibly condenses with ketone and ammonia to form the Δ^3-thiazoline. The first step in this reaction (thiolation = sulfhydrylation = base-catalysed replacement of an H atom α to the carbonyl group by a mercapto group) was described in 1962 by *W. A. Pryor* [2] as "the only known sulfur oxidation at a carbon atom that has an appreciable rate at 25 °C".

[*] Prof. Dr. F. Asinger and Dr. H. Offermanns
Institut für Technische Chemie der Technischen Hochschule
Alte Maastrichter Str. 2
51 Aachen (Germany)

[**] The articles in this series have been published in five volumes by Verlag Chemie, Weinheim/Bergstrasse. They have also been published in an English edition. The present article, together with additional tables and preparative procedures, will appear in Volume VI of the series.

[***] Simple syntheses and chemical behavior of new heterocyclic ring systems, part 2. Part 1: *F. Asinger* and *M. Thiel*, Angew. Chem. *70*, 667 (1958). Cf. also *F. Asinger, W. Schäfer, K. Halcour, A. Saus*, and *H. Triem*, Angew. Chem. *75*, 1050 (1963); Angew. Chem. internat. Edit. *3*, 19 (1964).

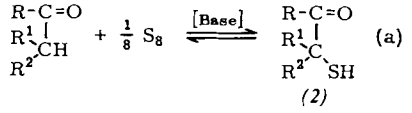
[1] *R. Wegler, E. Kühle*, and *W. Schäfer*, Angew. Chem. *70*, 351 (1958).

[2] *W. A. Pryor*: Mechanisms of Sulfur Reactions. McGraw-Hill, New York 1962.

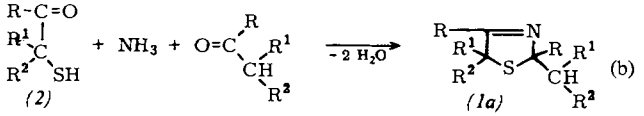
[3] *F. Asinger*, Angew. Chem. *68*, 377, 413 (1956).

This showed the possibility of studying the action of sulfur on suitable systems under mild conditions.

The formation of the Δ^3-thiazoline takes place in two steps.

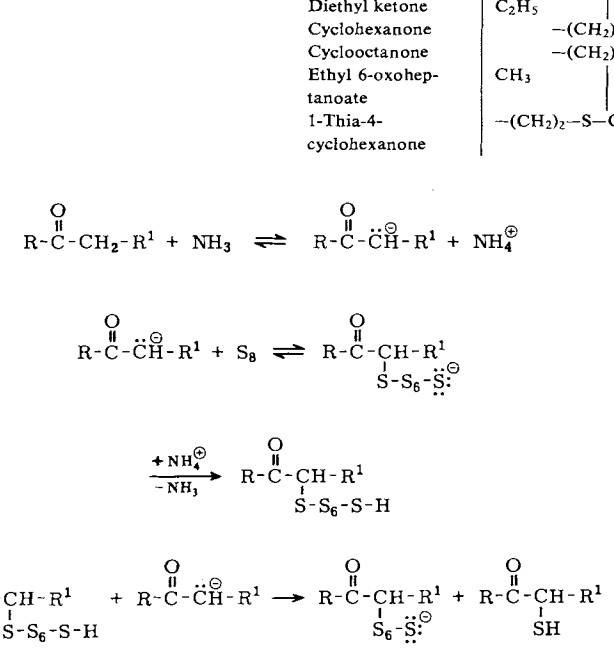


(a)



(b)

The first step (a), an α-thiolation, is an amine-catalysed ionic reaction induced by a carbanion (cf. [2], p. 154ff.) (R^2 = H).



The second step (ring formation) (b) may also be regarded as an α-aminoalkylation of an SH acid and subsequent stabilization by ring closure with elimination of water (cf. [4], p. 28ff.) (variant of the Mannich condensation).

A study of the two steps showed that both the thiolation reaction and the ring closure reaction are capable of generalization and can be applied to other systems. The result is a very powerful preparative tool [5].

[4] *H. Hellmann* and *G. Opitz*: α-Aminoalkylierung. Verlag Chemie, Weinheim/Bergstr. 1960.

[5] *F. Asinger et al.*, Forschungsbericht des Landes Nordrhein-Westfalen No. 1594. Westdeutscher Verlag, Köln and Opladen 1966.

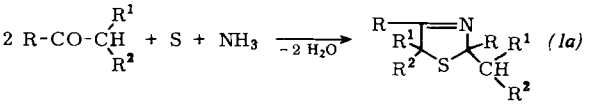
2. Δ^3-Thiazolines (Action of Sulfur and Ammonia on Ketones)

2.1. Syntheses

The action of elementary sulfur and gaseous ammonia on aliphatic, alicyclic, mixed aliphatic-alicyclic, and heterocyclic ketones having at least one H atom α to the carbonyl group, and which may also contain functional groups, leads at room temperature and normal pressure to substituted Δ^3-thiazolines *(1a)*, generally in excellent yields [3, 6]. The reaction is very widely applicable [5, 6] (for examples see Table 1).

The optimum conditions are as follows. An excess of ammonia is passed into a well-stirred suspension of the ketone

Table 1. Δ^3-Thiazolines *(1a)* prepared by the action of sulfur and ammonia on ketones (selection).



Ketone	R	R^1	R^2	Yield (%)	M.p. (°C)	B.p. (°C/mm)	Ref.
Diethyl ketone	C_2H_5	H	CH_3	85	–	96/12	[11]
Cyclohexanone	$-(CH_2)_4-$		H	80	81.5–82	162/15	[12]
Cyclooctanone	$-(CH_2)_6-$		H	62	–	150–152/0.5	[13]
Ethyl 6-oxoheptanoate	CH_3	H	$(CH_2)_3-CO_2C_2H_5$	80	–	140/10^{-4}	[14]
1-Thia-4-cyclohexanone	$-(CH_2)_2-S-CH_2-$		H	85	115	–	[13]

(1 mole) and sulfur (0.5 g-atom) at room temperature. After a short incubation period, the reaction mixture turns brown. The reaction is generally complete after 3–4 hours. To obtain optimum yields, the conditions must be varied to suit the ketone. In many cases it is advisable to carry out the reaction in anhydrous benzene (in the case of methyl isopropyl ketone) [7], in pyridine at 60 °C (7-tridecanone) [8], in dimethylformamide at 60 °C (aryl methyl ketones) [9], or in methanol (*N*-methyl- and *N*-benzylpiperidone) [10]. In some cases (*e.g.* with acetophenone and its derivatives) it is desirable to vary the proportions.

However, the synthesis also has its limitations. Cyclopentanone gives ill-defined resinous products. It has not so far been possible to prepare Δ^3-thiazolines from camphor, stearone, and isophorone [6]. Keto acids and their esters give Δ^3-thiazolines only when the keto group and the carboxyl group are so far

[6] *F. Asinger* and *M. Thiel*, Angew. Chem. *70*, 667 (1958).

[7] *M. Thiel, F. Asinger*, and *G. Reckling*, Liebigs Ann. Chem. *611*, 131 (1958).

[8] *F. Asinger, W. Schäfer, G. Herkelmann, H. Römgens, B. D. Reintges, G. Scharein*, and *A. Wegerhoff*, Liebigs Ann. Chem. *672*, 156 (1964).

[9] *F. Asinger* and *N. B. Desai*, unpublished.

[10] *F. Asinger, W. Schäfer*, and *H.-W. Becker*, Liebigs Ann. Chem. *674*, 57 (1964).

[11] *F. Asinger, M. Thiel*, and *E. Pallas*, Liebigs Ann. Chem. *602*, 37 (1957).

[12] *F. Asinger, M. Thiel*, and *H. Kaltwasser*, Liebigs Ann. Chem. *606*, 67 (1957).

[13] *F. Asinger, W. Schäfer, M. Baumann*, and *H. Römgens*, Liebigs Ann. Chem. *672*, 103 (1964).

apart that they no longer influence each other (*e.g.* 6-oxohexanecarboxylic acid and its esters [14]).

The reaction of aldehydes with sulfur and ammonia is complicated. Under the conditions used for ketones, Δ^3-thiazolines are obtained only in poor yields (maximum 10 %) from aldehydes; 2,3,5-trialkylated pyridines are also formed (yields 20–35 %) [14a].

Acetone reacts in a complicated manner with sulfur and ammonia [15, 15a].

Asymmetric ketones with at least one thiolatable H atom in each of the positions α to the carbonyl group give two isomeric α-mercapto ketones on thiolation; the ring-closure step consequently gives two isomeric Δ^3-thiazolines.

Investigations on asymmetric ketones have shown that the thiolation direction (expressed in the ratio of the isomeric Δ^3-thiazolines, which was determined by fractional precipitation of the picrates and, more recently, by gas-chromatographic analysis [16]) is very strongly dependent on the temperature:

20 °C : $CH_2 \gg CH > CH_3$

80 °C : $CH_2 > CH_3 > CH$

The addition of bases or solvents causes only a slight change in the isomer ratio (cf. [17], which contains further references).

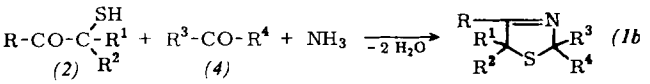
The ketone plays a double role in the synthesis of Δ^3-thiazolines. On the one hand it is thiolated to form the α-mercapto ketone, while it also functions as the oxo component for the irreversible ring closure in the second step. The substituents on the Δ^3-thiazoline are determined by the choice of ketone. Extensive variation (particularly with respect to the substituents in position 2) is possible in the synthesis from practically any α-mercapto oxo compounds (α-mercapto aldehydes, α-mercapto ketones), ammonia, and ketones, aldehydes or carbonyl compounds having functional substituents [6] (resynthesis).

A small selection of the Δ^3-thiazolines (total ≈ 180) prepared by us in this way is given in Table 2.

The α-mercapto oxo compounds are obtainable from α-halogeno carbonyl compounds and sodium hydrogen sulfide in alcoholic solution [18]. It is also possible to prepare an α-mercapto oxo compound by hydrolysis of one Δ^3-thiazoline [19] and to convert it into another Δ^3-thiazoline by reaction with any oxo component.

The condensation of α-mercapto aldehydes and ketones with carbonyl compounds and ammonia (α-amino-

Table 2. Δ^3-Thiazolines *(1b)* prepared from α-mercapto ketones or aldehydes *(2)*, carbonyl compounds *(4)*, and ammonia (resynthesis, selection).



(2) *(4)* *(1b)*

R	R^1	R^2	R^3	R^4	Yield (%)	B.p. (°C/mm)	Ref.
CH_3	H	H	H	H	62	66–68/20	[30]
CH_3	CH_3	H	C_2H_5	H	80	63–64/5	[6]
C_2H_5	CH_3	H	c-C_6H_{11}	H	92	100–102/1.5	[30]
CH_3	CH_3	H	CH	C_2H_5	80	63–64/5	[31]
C_2H_5	CH_3	H	$-(CH_2)_5-$		83	94–97/3	[30]
H	CH_3	CH_3	C_6H_5	H	34 [a]	106–108/0.5	[32]

[a] Yield based on α-bromoisobutyraldehyde.

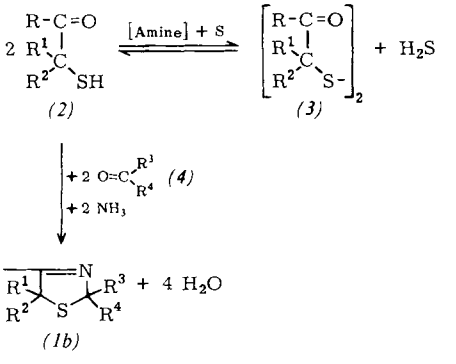
alkylation of an SH acid with subsequent stabilization by cyclization) is capable of generalization, and can be applied to special acyloins and to α-amino ketones.

The reaction of acyloins with oxo compounds and ammonia leads to Δ^3-oxazolines [20], while α-amino ketones give Δ^3-imidazolines [21].

The analogous ring closure reaction with β-mercapto oxo compounds leads to Δ^3-dihydro-1,3-thiazines [22, 22a], while 2,3,4,5-tetrahydropyrimidines [23] can be obtained from β-amino ketones.

The action of elementary sulfur on α-mercapto ketones in the presence of traces of ammonia or amine leads *via* a vigorous reaction to almost quantitative formation of α,α′-diketo disulfides, with liberation of hydrogen sulfide [24]. The reaction is a special case of the amine-catalysed dehydrogenation of thiols to disulfides by elementary sulfur, which was discovered by *McMillan* and *King* [25]. It is reversible if the α-mercapto oxo compound is removed from the equilibrium by other reactions.

Thus the action of hydrogen sulfide and ammonia on a mixture of α,α′-diketo disulfides and oxo components



(2) *(3)* *(4)* *(1b)*

[14] *F. Asinger, M. Thiel, H. Sedlak, O. Hampel,* and *R. Sowada,* Liebigs Ann. Chem. *615*, 84 (1958).

[14a] *F. Asinger, H. Offermanns,* and *P. Crozet,* unpublished.

[15] *M. Thiel* and *F. Asinger,* Liebigs Ann. Chem. *610*, 17 (1957).

[15a] *F. Asinger, H. Offermanns,* and *F. Abo Dagga,* unpublished.

[16] *F. Asinger, W. Schäfer, B. D. Reintges, A. Wegerhoff,* and *G. Scharein,* Liebigs Ann. Chem. *683*, 121 (1965).

[17] *F. Asinger, W. Schäfer, K. Halcour, A. Saus,* and *H. Triem,* Angew. Chem. *75*, 1050 (1963); Angew. Chem. internat. Edit. *3*, 19 (1964).

[18] *T. Bacchetti* and *A. Sartori,* Gazz. chim. ital. *83*, 665 (1953).

[19] *F. Asinger, W. Schäfer,* and *G. Herkelmann,* Liebigs Ann. Chem. *672*, 179 (1964).

[20] *J. R. Gaines* and *G. R. Hansen,* J. heterocyclic Chem. *1*, 96 (1964).

[21] *F. Asinger, M. Thiel,* and *R. Sowada,* Mh. Chem. *90*, 402 (1959).

[22] *F. Asinger, M. Thiel,* and *W. Höringklee,* Liebigs Ann. Chem. *610*, 1 (1957); *M. Thiel, F. Asinger,* and *G. Trümpler, ibid. 619*, 137 (1958).

[22a] *F. Asinger* and *M. Fischer,* J. prakt. Chem. [4], *35*, 81 (1967).

[23] *F. Asinger, M. Thiel,* and *H. Baltz,* Mh. Chem. *88*, 464 (1957).

[24] *F. Asinger, M. Thiel,* and *H. G. Hauthal,* Liebigs Ann. Chem. *615*, 70 (1958).

[25] *F. H. McMillan* and *J. A. King,* J. Amer. chem. Soc. *70*, 4143 (1948).

gives Δ^3-thiazolines in excellent yields (modified resynthesis) [24, 33–36].

This process has proved particularly useful when the tendency toward desulfurization, *i.e.* the elimination of sulfur with reformation of the ketone or else the formation of epiminodithiane, is so strong in the presence of ammonia (see below) that resynthesis fails. Good yields of thiazoline are also obtained in these cases if *S*-acetylated α-mercapto ketones are used; on reaction of these compounds with ammonia and carbonyl compounds, one mole of acetamide is formed per mole of Δ^3-thiazoline [26].

$$\underset{(5)}{R\text{-}CO\text{-}CR^1R^2\text{-}S\text{-}CO\text{-}CH_3} + NH_3 + \underset{(4)}{R^3\text{-}CO\text{-}R^4} \longrightarrow \underset{(1b)}{\text{thiazoline}}$$

The *S*-acetylated α-mercapto ketones are obtained by acetylation of monomeric or even dimeric α-mercapto ketones with acetic anhydride in pyridine or by reaction of α-halogeno ketones with sodium acetothiolate [26].

Δ^3-Thiazolines can also be synthesized by the reaction of alkylidene vinylamines *(6)* (which can be prepared from secondary aliphatic aldehydes and ammonia) [27] with sulfur.

$$\underset{(6)}{\text{alkylidene vinylamine}} + S \longrightarrow \underset{(1c)}{\text{thiazoline}}$$

The α-thiolation of the condensation product of 2 moles of aldehyde and 1 mole of ammonia (= enazomethine) is followed by an intramolecular cycloaddition of the thiol to the olefinic double bond with formation of the stable Δ^3-thiazoline ring system. This possibility was first described in 1959 [28] und was recently re-examined by us [29]. We studied it in detail for the case of isobutylidene-β β-dimethylvinylamine and applied it to other alkylidenevinylamines. By the addition of solvents and special amines, it is possible [29] to lower the reaction temperature from 140 °C to 65 °C, and even to 20 °C and to double the yield to 80 % (see Table 3).

Table 3. 2,5,5-Trialkyl-substituted Δ^3-thiazolines *(1c)* prepared from alkylidenevinylamines *(6)* (0.1 mole) and sulfur (0.4 g-atom).

$$\underset{(6)}{\text{alkylidene vinylamine}} \xrightarrow{S} \underset{(1c)}{\text{thiazoline}}$$

R	R^1	Conditions	Yield (%)	B.p. (°C/mm)	Ref.
CH_3	CH_3	[a]	40	55–56/5	[28]
CH_3	CH_3	[b]	80	65/7	[29]
CH_3	n-C_3H_7	[a]	40	90/3	[28]
C_2H_5	C_2H_5	[b]	65	74–75/0.1	[29]
C_2H_5	n-C_4H_9	[b]	52	110–111/0.1	[29]

[a] Solvent-free, 140 °C.

[b] In methanol with the addition of 0.1 mole of diazabicyclooctane per 0.1 mole of *(6)*, 65 °C.

2.2. Properties and Reactions

The alkyl-substituted Δ^3-thiazolines are colorless liquids having a musty odor. As the molecular weight increases, the odor becomes similar to that of terpene and finally almost completely disappears. The Δ^3-thiazoline formed from cyclohexanone is an exception in that it is crystalline and almost odorless [12], while the Δ^3-thiazoline derived from cycloheptanone [35] and that formed by the reaction of α-mercaptocyclopentanone with cyclopentanone and ammonia [35] are again liquid. Δ^3-Thiazolines with aromatic substituents are frequently obtained in the crystalline form.

The compounds can in many cases be characterized in the form of the picrates which melt between 90 and 150 °C.

The hydrochlorides are directly obtainable only in exceptional cases. In other cases they can be obtained *via* the hydrochlorides of the thiazolidine-4-carbonitriles by elimination of HCN (see below). Some Δ^3-thiazolines form stable adducts with BF_3 [29]. The Δ^3-thiazolines are insoluble in water but soluble in alcohols, chlorinated hydrocarbons, ether, benzene, and petroleum ether.

The principal reactions of the Δ^3-thiazolines are shown in Scheme 1.

Attempts to reduce Δ^3-thiazolines with sodium and alcohol, sodium in liquid ammonia, or aluminum in the presence of potassium hydroxide solution or moist ether did not yield uniform results. On the other hand, the Δ^3-thiazolines are very smoothly hydrogenated with lithium tetrahydridoaluminate; this reaction results, not only in the hydrogenation of the azomethine bond, but also in hydrogenolytic ring cleavage between

[26] *F. Asinger, W. Schäfer,* and *N. B. Desai,* unpublished.

[27] *A. Lipp,* Liebigs Ann. Chem. *205,* 4 (1880); *211,* 345 (1882); *R. H. Hasek, E. U. Elan,* and *J. C. Martin,* J. org. Chemistry *26,* 1822 (1961); *J. W. Clark* and *A. L. Wilson,* US-Pat. 2319848 (May 25, 1943), Carbide and Carbon Chemicals Corp.; Chem. Abstr. *37,* 6275 (1943).

[28] *H. Schade* and *M. Thiel,* DAS 1063602 (March 13, 1957), Leuna-Werk.

[29] *F. Asinger* and *M. Schröder,* unpublished.

[30] *F. Asinger, M. Thiel,* and *G. Esser,* Liebigs Ann. Chem. *610,* 33 (1957).

[31] *F. Asinger, M. Thiel,* and *I. Kalzendorf,* Liebigs Ann. Chem. *610,* 25 (1957).

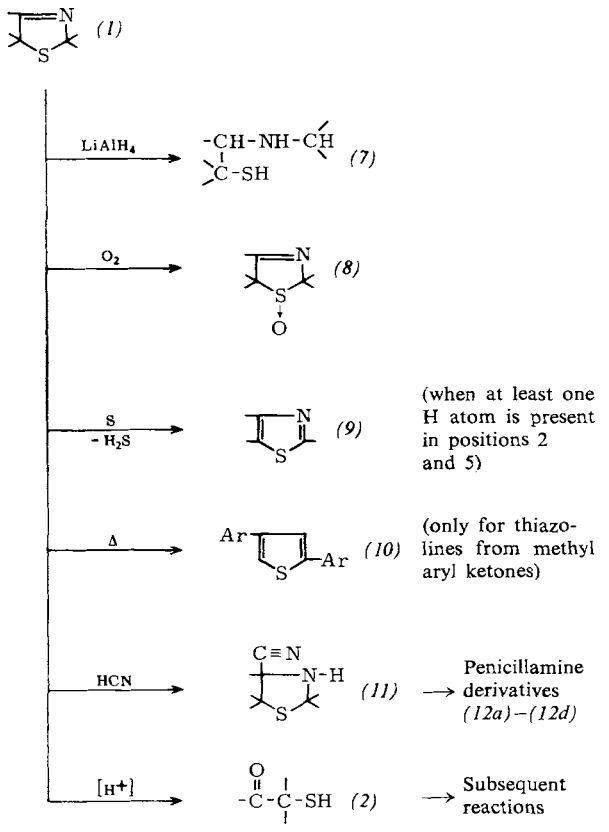
[32] *M. Thiel, F. Asinger,* and *K. Schmiedel,* Liebigs Ann. Chem. *611,* 121 (1958).

[33] *F. Asinger, M. Thiel, W. Dathe, O. Hampel, E. Mittag, E. Plaschil,* and *C. Schröder,* Liebigs Ann. Chem. *639,* 146 (1961).

[34] *F. Asinger, M. Thiel, P. Püchel, F. Haaf,* and *W. Schäfer,* Liebigs Ann. Chem. *660,* 85 (1962).

[35] *F. Asinger, M. Thiel, H. Usbeck, K.-H. Gröbe, H. Grundmann,* and *S. Tränkner,* Liebigs Ann. Chem. *634,* 144 (1960).

[36] *F. Asinger, H. Diem,* and *An Sin-Gun,* Liebigs Ann. Chem. *643,* 186 (1961).



Scheme 1. Reactions of the Δ^3-thiazolines *(1)*.

S and C-2 with formation of *N*-substituted cysteamines *(7)* [37].

Δ^3-Thiazolines are generally stable and can be stored for long periods without deteriorating. However, those derived from cycloaliphatic ketones are converted into Δ^3-thiazoline *S*-oxides *(8)* by air [13].

2,2-Pentamethylene-4,5-tetramethylene-Δ^3-thiazoline and the Δ^3-thiazolines derived from alkylcyclohexanones are suitable for use as antioxidants for polyolefins [38]. The superiority of their properties as compared with those of other compounds containing sulfur is due to the ease with which these thiazolines autoxidize to form *S*-oxides.

The Δ^3-thiazolines obtained from primary or secondary α-mercapto ketones or aldehydes, aldehydes, and ammonia, which contain C–H bonds in positions 2 and 5, can be smoothly dehydrogenated to thiazoles *(9)*, preferably by heating with sulfur at about 130 °C [39–41]. $FeCl_3$, $K_3[Fe(CN)_6]$, K_2Cr_2O, and hydrogen peroxide are less suitable than sulfur powder for this novel thiazole synthesis. The yields are about 80 %.

Δ^3-Thiazolines formed by the reaction of acetophenone and ring-substituted acetophenones with

[37] *M. Thiel, F. Asinger, K. Häussler*, and *Th. Körner*, Liebigs Ann. Chem. *622*, 107 (1959).

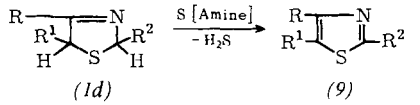
[38] *C. Heuck et al.*, German Pat. 1096599 (June 19, 1958), Farbwerke Hoechst; Chem. Abstr. *55*, 24115 (1961).

[39] *F. Asinger, M. Thiel*, and *L. Schröder*, Liebigs Ann. Chem. *610*, 49 (1957).

[40] *M. Thiel, F. Asinger*, and *M. Fedtke*, Liebigs Ann. Chem. *615*, 77 (1958).

[41] *F. Asinger, L. Schröder*, and *S. Hoffmann*, Liebigs Ann. Chem. *648*, 83 (1961).

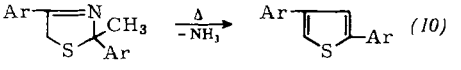
Table 4. Thiazoles prepared from Δ^3-thiazolines by dehydrogenation (selection).



(1d) *(9)*

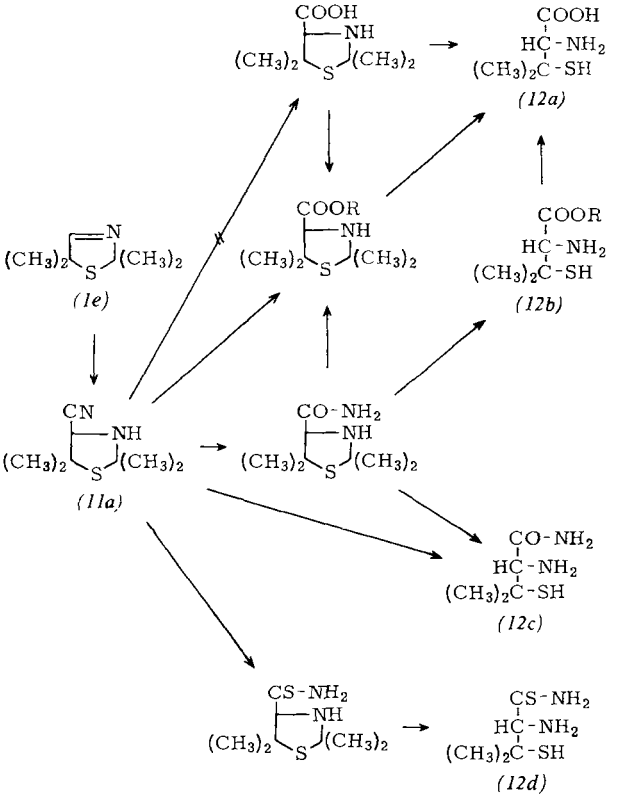
R	R^1	R^2	Yield (%)	B.p. (°C/mm)	Ref.
CH_3	H	H	52	60–61/16	[39]
n-C_3H_7	H	C_2H_5	84	97.5–98/15	[8]
CH_3	H	C_6H_5	80	145–147/16	[33]
C_2H_5	CH_3	CH_3	93	66–68/11	[39]
$-(CH_2)_4-$		CH_3	89	102/11	[35]

sulfur and ammonia [9] can be pyrolysed by heating at about 250 °C for 5 to 15 hours, the products being 2,4-diarylthiophenes *(10)* [9]. The yield when Ar = C_6H_5 is 56 %.



(10)

Anhydrous hydrogen cyanide adds readily to the azomethine bond of many Δ^3-thiazolines at room temperature [42]. The resulting thiazolidine-4-carbonitriles *(11)* are more or less stable, depending on their purity and on the nature and number of substituents in positions 2 and 4; however, they are always stable in the form of their hydrochlorides. No relationship could be found between structure and stability. Thiazolidine-4-carbonitriles that are not quite pure decompose much more rapidly.



Scheme 2. Reactions of thiazolidine-4-carbonitriles, illustrated for the case of 2,2,5,5-tetramethylthiazolidine-4-carbonitrile [42, 42a].

[42] *F. Asinger, E.-C. Witte*, and *W. Schäfer*, Liebigs Ann. Chem. *697*, 140 (1966); *F. Asinger, W. Schäfer*, and *E.-C. Witte*, Angew. Chem. *76*, 273 (1964); Angew. Chem. internat. Edit. *3*, 313 (1964).

[42a] *F. Asinger, H. Offermanns*, and *M. Ghyczy*, unpublished.

The reactions of the thiazolidine-4-carbonitriles may be illustrated for the case of 2,2,5,5-tetramethylthiazolidine-4-carbonitrile *(11a)*, (see Scheme 2), which is particularly important for the preparation of penicillamine and its derivatives *(12a)–(12d)*.

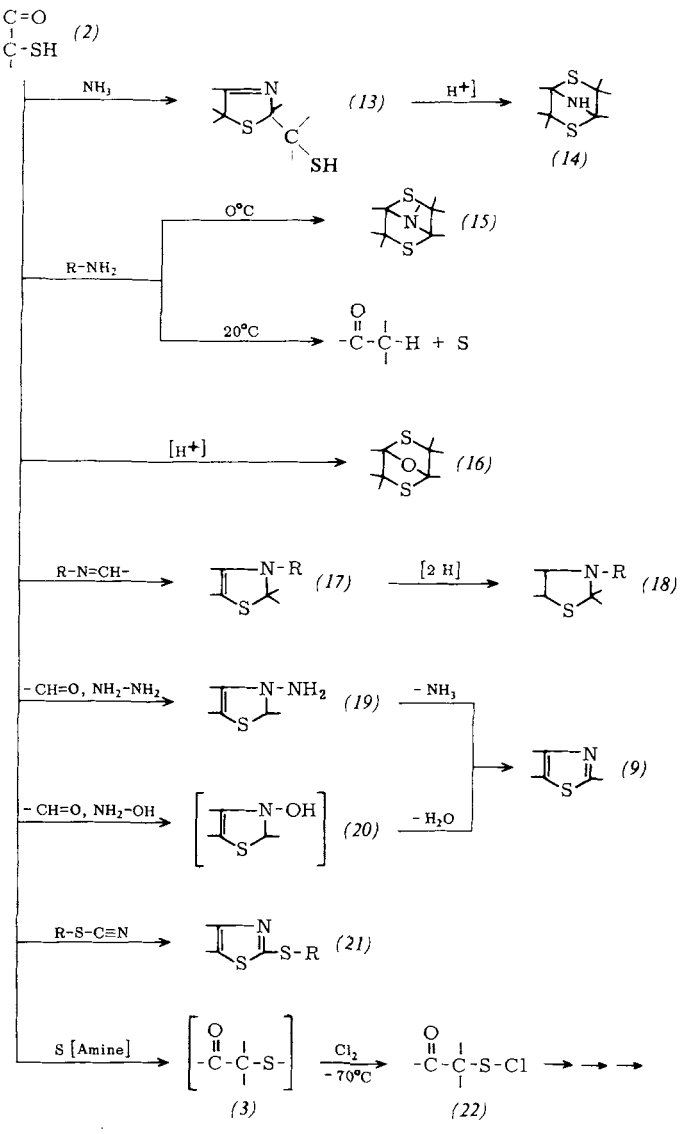
A general property of the Δ^3-thiazolines is their ability to undergo hydrolysis by aqueous acids with formation of α-mercapto ketones or aldehydes, oxo compounds, and ammonium salts (reversal of ring formation)[19].

The rate of hydrolysis is strongly dependent on the nature, number, and position of the substituents on the thiazoline ring. The time taken to reach a degree of hydrolysis of 50 % is *e.g.* between 10 min and 85 hours for methyl-substituted Δ^3-thiazolines. A substituent in position 2 has an accelerating influence; a substituent on C-4, on the other hand, strongly inhibits hydrolysis, an effect that can be intensified by additional substitution on C-5. Two substituents on the same C atom intensify the effect in the same direction. It is possible on the one hand to prepare Δ^3-thiazolines that are practically no longer hydrolysable, and which form stable hydrochlorides (which are otherwise obtainable only by the elimination of HCN from 4-cyanothiazolidine hydrochlorides[42]). On the other hand, it is also possible to prepare readily hydrolysable Δ^3-thiazolines whose acid hydrolysis provides a favorable route to α-mercapto ketones, which is superior in most cases to the other methods of preparation, *e.g. via* α-halogeno ketones, thioesters, or Bunte salts.

The hydrolysis is best carried out with dilute acetic acid, the low dissociation of which suppresses the troublesome formation of epoxydithiane from the α-mercapto ketone.

If the rate of hydrolysis is too low and self-condensation with ammonium acetate (see below) takes place, the hydrolysis is carried out with dilute hydrochloric acid and the α-mercapto ketone is removed by steam distillation.

The convenient 2-stage process[19] for the preparation of α-mercapto ketones by formation and hydrolysis of Δ^3-thiazolines, which proceeds in excellent yields without the use of high temperatures or pressures, led us to study in detail the behavior of the reactive 1,3-bifunctional α-mercapto ketones.

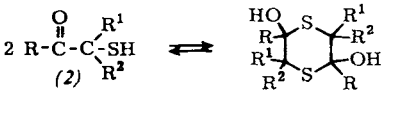


Scheme 3. Reactions of the α-mercapto ketones.

3. Syntheses with α-Mercapto Ketones

The reactions of the α-mercapto ketones are shown in Scheme 3.

The lower α-mercapto ketones *(2)* are generally liquid (exception: α-mercaptoacetone, m.p. 75–76 °C[43]) and have an extremely unpleasant odor. They frequently exhibit a double molecular weight, so that an equilibrium with a dithiane form must be assumed.



(For the association behavior of α-mercapto ketones in CCl_4, see[44].)

Under the influence of mineral acids, many α-mercapto ketones form 2,5-epoxy-1,4-dithianes *(16)*. This reaction can be troublesome in the preparation of α-mercapto ketones by hydrolysis of Δ^3-thiazolines.

In the presence of ammonia, α-mercapto ketones in general undergo self-condensation to form 2-mercaptoalkyl-Δ^3-thiazolines *(13)*, which exist in acidic media as 2,5-epimino-1,4-dithianes *(14)* (intramolecular addition of SH to the azomethine group). *N*-Substituted epiminodithianes *(15)* are formed when primary amines or carbonyl reagents such as phenylhydrazine, hydroxylamine, and semicarbazone are allowed to react with α-mercapto ketones at low temperatures. The action of primary amines on α-mercapto ketones at or above room temperature yields ketones and sulfur (in the form of alkylammonium polysulfides). In this desulfurization reaction[11] (cf.[17]), which is the reverse of the α-thiolation, the positionally isomeric ketones are formed as well as the expected ketone. Thus the desulfurization of 2-mercapto-3-pentanone leads to both 2-pentanone and 3-pentanone, while that of α-mercaptobutyrophenone yields all three positionally isomeric 1-phenylbutanones[45]. This desulfurization reaction is very important to the interpretation of the Willgerodt-Kindler reaction. Pure secondary amines desulfurize α-mercapto ketones only to a small extent; tertiary amines react with α-mercapto ketones only above 70 °C, to form hydrogen sulfide and non-uniform polymeric products[45a]. The desulfurizing action of ammonia has so far been ob-

[43] *B. Groth*, Dissertation, Technical University, Stockholm, 1928.

[44] *G. Geiseler* and *F. Stache*, Chem. Ber. *94*, 337 (1961).

[45] *F. Asinger*, *H. Offermanns*, and *H.-D. Köhler*, unpublished.

[45a] *W. Pürschel*, Diploma Thesis, Technische Hochschule Aachen, 1963; and literature cited there.

served only with 1-mercapto-1-phenylpropanone, since the rapid formation of epimonodithiane occurs in other cases [40].

If primary amines are allowed to act, not on α-mercapto ketones alone (except tertiary), but on a mixture of the ketone and an aliphatic aldehyde at about 0 °C, epiminodithiane formation and desulfurization are completely suppressed, and Δ^4-thiazolines *(17)* are formed by an exothermic reaction [46].

Instead of starting with an aldehyde and an amine, aldimines may be allowed to react directly with α-mercapto ketones [47]. Ketimines and the components of ketimines, *i.e.* ketones and primary amines, do not react with α-mercapto ketones to form Δ^4-thiazolines. The result is desulfurization, together with other reactions that have not yet been clarified. (An exception is cyclohexanone.) The reaction of α-mercapto ketones with cyclohexanone and primary amines or directly with *N*-alkylketimines of cyclohexanone leads smoothly to the corresponding Δ^4-thiazolines.

α-Mercapto ketones can also react with aldehydes (or cyclohexanone) and esters of α-amino acids (or their hydrochlorides), or with the Schiff bases formed by these components, to form esters of Δ^4-thiazolin-3-ylacetic acids [47a].

The Δ^4-thiazolines *(17)*, which are colorless to yellow liquids, are generally less stable than Δ^3-thiazolines. They have a fixed enamine structure, and so can be hydrogenated to thiazolidines *(18)* by formic acid at 50–60 °C [48]; this offers a new route to the thiazolidines. Some examples of the synthesis and hydrogenation of Δ^4-thiazolines are given in Table 5.

The reaction of primary or secondary α-mercapto ketones with aldehydes and hydrazine leads to 3-amino-Δ^4-thiazolines *(19)* [48], which lose ammonia to form thiazoles *(9)* on treatment with acids. Whereas Δ^3- and Δ^4-thiazolines are decomposed again by mineral acids, *i.e.* their formation is reversed, the hydrolysis is suppressed in this case in favor of thiazole formation.

The reaction of α-mercapto ketones with aldoximes leads to the formation of thiazoles and water [48]. The postulated intermediate 3-hydroxy-Δ^4-thiazoline *(20)* has not been isolated. The last two reactions are new thiazole syntheses. Certain α-mercapto ketones react with both aliphatic and aromatic thiocyanates to give *S*-substituted 2-mercaptothiazoles *(21)* [49].

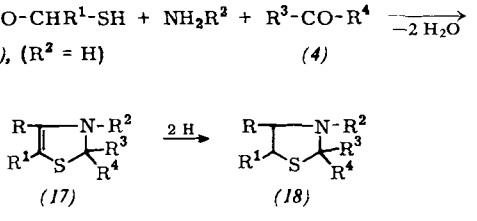
As was mentioned earlier, α-mercapto ketones can be smoothly oxidized with sulfur in the presence of catalytic quantities of amine or ammonia to give α,α'-dioxo sulfides *(3)* [24] (modified McMillan-King reaction).

α,α'-Dioxo disulfides react readily with stoichiometric quantities of liquid chlorine in methylene chloride at −70 to −80 °C to form β-oxo sulfenyl chlorides *(22)*, which cannot be isolated as such. Their existence was shown by secondary reactions, *e.g.* with triethyl phosphite [50].

Tertiary β-oxosulfenyl chlorides react with ammonia or amines to give moderate yields of β,β'-dioxosulfenylimides or β-oxosulfenylamides which can be isolated [50,51].

Primary β-oxosulfenyl chlorides react with secondary amines with dehydrogenative rearrangement and formation of α-oxothioamides. The yield of α-oxothioamide is considerably increased by the addition of sulfur [52,53].

Table 5. Δ^4-Thiazolines *(17)* prepared from primary or secondary α-mercapto ketones, oxocomponents, and primary amines (or from α-mercapto ketones and aldimines) [46,47] and thiazolidines *(18)* prepared by hydrogenation of the corresponding Δ^4-thiazolines *(17)* with formic acid [48] (selection).



(2), (R^2 = H) *(4)*

(17) *(18)*

R	R^1	R^2	R^3	R^4	*(17)* Yield (%)	*(17)* b.p. (°C/mm)	*(18)* Yield (%)	*(18)* b.p. (°C/mm)
C_2H_5	CH_3	CH_3	CH_3	H	63	38–40/0.4	44	78–80/12
C_2H_5	CH_3	n-C_4H_9	$CH(CH_3)_2$	H	76	77–78/0.5	65	81–82/0.5
C_2H_5	CH_3	n-C_3H_7	$-(CH_2)_5-$		70	95/0.5	47	103–104/13
C_2H_5	CH_3	CH_3	C_6H_5	H [a]	85	138–139/3 m.p. 58 °C	78	105–109/0.6
$-(CH_2)_4-$		CH_3	C_6H_5	H [a]	67	180/6 m.p. 37 °C	—	—

[a] Prepared from *(2)*, (R^2 = H), and benzylidenemethylamine.

[46] *F. Asinger, M. Thiel*, and *H. G. Hauthal*, Liebigs Ann. Chem. *622*, 83 (1959).

[47] *K. Rühlmann, M. Thiel*, and *F. Asinger*, Liebigs Ann. Chem. *622*, 94 (1959).

[47a] *F. Asinger, H. Offermanns*, and *C. Dudeck*, unpublished.

[48] *F. Asinger, M. Thiel*, and *H. G. Hauthal*, Liebigs Ann. Chem. *634*, 131 (1960).

[49] *F. Asinger* and *K. Fabian*, unpublished.

[50] *F. Asinger, M. Thiel*, and *W. Schäfer*, Liebigs Ann. Chem. *637*, 146 (1960).

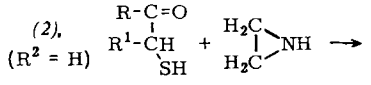
[51] *P.-F. Müting*, Dissertation, Technische Hochschule Aachen, 1962.

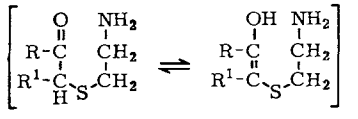
[52] *F. Asinger, W. Schäfer, G. Baumgarte*, and *P. F. Müting*, Liebigs Ann. Chem. *661*, 95 (1963).

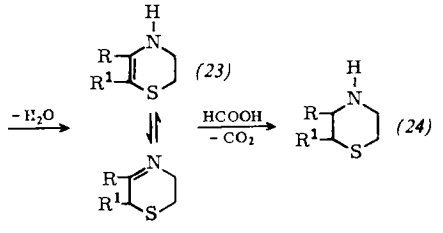
[53] *F. Asinger, W. Schäfer*, and *A. Saus*, Mh. Chem. *96*, 1272 (1965).

4. 5,6-Dihydro-4*H*-1,4-thiazines, 5,6,8,8a-Tetrahydrothiazolo[2,3-*c*]-1,4-thiazines, and Thiomorpholines (Action of Sulfur and Ethylenimine on Ketones)

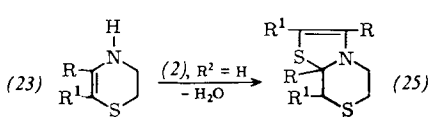
The action of ethylene on primary or secondary α-mercapto ketones (special case of the action of a secondary amine on α-mercapto ketones) leads to a new class of substances, *i.e.* the 5,6-dihydro-4*H*-1,4-thiazines *(23)* [54,55] [*].







The equilibrium between the azomethine and the enamine forms lies completely on the enamine side. 5,6-Dihydro-4*H*-1,4-thiazines can be acetylated at the nitrogen and can react with phenyl isocyanate; their reduction with formic acid (cf. [56]) yields thiomorpholines *(24)* [54,55]. The 5,6-dihydro-4*H*-1,4-thiazines are also characterized by the ease of addition of an excess of α-mercapto ketone. This leads smoothly to 5,6,8,8a-tetrahydrothiazolo[2,3-*c*]-1,4-thiazines *(25)* [54, 55], which can be reduced by formic acid to the perhydrogenated products.



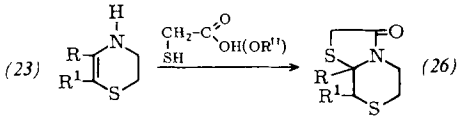
Further investigations on the simultaneous formation of the compounds *(23)* and *(25)* have shown that the preferential formation of one form or the other does not depend mainly on the molar ratio of α-mercapto ketone to ethylenimine, as might at first be assumed; the reaction temperature is a much more important factor. If the α-mercapto ketone is added dropwise to boiling ethylenimine, the temperature (which is initially determined by the boiling point of ethylenimine) being gradually raised to 70–75 °C, *(23)* is obtained in 95 % yield. On the other hand, if the reaction is carried out at −20 °C, *(25)* is obtained in 80 % yield. The results are given in Table 6 for the reaction of 2-mercapto-3-pentanone with ethylenimine [54] (for further examples see [54,55]).

Table 6. Temperature-dependence of the reaction of ethylenimine (1.3 mole) with 2-mercapto-3-pentanone (1 mole) (R = C_2H_5, R^1 = CH_3)

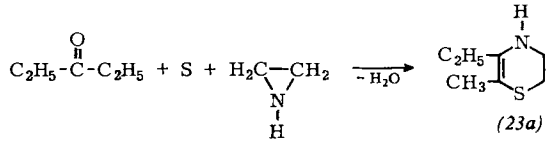
Temp. (°C)	Yield of (%)	
	(23a)	*(25a)*
60 → 75	95	–
60	86	4
40	78	12
20	50	36
0	21	66
−20	10	78

5,6-Dihydro-4*H*-1,4-thiazines can also be prepared from α-bromo ketones and cysteaminesodium. This reaction also serves as structural evidence. The problems involved in the reaction of tertiary α-mercapto ketones with ethylenimine and the reaction of propylenimine with α-mercapto ketones will not be discussed here [55].

5,6-Dihydro-4*H*-1,4-thiazines react with α-mercapto carboxylic acids or their esters to form 5,6,8,8a-tetrahydro-3-oxothiazolidine[2,3-*c*]-1,4-thiazines *(26)* [57].



As was shown in the case of 3-ethyl-2-methyl-5,6-dihydro-4*H*-1,4-thiazine *(23a)*, the dihydro-1,4-thiazines are also directly obtainable from ketones, sulfur, and ethylenimine [58]. *(23a)* is formed in a yield of about 80 %.



When elementary selenium is used in the reaction instead of sulfur [59], 3-ethyl-2-methyl-5,6-dihydro-4*H*-1,4-selenazine is formed in a yield of more than 50 %. So far as we know, this is the first direct selenation of a CH acid.

Unlike the selenazines, Δ³-selenazolines cannot be prepared either directly from ketone, selenium, and ammonia or *via* α-hydroseleno ketones (the reaction of α-halogeno ketones with sodium hydrogen selenide leads to deposition of selenium and resinification) [59]. At present we are investigating whether the thiazine and selenazine synthesis is as generally applicable as the action of sulfur and ammonia on ketones.

5. Δ³-Imidazoline-5-thiones (Action of Sulfur and Ammonia on Methyl Ketones)

5.1. Syntheses

Methyl ketones occupy a special place in the synthesis of Δ³-thiazolines. Methyl ketones having at least one H atom in the other α position preferentially give

[54] *F. Asinger, F. J. Schmitz,* and *S. Reichel,* Liebigs Ann. Chem. *652,* 50 (1962).

[55] *F. Asinger, H. Diem,* and *W. Schäfer,* Mh. Chem. *95,* 1335 (1964).

[*] According to IUPAC rules A-216, A-23.1 and A-23.2, these compounds are named 3,4-dihydro-2*H*-1,4-thiazines.

[56] *N. J. Leonard* and *F. P. Hauck jr.,* J. Amer. chem. Soc. *79,* 5279 (1957).

[57] *F. Asinger, H. Diem,* and *W. Schäfer,* Mh. Chem. *95,* 1391 (1964).

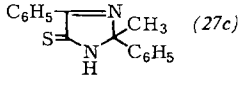
[58] *F. Asinger, W. Pürschel,* and *K. H. Lim,* unpublished.

[59] *F. Asinger* and *H. Berding,* unpublished.

the Δ^3-thiazoline, which is not formed by thiolation of the methyl group. Methyl ketones in which only the methyl group is available for thiolation have proved inert under the standard conditions of the Δ^3-thiazoline synthesis (acetophenone [34, 60], pinacolone [61]). Acetophenone gives only 11 % of 2-methyl-2,4-diphenyl-Δ^3-thiazoline together with 4 % of a yellow crystalline compound $C_{16}H_{14}N_2S$ [34, 52, 60, 61] (see below).

Since similar yellow crystalline compounds are also formed in the reactions of other methyl ketones (methyl isopropyl ketone, methyl neopentyl ketone, methyl cyclohexyl ketone) with sulfur and ammonia, this behavior seemed to be a pecularity of the methyl ketones. Acetophenone was of particular interest, since it is the classic ketone for the Willgerodt and Willgerodt-Kindler reactions, and we hoped to obtain an understanding of these reactions.

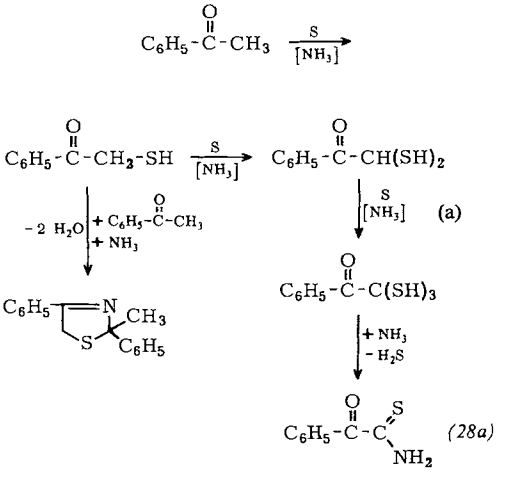
The yellow crystalline compound formed in a 4 % yield from acetophenone, sulfur, and ammonia under standard conditions was identified by degradation reactions and comparison synthesis as 2-methyl-2,4-diphenyl-Δ^3-imidazoline-5-thione *(27c)* [62].



(27c)

The yield of *(27c)* can be increased to more than 90 % if 8 g-atoms of sulfur are used per mole of acetophenone (though only 1.5 g-atoms are theoretically required), the reaction being carried out in methanol and ammonia being passed into the mixture for about 24 hours at 20 °C and normal pressure [52] (see Table 7).

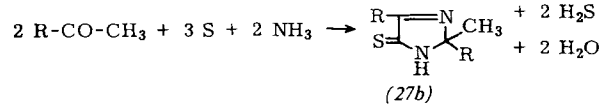
The reaction is applicable to many other methyl aryl ketones. The yields obtained with methyl heteroaryl ketones are considerably lower. With aliphatic methyl ketones, Δ^3-thiazoline formation generally predominates; however, even in this case formation of Δ^3-imidazoline-5-thiones can be made the principal reaction by the addition of one mole of piperidine per mole of ketone.



Like the Δ^3-thiazoline formation, the formation of Δ^3-imidazoline-5-thiones can be broken down into two steps (illustrated for acetophenone):

(a) formation of phenylglyoxylic thionamide; (b) ring closure.

Table 7. 2,2,4-Trisubstituted Δ^3-imidazoline-5-thiones *(27b)* prepared from methyl ketones, sulfur, and ammonia (molar ratio ketone: sulfur = 1:8; 24 hours at 20 °C) (selection).



(27b)

Ketone	R	M.p. (°C)	Solvent	Yield (%)	Ref.
Acetophenone	C_6H_5	182	CH_3OH	90	[52]
p-Fluoroacetophenone	*p*-F—C_6H_4	186	CH_3OH	69	[52]
p-Chloroacetophenone	*p*-Cl—C_6H_4	161	CH_3OH	89	[52]
3,4-Dichloroacetophenone	3,4-Cl_2—C_6H_3	185—186	CH_3OH	58	[63]
p-Methoxyacetophenone	*p*-CH_3O—C_6H_4	187	CH_3OH	96	[52]
p-Aminoacetophenone	*p*-NH_2—C_6H_4	171	CH_3OH	74	[52]
α-Acetylnaphthalene	α-Naphthyl	247	CH_3OH	40	[52]
β-Acetylnaphthalene	β-Naphthyl	185	CH_3OH	85	[52]
2-Acetylthiophene	2-Thienyl	174	CH_3OH	38	[52]
3-Acetylpyridine	3-Pyridyl	179—181	CH_3OH	26	[63]
Methyl isopropyl ketone	$(CH_3)_2CH$	92	[a]	32	[63a]
Pinacolin	$(CH_3)_3C$	147—148	[a]	65	[63a]
Pinacolin	$(CH_3)_3C$	147—148	—	21	[61]
Methyl cyclohexyl ketone	Cyclohexyl	156	—	22	[64]

[a] Addition of 1 mole of piperidine per mole of ketone.

The formation of phenylglyoxylic thionamide *(28a)* is due to multiple thiolation of the acetophenone [66]. This explains the high sulfur requirement in the reaction. The final result is the oxidative replacement of all the H atoms of the methyl group in acetophenone by SH groups. It is not yet possible to decide whether this substitution takes place simultaneously

[60] *F. Asinger* and *S. Vogelsang*, unpublished.

[61] *F. Asinger, M. Thiel, G. Peschel*, and *K.-H. Meinicke*, Liebigs Ann. Chem. *619*, 145 (1958).

[62] *F. Asinger, F. Haaf, H. Meisel*, and *G. Baumgarte*, Angew. Chem. *73*, 706 (1961).

[63] *F. Asinger, W. Schäfer*, and *G. Kriebel*, Mh. Chem. *96*, 69 (1965); cf. *G. Kriebel*, Dissertation, Technische Hochschule Aachen, 1965.

[63a] *F. Asinger* and *G. Kriebel*, unpublished.

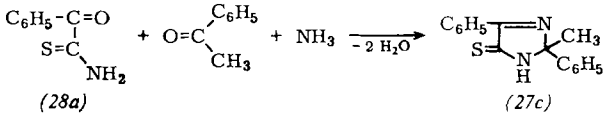
[64] *F. Asinger, W. Schäfer*, and *F. Haaf*, Liebigs Ann. Chem. *672*, 134 (1964).

[65] *F. Asinger* and *F. Gentz*, Mh. Chem. *96*, 1461, 1473 (1965).

[66] *F. Asinger, W. Schäfer*, and *A. Saus*, Mh. Chem. *96*, 1278 (1965).

(to the trimercapto ketone stage) or stepwise *via* the dimercapto compound, the thioaldehyde, or the products of their further reaction with ammonia (aminomercapto compound, α-oxoaldimine); however, this is of no importance to the interpretation of the course of the reaction. Those cases in which the ketimine formation is allowed to precede the α-thiolation in order to increase the acidity of the α-CH group will not be discussed here (see, however, [66, 67]).

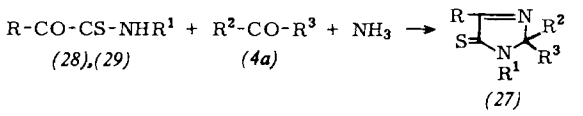
The second step (b) as in the Δ^3-thiazoline formation, involves the α-aminoalkylation of an N–H acid compound (cf. [4], p. 64) and subsequent stabilization by ring closure with elimination of water.



(28a) *(27c)*

Since we have been able to develop efficient syntheses both for *N*-unsubstituted *(28)* and for *N*-monosubstituted *(29)* α-oxothionamides, many Δ^3-imidazoline-5-thiones *(27)*, particularly with a substituent (of almost any type) in position 2, are now available by reaction of these α-oxothionamides with ketones and ammonia (see Table 8).

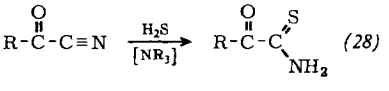
Table 8. Δ^3-Imidazoline-5-thiones prepared from α-oxothionamides, ketones, and ammonia (selection) [65, 69].



(28), (29) *(4a)* *(27)*

R	R^1	R^2	R^3	Yield (%)	M.p. (°C)
C_6H_5	H	CH_3	CH_3	77	187–191
i-C_4H_9	H	$-(CH_2)_5-$		78	131–133
$(CH_3)_3C-CH_2$	H	CH_3	CH_3	72	137–139
3,4,5-$(CH_3O)_3-C_6H_2$	H	$-(CH_2)_5-$		91	208
C_6H_5	n-C_3H_7	$-(CH_2)_5-$		92	118
C_6H_5	CH_3	C_6H_5	CH_3	54	96
$(CH_3)C$	n-C_4H_9	$-(CH_2)_5-$		48	64

N-Unsubstituted α-oxothionamides *(28)* are obtained by base-catalysed (triethylamine) addition of H_2S to acyl or aroyl cyanides, in accordance with the equation:

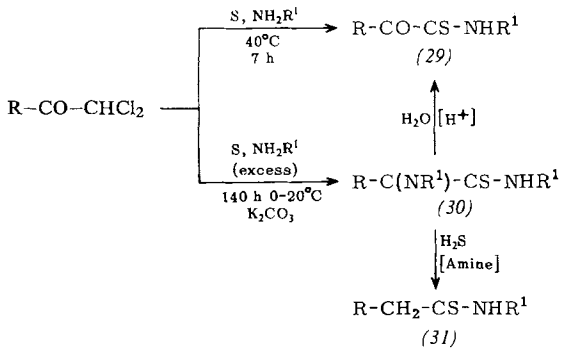


(28)

This reaction must be carried out in nonpolar solvents such as n-heptane or ether [68, 69].

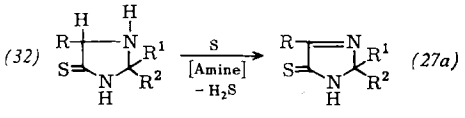
We were also able to prepare *N*-monosubstituted α-oxothionamides *(29)* readily by the action of primary amines and sulfur in boiling ether on α-oxodichloro compounds of the type R–CO–$CHCl_2$ (R = alkyl or aryl) [69], the residue R^1 depending on the amine used.

Under different conditions [70] (increase in the quantity of amine, addition of potash, and increase in the reaction time to 140 hours, the reaction temperature being lowered to 20 °C), the reaction leads to yields of more than 70 % of α-ketiminothionamides *(30)*, which can be quantitatively converted into α-oxothionamides *(29)* by hydrolysis with dilute acetic acid.



The ketiminothionamides can be converted into the Willgerodt-Kindler products *(31)* by the introduction of hydrogen sulfide even at room temperature [70].

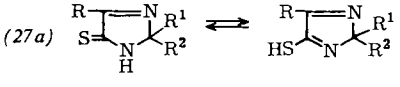
Another method for the synthesis of Δ^3-imidazoline-5-thiones *(27a)* is the dehydrogenation of imidazolidine-4-thiones *(32)* by heating with sulfur in the presence of catalytic quantities of amine [62, 71].



(32) *(27a)*

5.2. Reactions

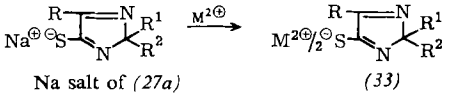
The intensely yellow, highly crystalline, and very stable Δ^3-imidazoline-5-thiones are cyclic thionamides. They are tautomeric with mercapto-2*H*-imidazoles.



(27a)

The position of the equilibrium depends on the basicity of the reaction medium, and it is possible to prepare derivatives both of the thionamide and of the thiolimine form. The reactions can be illustrated by the case of 2-methyl-2,4-diaryl-Δ^3-imidazoline-5-thiones *(27b)* and *(27c)*.

Solutions of the Δ^3-imidazoline-5-thiones in dilute NaOH form salts with bivalent metal ions [72].



Na salt of *(27a)* *(33)*

$M=Cu^{2\oplus}$, $Cd^{2\oplus}$, $Hg^{2\oplus}$
Yield = 58 to 92 %

$R=R^1=C_6H_5$,
$R^2=CH_3$

Reduction of the azomethine bond of the Δ^3-imidazoline-5-thione with magnesium in methanol leads to imidazolidine-4-thiones in 60 % yield [72]. Poorer

[67] *A. Saus*, Dissertation, Technische Hochschule Aachen, 1963.

[68] *F. Asinger* and *F. Gentz*, Angew. Chem. *75*, 577 (1963); Angew. Chem. internat. Edit. *2*, 397 (1963).

[69] *F. Asinger*, *A. Saus*, *H. Offermanns*, and *H.-D. Hahn*, Liebigs Ann. Chem. *691*, 92 (1966).

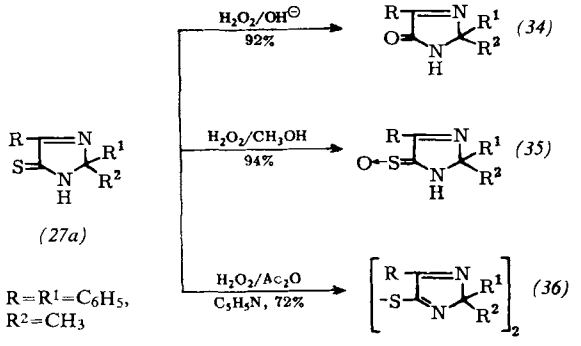
[70] *F. Asinger* and *H. Offermanns*, Mh. Chem., in press.

[71] *F. Asinger*, *W. Schäfer*, *H. Meisel*, *H. Kersten*, and *A. Saus*, Mh. Chem. *98*, 338 (1967).

[72] *F. Asinger*, *W. Schäfer*, *A. Wegerhoff*, and *G. Kriebel*, Mh. Chem. *97*, 792 (1966).

yields are obtained with $NaBH_4$. Reduction with $LiAlH_4$ in ether at 35 °C leads to ring cleavage and removal of the sulfur as hydrogen sulfide, with formation of a mixture of two structurally isomeric diamines [72].

The oxidation reactions are shown in Scheme 4 [72]. They lead to products in which exocyclic sulfur remains on the ring, but in a higher oxidation state, or is replaced by oxygen.



Scheme 4. Action of oxidizing agents on Δ^3-imidazoline-5-thione.

Electrophilic substitution is possible either on the N of the thionamide form or on the S of the thiolimine form, depending on the reaction medium and the attacking agent [64, 72].

Benzoylation yields an N^1-benzoyl derivative of the thionamide form (together with a little *S*-benzoyl compound); acetylation with acetic anhydride follows a similar course (yield 70 %). Substitution with electrophilic reagents in aqueous alkaline media leads to thiolimine derivatives. Methylation with dimethyl sulfate gives the 4-methylmercapto compound in a yield of 83 %. Benzoylation in the presence of pyridine leads to the *S*-benzoyl compound. The corresponding thiolimine derivatives are also formed on benzylation and on reaction with chloroacetic acid or with α-bromoacetophenone.

The 4-mercapto group of the thiolimine form can be smoothly replaced by nucleophilic substitution [72].

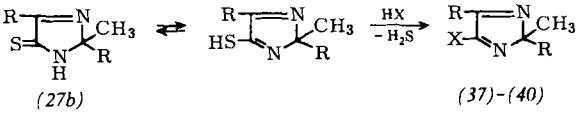
Reaction with PbO in methanol in the presence of ammonia leads to the 4-methoxy-2*H*-imidazole *(37a)* [64]. Sulfuryl chloride reacts to give a 4-chloro-2*H*-imidazole *(38a)* [72]; this is a novel cyclic imide chloride, which can enter into many reactions. The reaction with ammonia [73] (at 80 °C in ethylene glycol) or with primary or secondary amines [74] provides a simple route to 4-amino- or 4-alkylamino-2*H*-imidazoles *(39)–(40)*.

Derivatives of the thiolimine form are listed in Table 9.

The 4-amino- and alkylamino-2*H*-imidazoles *(39)* to *(40)* are nearly all colorless, highly crystalline substances. They can be converted back into the Δ^3-imidazoline-5-thiones by the introduction of hydrogen sulfide.

The reaction of the Δ^3-imidazoline-5-thiones *(27)*, as well as of the bis(2*H*-imidazol-4-yl) disulfides *(36)* (cf. Scheme 4) with sulfuryl chloride in the presence of MgO (or better, CaO) leads to good yields of 4-chloro-2*H*-imidazoles *(38a)*. The reaction of the 4-chloro-2*H*-imidazoles *(38a)* with aromatic amines

Table 9. Derivatives *(37)* to *(40)* of the tautomeric thiolimine form of the Δ^3-imidazoline-5-thiones *(27b)*.



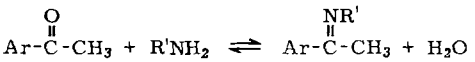
(27b) *(37)-(40)*

	R	X	Yield (%)	B.p. (°C/mm m.p. (°C)
(37a)	C_6H_5	CH_3O	55	34
(38a)	C_6H_5	Cl	85	132–133/0.1
(39a)	C_6H_5	NH_2	88	147–148
(39b)	*p*-F–C_6H_4	NH_2	93	173–174
(39c)	*p*-Cl–C_6H_4	NH_2	82	190–191
(39d)	*p*-CH_3O–C_6H_4	NH_2	63	163–165
(39e)	β-Naphthyl	NH_2	47	173–174
(40a)	C_6H_5	$NHCH_3$	78	105–106
(40b)	C_6H_5	NH-n-C_4H_9	90	48–49
(40c)	C_6H_5	NH-Cyclohexyl	83	121–122
(40d)	*p*-CH_3–C_6H_4	NH-n-C_3H_7	50	73
(40e)	*p*-CH_3–C_6H_4	Piperidino	58	101
(40f)	3,4-$(CH_3)_2$–C_6H_3	$NHCH_2$–CH=CH_2	92	87

yield 4-arylamino-2*H*-imidazoles that are not obtainable by direct reaction of the Δ^3-imidazoline-5-thiones [74]. Similarly, 5-selenoxo-Δ^3-imidazolines, which cannot be directly prepared by the action of selenium and ammonia on methyl ketones [59], can be synthesized by the reaction of *(38a)* with hydrogen selenide.

6. 8-Alkylamino-8-aryl-1,2,3,4,5,6-hexathiocane-7-thiones (Action of Sulfur and Primary Amines on Methyl Aryl Ketones)

Acetophenone and ring-substituted acetophenones react even at room temperature with primary aliphatic amines to form *N*-alkylketimines *(41)* of the acetophenones [66, 75, 76].



(41)

Quantitative IR measurements [66, 76] have shown that this reaction is strongly dependent on the polarity of the solvent, the substituents on the phenyl nucleus, and the catalyst. The acetophenone imines can be readily synthesized from acetophenone and primary amines with acid catalysis (glacial acetic acid).

Apart from the catalytic effect of acids (glacial acetic acid, *p*-toluenesulfonic acid, *etc.*), dehydrating agents (K_2CO_3), and polar solvents (CH_3OH), the favorable influence of catalytic quantities of elementary sulfur on the ketimine formation is particularly interesting.

Acetophenone reacts with n-butylamine at room temperature in the presence of elementary sulfur (0.25 g-atom per mole of ketone) to give a 44 % yield of the *N*-(n-butyl)ketimine of acetophenone. When the quantity of sulfur is increased to 0.5 g-atom per mole of

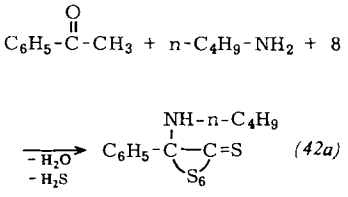
[73] *F. Asinger, W. Schäfer,* and *A. V. Grenacher,* Mh. Chem. *96,* 741 (1965).

[74] *F. Asinger, W. Schäfer,* and *G. Kriebel,* Mh. Chem. *97,* 1108 (1966).

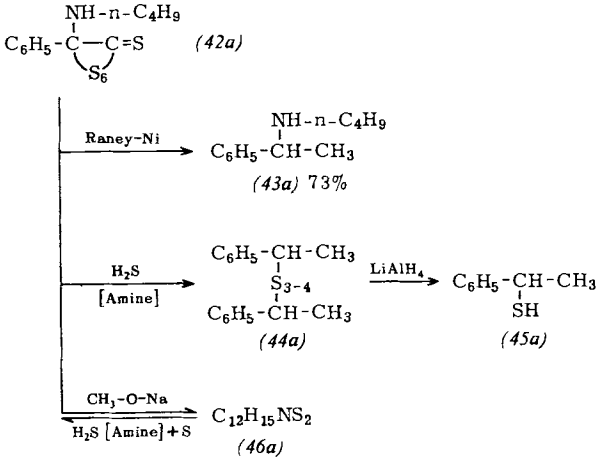
[75] *F. Asinger* and *K. Halcour,* Mh. Chem. *95,* 24 (1964).

[76] *F. Asinger* and *H. Offermanns,* unpublished.

ketone, the yield of ketimine falls to 26 %[75]. A further increase in the quantity of sulfur (molar ratio ketone : amine : sulfur = 1:2:8; CH_3OH as solvent) gives a yellow crystalline product $C_{12}H_{15}NS_7$ in 20 % yield[77]. If acetophenone imine is used instead of acetophenone (molar ratio imine : amine : sulfur = 1:2:8), the compound $C_{12}H_{15}NS_7$ is formed in 65 % yield[77]. The yellow crystalline compound formed from acetophenone, n-butylamine, and sulfur is 8-n-butylamino-8-phenyl-1,2,3,4,5,6-hexathiocane-7-thione *(42a)*[77]. No compounds of this class had previously been known.



The degradation reactions of *(42a)* are shown in Scheme 5.

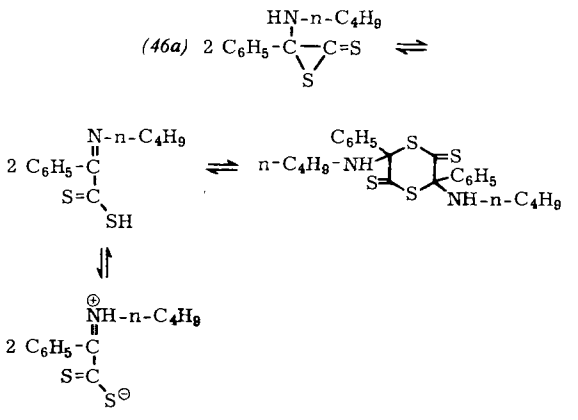


Scheme 5. Degradation reactions of the 8-alkylamino-8-phenyl-1,2,3,4,5,6-hexathiocane-7-thiones, illustrated by the case of the 8-n-butylamino product *(42a)* [77].

The hydrogenation of *(42a)* with Raney nickel, which is accompanied by removal of sulfur, yields *N*-n-butyl-(α-methylbenzyl)amine *(43a)*. The reduction of *(42a)* with hydrogen sulfide in the presence of amine leads to bis-(α-methylbenzyl)polysulfides *(44a)*, which can be reduced with $LiAlH_4$ to 1-phenylethylthiol *(45a)*.

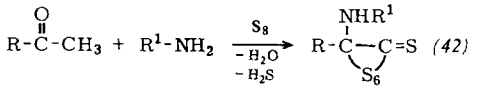
When sodium methoxide is allowed to act on *(42a)* at room temperature, 5 g-equivalents of sulfur separate out with formation of a new crystalline compound $C_{12}H_{15}NS_2$ *(46a)*, which can be converted back into *(42a)* by reaction with sulfur in the presence of amine.

The compound $C_{12}H_{15}NS_2$ is assigned the 3-n-butylamino-3-phenylthiirane-2-thione structure *(46a)*. The reactions of this thiirane can be readily explained if a number of tautomeric equilibria are taken into account.



The yields of hexathiocane (20 % with n-butylamine as the amine component) can be considerably improved if the molar ratio of ketone : amine : sulfur is changed from 1:2:8 to 1:7:10 and the reaction time reduced from 80 to 18 hours[76]. The hexathiocanes prepared under optimum conditions are listed in Table 10.

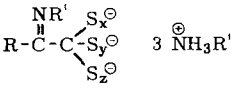
Table 10. 8-Alkylamino-8-aryl-1,2,3,4,5,6-hexathiocane-7-thiones *(42)* prepared by the reaction of aryl methyl ketones (0.1 mole) with primary amines (0.7 mole) and sulfur (1.0 g-atom) in methanol (50 ml) at room temperature; reaction time 18 hours [76,78] (selection).



R	R^1	M.p. (°C)	Yield (%)
C_6H_5	CH_3	145—146	73
C_6H_5	C_2H_5	139	82
C_6H_5	n-C_4H_9	109—110	80
C_6H_5	Cyclohexyl	145	63
4-Pyridyl	n-C_4H_9	139—139.5	65

The first step in the hexathiocane formation is the formation of the *N*-alkylketimine of the methyl aryl ketone. This results in a considerable increase in the acidity of the α C—H group[79].

In the presence of a large excess of primary amine (thiophilic reagent), the S_8 rings are cleaved into sulfane chains, which then add on to the carbanions formed by the basic action of the amine. The result is triple thiolation.



The sulfane chain, which has exactly the "right" chain length (x, y, or z = 6) after partial degradation, adds to the azomethine bond to form the hexathiocane ring. Further degradation of the remaining sulfane

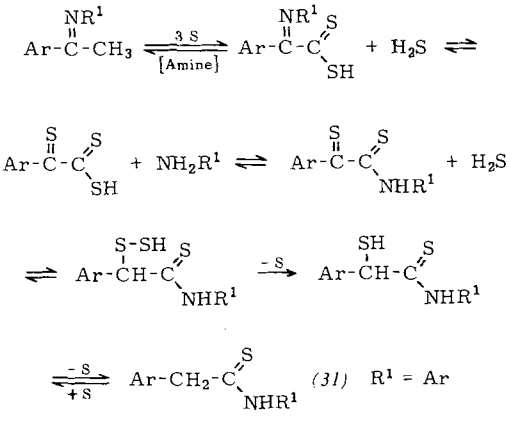
[77] *F. Asinger, H.-W. Becker, W. Schäfer,* and *A. Saus,* Mh. Chem. *97,* 301 (1966); cf. *F. Asinger, W. Schäfer,* and *H.-W. Becker,* Angew. Chem. *77,* 41 (1965); Angew. Chem. internat. Edit. *4,* 71 (1965).

[78] *F. Asinger, H. Offermanns,* and *F. Abo Dagga,* unpublished.

[79] *V. E. Haury, E. Cerrito,* and *S. A. Balard,* US-Pat. 2418173 (April 1, 1947); Chem. Abstr. *41,* 4510d (1947); *V. E. Haury* and *S. A. Balard,* French Pat. 951655 (Aug. 7, 1947); Chem. Zbl. *1950,* II 1876; *J. Mosjew, A. Inasinski, K. Kubiczek,* and *J. Zawrjkraj,* Roczn. Chem. *34,* 1169 (1960); Chem. Abstr. *55,* 15387 a-d (1961).

chains and reaction with $\overset{\oplus}{N}H_3R$ leads to the formation of the 8-alkylamino-8-aryl-1,2,3,4,5,6-hexathiocane-7-thione. No pentathiepane, tetrathiane, or trithiolane rings were found.

Reaction of ketimines of acetophenone, not with excess primary amine and a large quantity of sulfur in methanol at room temperature (hexathiocane yield >80 %), but with the stoichiometric quantity of sulfur in the presence of tertiary amine in DMF, preferably at 65 °C, the formation of hexathiocane is completely



Scheme 6.

suppressed, and the Willgerodt-Kindler product (*N*-monosubstituted arylacetic thionamide) *(31)* is formed in a yield of more than 80 %[76].

The formation of the Willgerodt-Kindler product from the ketimine is assumed to proceed as shown in Scheme 6[76].

The reactions of the ketimine, on the one hand to form the hexathiocanethione *(42)* and on the other to form the Willgerodt-Kindler product *(31)*, show that there is a close connection between the base-catalysed thiolation reaction (of preparative interest for the synthesis of new heterocycles) and the original Willgerodt and Willgerodt-Kindler reaction, though it is not yet possible to collect all the existing knowledge of the thermal and base-catalysed action of sulfur on organic systems in a common scheme.

Acknowledgment: F. A. wishes to thank Dr. H. Offermanns, Dr. W. Schäfer, and Dr. M. Thiel, who have made most valuable contributions to the development of this field of study, as well as a great number of co-workers, whose names appear in the references, for their enthusiastic cooperation.

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Translated by Express Translation Service. London

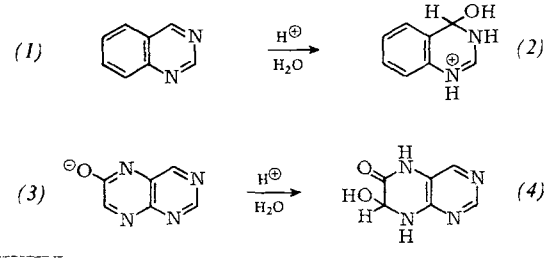
Hydration of C=N Bonds in Heteroaromatic Substances[**]

BY A. ALBERT[*]

Many aromatic N-heterocycles add water across the C=N double bond. Methods are described for recognizing this phenomenon and for diagnosis of the site of attack. These methods are extended to the determination of (a) the ionization constants of unstable states (whether hydrated or anhydrous), (b) the ratio of hydrated to anhydrous forms at equilibrium, and (c) the rate constants of hydration. The features that stabilize hydration in a molecule are discussed. The literature through 1965 and 1966 is reviewed with special reference to the emergence of new principles, such as di-hydration and the shifting of hydration within a molecule.

1. Introduction

In 1952, we became convinced that quinazoline, and some of the pteridines, had ultraviolet spectra and ionization constants that were absolutely incompatible with the orthodox formulation of these molecules. By 1955, we had eliminated the more obvious explanations, such as ring-opening, and decided that water was being added across the C=N bond of at least one ionic species in each case[1,2]. For example, quinazoline has a stable anhydrous neutral species *(1)*, but the cation is stable only as the hydrated form *(2)*. This means that as soon as the cation corresponding to *(1)* is formed (by the addition of dilute acid), it is rapidly hydrated to *(2)*. Again the anion of 6-hydroxypteridine *(3)*, when made neutral, quickly becomes hydrated to *(4)*.



[*] Prof. A. Albert
Department of Medical Chemistry, The John Curtin School of Medical Research, Australian National University
Canberra (Australia)

[**] Substance of a plenary lecture given at the First German Heterocyclic Symposium, Stuttgart, October 5th, 1966.

[1] *A. Albert*, J. chem. Soc. (London) *1955*, 2690; *A. Albert, D. J. Brown*, and *H. C. S. Wood, ibid. 1956*, 2066; *A. Albert*, Special Publ., chem. Soc. (London) *3*, 138 (1955).

[2] *D. J. Brown* and *S. F. Mason*, J. chem. Soc. (London) *1956*, 3443.

Before reviewing recent work on the hydration of heteroaromatic molecules, it is necessary first to summarize the principal methods which we have found to be most reliable for studying the phenomena of C=N hydration.

2. Diagnosis and Location of Covalent Hydration

It should be clear that obstinate retention of water in an analytical specimen is no evidence of covalent hydration. This is very often due to water of crystallization, held by lattice forces and not by covalent bonds. Covalent hydration is often unrecognized in elementary analysis because the hydrated ionic species is seldom subjected to analysis (this was the fate of quinazoline before 1961).

The four most useful indications of covalent hydration have proved to be: anomalous ionization constants (measured as pK_a values), anomalous ultraviolet spectra, anomalous infrared spectra, and anomalous nuclear magnetic resonance spectra. Of these, the first two are the most valuable, at least early in the investigation, because they can be used in a swamping excess of water, thus taking advantage of the mass action effect and also reproducing biological conditions.

The principal anomalies of ionization constants caused by covalent hydration are (a) bases are usually strengthened and (b) acids weakened; these results would be expected for the deletion of a double bond. The change is marked; the anomalous constant differs about one thousand-fold from the norm, which can be that of a *C*-methyl derivative, or else a calculated value[3]. Sometimes an anomalous value can be detected in a table of pK_a values; otherwise the anomaly is found when the pK_a is measured, using one of the simple procedures in a manual[4]. If the hydration is slow, hysteresis should be seen during potentiometric titration.

In UV spectra, the usual anomaly caused by covalent hydration is a large shift of the absorption to shorter wavelengths, which is consonant with the deletion of a double bond. (Normally the long-wavelength peak in the spectrum of a substance does not shift more than 10 nm when an ion is formed from the neutral species.) Further, according to the R. Norman Jones rule[5] the UV spectrum of the anion of a hydroxy derivative should be identical with that of the neutral species of the corresponding primary amine. If hydration is suspected in the neutral species, the spectra obtained in water and hexane should be compared: the latter often shows less or none of the anomaly depending on how strongly the water is held. If hydration is suspected in the cation, the spectrum in dilute mineral acid should be compared with that in a more concentrated acid where the thermodynamic activity of the water is much less[6,7].

The IR spectra should show lack of the vibrations ascribable to $-NH_2$ and $-CHO$, which would arise from ring-opening (the $-CHO$ group can also be sought with *p*-nitrophenylhydrazine which is effective at a pH as high as 3.8).

Suitable NMR spectra cannot usually be obtained for the neutral species, which are seldom soluble enough in water; and other solvents have not the same likelihood of permitting full hydration. NMR spectra of anions and cations should show an aliphatic-type peak upfield, at about $\tau = 4$, if hydration has occurred.

The most reliable method for locating the site of hydration is to examine the homologue which has a methyl group attached to that carbon atom which is thought to carry the hydroxyl group. If the location is correct, all the anomalies mentioned above will disappear. Thus in Fig. 1, it is seen that the UV

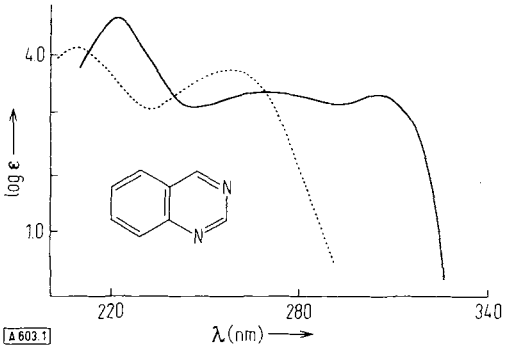


Fig. 1. UV spectra of quinazoline in water, ——: neutral species; ·····: cation.

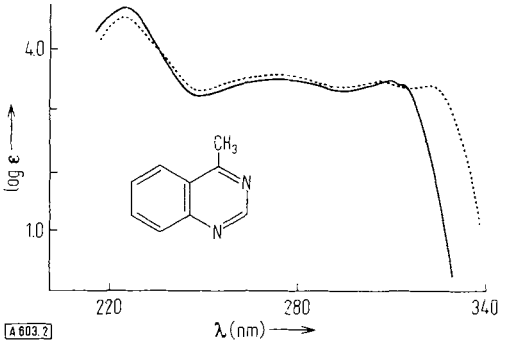


Fig. 2. UV spectra of 4-methylquinazoline in water, ——: neutral species, ·····: cation.

spectrum of quinazoline has moved, anomalously, to shorter wavelengths for the cation, whereas Fig. 2 shows that the spectrum of the cation of 4-methylquinazoline is normal. This indicates that quinazoline is hydrated in the 4-position, a conclusion which other tests confirm [7]. Another useful method is to oxidize the hydroxy group gently to a carbonyl group and to compare the product with substances of known constitution[2]. Hydrogen peroxide in 1 N sulfuric acid, potassium permanganate, and alkaline potassium ferricyanide have proved suitable if used at room temperature. NMR spectroscopy and comparison of the UV spectrum with UV spectra of known dihydro derivatives are further methods which can be used for locating the site of hydration.

3. Equilibrium Methods and Kinetic Methods

Figure 3 shows the equilibria involved in hydration processes. The relevant ionization equilibria are twofold: (a) between A and $AH^{\oplus}$ (the anhydrous

[3] *J. Clark* and *D. D. Perrin*, Quart. Rev. (chem. Soc., London) *18*, 295 (1964); *G. B. Barlin* and *D. D. Perrin*, *ibid. 20*, 75 (1966).

[4] See, *e. g.*, *A. Albert* and *E. P. Serjeant*: Ionization Constants of Acids and Bases, A Laboratory Manual. Methuen and Co. Ltd., London 1962.

[5] *R. Norman Jones*, J. Amer. chem. Soc. *67*, 2127 (1945); *A. Albert*, Quart. Rev. (chem. Soc., London) *6*, 197 (1952).

[6] Sulfuric acid (50% w/w) has been successfully used for this purpose [7]; a useful alternative, free from any danger of forming a dication is anhydrous dichloroacetic acid with a Hammett acidity function (H_0) of -0.9 [7].

[7] *A. Albert*, *W. L. F. Armarego*, and *E. Spinner*, J. chem. Soc. (London) *1961*, 2689,5267.

neutral species and the anhydrous cation) and (b) between B and $BH^{\oplus}$ (the corresponding hydrated pair). These equilibria are instantaneous (perhaps 10^{-6} seconds). There are also time-dependent equilibria between A and B, and between $AH^{\oplus}$ and $BH^{\oplus}$ with half-times of 0.01 to 4000 seconds. It is usually found that A and $BH^{\oplus}$ are stable species, whilst B and $AH^{\oplus}$

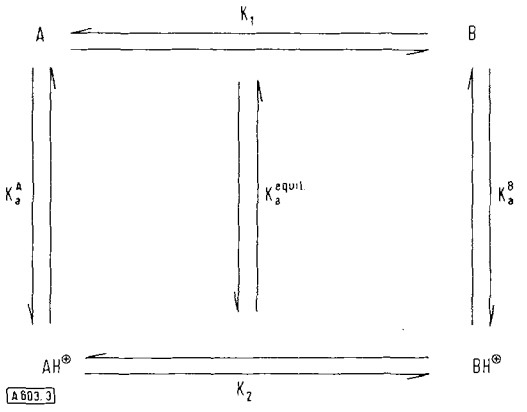


Fig. 3. The equilibria in covalent hydration: A, anhydrous form. B, hydrated form. $AH^{\oplus}$, cation of anhydrous form. $BH^{\oplus}$, cation of hydrated form.

are unstable (*i.e.* they rapidly lose and gain water, respectively). By the use of *Chance*'s rapid-reaction apparatus (Fig. 4) [8] it is possible to obtain UV spectra of the unstable species and to calculate the four equilibrium constants shown on the periphery of Fig. 3. If a conventional apparatus is used for determining pK_a values, the observations are spread over 20 minutes or more and a different ionization constant is obtained, namely $K_a^{equil.}$, which is a composite of

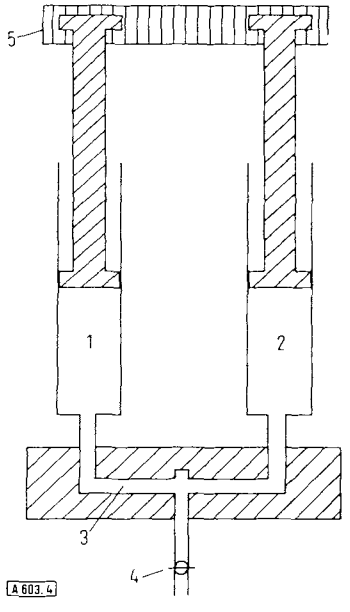


Fig. 4. Diagram of the *Britton Chance* [8,9] mixing apparatus for studying rapid reactions. 1,2: storage vessels; 3: mixing chamber; 4: tap; 5: handle for pressing down piston.

[8] *B. Chance*, J. Franklin Inst. *229*, 455, 613, 737 (1940); in *S. Friess* and *A. Weissberger*: Rates and Mechanisms of Reactions, Technique of Organic Chemistry. Interscience, New York (1953), Vol. 8, p 690.

[9] *D. D. Perrin*, Advances heterocyclic Chem. *4*, 43 (1965); *Y. Inoue* and *D. D. Perrin*, J. physic. Chem. *66*, 1689 (1962).

the values K_a^A, K_a^B, K_1, and K_2 Although $K_a^{equil.}$ is not a pure constant, it has a use as we shall see later. The mixing apparatus shown in Fig. 4 (for details of construction see ref. [9]) is suitable for reactions whose half-times are not less than one second.

The left-hand cylinder 1 of the mixing apparatus is filled with an equilibrated solution of one ionic species (say, the neutral species) and into cylinder 2 is put a buffered solution at a pH suitable for the liberation of a different ionic species (say, the cation). The outflow from the mixing apparatus is allowed to fall into an ultraviolet spectrophotometer cell 3, the bottom of which is fitted with a tap. To obtain the spectrum of the unstable species, it is only necessary to leave open the tap of the spectrophotometer cell, and let the automatic instrument record the spectrum while the pistons of the mixing apparatus are steadily pushed down (by means of the handle 5). To obtain the pK_a of the unstable species, a series of buffers are, in turn, placed in the cylinder 2, and the variation in optical density measured. The values obtained at different pH values are plotted as shown in Fig. 5a [10]. The pK_a value is obtained from this graph by drawing a vertical line through the point where there is the least increment in pH per unit change in density; the point where it intercepts the pH axis is the pK_a. More accurate values of pK_a are obtained by averaging individual values calculated directly from the data and corresponding to various sections of the curve. When the rate of change is too great to obtain reliable points for a plot such as that shown in Fig. 5, the required result can still be obtained, but not so quickly, by recording density changes with time for one buffer solution. The resulting straight-line plot of these values (see Fig. 5b), if back-extrapolated to zero time, gives one of the necessary density values from which to calculate the pK_a.

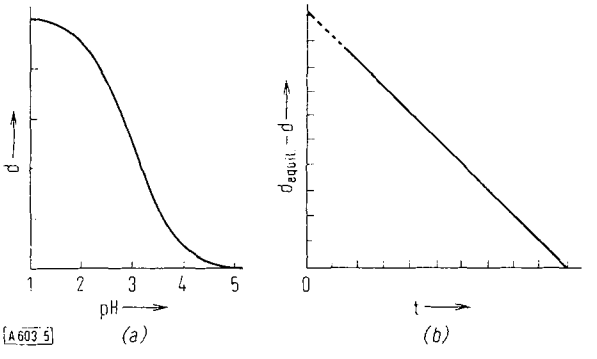


Fig. 5. (a) Plot of optical density against pH for a continuously flowing mixture (for determination of ionization constant of an unstable ionic species). (b) Plot of optical density against time for a stationary mixture.

The graphical representation shown in Fig. 5b has also been used to study the kinetics of these reactions [9,11], which were found to be first-order (at any constant pH), and catalysed by both acid and alkali. The half-times for the reactions are obtained from the equation:

$$t_{1/2} = 0.301/K_{obs} \qquad (1)$$

where K_{obs} is the observed velocity constant obtained by the use of logarithms to the base 10. Microscopic velocity constants (for the hydration and also for the

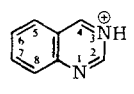
[10] These measurements are made at a single wavelength chosen from knowledge of the UV spectrum of the unstable species, *e.g.* 230 nm is suitable for the anhydrous cation of quinazoline, which necessarily has almost the same spectrum as that of 4-methylquinazoline (see Fig. 2).

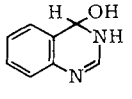
[11] *Y. Inoue* and *D. D. Perrin*, J. chem. Soc. (London) *1963*, 2648, 3936, 4803, 5166.

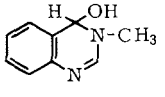
dehydration, exclusively) are then calculated, and plots of these constants against pH enable rate-pH profiles to be plotted. The hydration and dehydration rate curves for a single compound have different pH maxima, and intersect at low pH values [11].

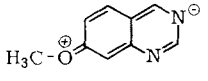
Because many ionization constants for anhydrous species are low, and hence have to be measured in a region where hydrogen-ion catalysis is very fast, an auxiliary apparatus was needed, one capable of handling $t_{1/2}$ values as low as 0.03 second. A quartz capillary tube served as the optical cell. A beam of monochromatic light was passed through cylindrical quartz lenses, placed both in front of and behind this cell, and made to fall on a photomultiplier tube. The output of the latter was applied, in a single sweep, to a cathode-ray oscilloscope. The tracings were then recorded by rapid-repeat photography. No more than 3 milliseconds elapsed between the time of mixing the reagents (mechanical drive was used on pistons) and the arrival of the mixture in the observation cell [12].

With the help of this new apparatus the pK_a of anhydrous quinazoline was measured [12], *i.e.* for the equilibrium *(1)* ⇌ *(5)*, and found to be 1.95, whereas that of hydrated quinazoline, *i.e.* for the equilibrium *(2)* ⇌ *(6)*, was 7.77. The latter value was suitably obtained with the original apparatus because the rate is not too fast between pH 4 and 10 [7]. These two pK_a values (1.95 and 7.77) are very different from the previously accepted pK_a of quinazoline, 3.51, which is only an equilibrium value. The value 1.95 for anhydrous quinazoline agrees well with a value calculated from the pK_a (2.52) of 4-methylquinazoline (known to be largely anhydrous) by substracting the usual 0.7 increment due to an α-methyl group. The value 7.77 for hydrated quinazoline is also reasonable because 4-hydroxy-3-methyl-3,4-dihydroquinazoline *(7)*, which does not lose methanol, has a pK_a value of 7.64. All these ionization constants were determined at 20 °C, in water [7].

(5) 


(6)

(7) 


(8)

In those cases where the cation is highly hydrated, such as quinazoline, it is easy to calculate the ratio of hydrated to anhydrous molecules in the neutral species, at equilibrium, by equation (2):

$$\frac{[B]}{[A]} = \frac{K_a^B}{K_a^{equil.} - K_a^B} \quad (2)$$

$$K_a^B = \frac{[H^{\oplus}] \cdot [B]}{[BH^{\oplus}]} \quad (3)$$

$$K_a^{equil.} = \frac{[H^{\oplus}]\,([A] + [B])}{[AH^{\oplus}] + [BH^{\oplus}]} \quad (4)$$

Equation (2) is derived directly from equations (3) and (4) after rejection of the term $[AH^{\oplus}]$ (rejected because no appreciable proportion of anhydrous cation is present). Some of the ratios obtained in this way for neutral species are given in Table 1. It can be seen that the degree of hydration is small but increases as the number of doubly bound nitrogen atoms increases. By constructing analogous equations, the ratio of anhydrous to hydrated cations can also be calculated [9].

Table 1. Ratio of hydrated (B) to anhydrous neutral species (A) in some azanaphthalenes (at equilibrium, in water at 20 °C).

Azanaphthalene	[B] : [A]
1,3-Di- (quinazoline)	1:10000
1.3,5-Tri-	1:200
1,3,7-Tri-	1:50
1,3,8-Tri-	1:500
1,3,5,8-Tetra- (pteridine)	1:4

A *C*-methyl group represses hydration only when it is attached to that carbon atom which is to be hydroxylated, an effect which is largely steric but partly electronic (see Section 7). However, a powerfully mesomeric (+M) group can exert a strong repressive effect from a distance. Thus a methoxy, amino-, or hydroxy group inserted in the 7-position of quinazoline, as in *(8)*, lowers hydration of the cation from 100 to 22 per cent [13].

4. Causes of Hydration

Until 1965, the only heteroaromatic substances known to hydrate covalently were polyazanaphthalenes, so that most of the original work on the causes of hydration was carried out using these substances. Table 1 shows that the hydration of neutral species increases as the number of ring-nitrogen atoms rises (cations are hydrated more strongly than neutral species but also observe this order). It seems that one feature necessary for hydration is the presence of an electron-withdrawing center, one so powerful that the π-electron layer (on the persistence of which normal aromatic stability depends) is depleted. As a result, a highly polarized double bond becomes isolated from Kekulé-type conjugation, and reactions typical of such a bond can take place. A doubly bonded nitrogen atom has the electron-withdrawing force of a nitro group. The presence of several doubly bonded nitrogen atoms in one nucleus can weaken its aromatic character, especially if they are placed 1,3 to one another so that their separate effects are completely additive. We have found that many nucleophilic reagents, such as methanol, malononitrile, and acetylacetone can easily be added to the 3,4 double bond of 2-hydroxypteridine [14] and 2-aminopteridine [15].

However, water is a weaker nucleophile than these substances and is not likely to be strongly bound unless some other force operates. Resonance has been found to supply the extra influence that makes the hydrated

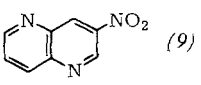
[12] *J. Bunting* and *D. D. Perrin*, J. chem. Soc. (London) *B 1966*, 433, 436.

[13] *W. L. F. Armarego*, J. chem. Soc. (London) *1962*, 561.

[14] *A. Albert* and *C. F Howell*, J. chem. Soc. (London) *1962*, 1591.

[15] *A. Albert* and *J. J. McCormack*, J. chem. Soc. (London) *C 1966*, 1117.

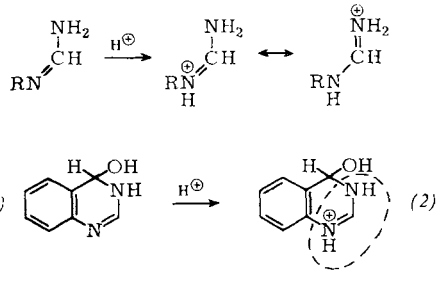
forms stable. Thus, water cannot be added to the 4-nitroisoquinoline cation whereas the quinazoline cation is fully hydrated. Again 3-nitro-1,5-naphthyridine *(9)* does not undergo hydration, but 1,3,5-



(9)

triazanaphthalene does so. No hydration could be detected in quinoline, isoquinoline, cinnoline, phthalazine, or quinoxaline.

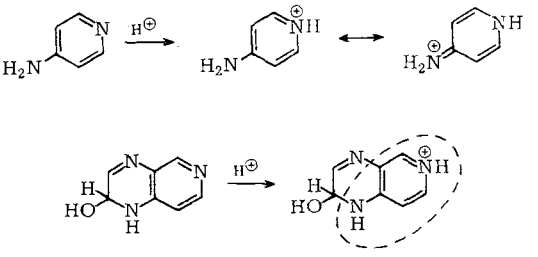
The stabilization of the cation of quinazoline in the hydrated state is ascribed to the amidinium-type resonance which is possible only in this state. This resonance, well-known in the aliphatic amidines, is much more strongly developed in the cations than in the neutral species because the latter have a separation of charge which is destabilizing [16]. The highly basic character of amidines is a result of this resonance. Scheme 1 shows how the amidinium resonance is present in the hydrated quinazoline cation and how it is responsible for stability in such a compound; this applies also to higher azalogues of quinazoline and many of their derivatives. The guanidine-type resonance found in 2-aminoquinazoline is an obvious extension of this.



Scheme 1. The amidinium cation as a model for the stabilization of the quinazoline cation *(2)*.

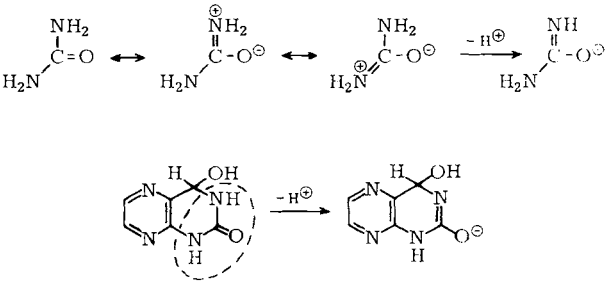
The 4-aminopyridinium-type resonance, one of the most interesting stabilizers of hydration, is a vinylogous amidinium resonance. The far greater resonance possible in the cation (as compared to the neutral species) of 4-aminopyridine makes the substance ten thousand times stronger a base than pyridine [17]. The stability of the 4-aminopyridinium resonance depends on the equality in energy of a *p*-quinonoidal conjugation and a benzenoid conjugation. The simplest hydrating azanaphthalene with this conjugation is 1,4,6-triazanaphthalene (see Scheme 2). 6-Hydroxypteridine also is stabilized as the hydrate because of this resonance. A 2-aminopyridinium resonance is also known, but it is weaker and, for the present purposes, of only borderline interest. The amidine anion type of resonance, which stabilizes the anion of pteridine, will be discussed later.

The urea-type resonance, yet another stabilizing influence, is significant mainly in the neutral species. It



Scheme 2. The 4-aminopyridinium cation as a model for the stabilization of various azanaphthalene cations as hydrates.

is almost ineffective in the anionic species because one of the two possible canonical forms would have to carry the negative charge on the nitrogen atom, and hence would not be equivalent to that carrying the charge on the much more electro-negative oxygen atom. In Scheme 3, the urea resonance is illustrated and an example is given of a substance, 2-hydroxypteridine, whose hydrate (it is hydrated in the neutral species only) owes its stability to this type of resonance.



Scheme 3. The urea molecule as a model for the stabilization of 2-hydroxypteridine (neutral species) as hydrate.

5. Recent Results from Other Systems

Attempts have been made to elicit hydration in the purine *(10)* series, both to extend the phenomenon beyond the azanaphthalene series and also to obtain substances with which the supposed activity of hydrated purines as enzyme substrates [18] could be tested. Since published tables of ionization constants and UV spectra of the known purines revealed no anomalies, it was decided to prepare purines with an electron-attracting substituent in the 8-position (both with and without a hydroxy group in the 2-position).

Although purines of this type would be among the most likely to show evidence of hydration, none was found to hydrate [19]. However, the cation of 8-azapurine *(11)* was strongly hydrated, as were the cations of its 2-amino, 2-hydroxy, and 2-mercapto derivatives. This hydration was detected by the use of ionization constants and UV spectroscopy. The hydrating hydroxyl group was found to enter the 6-position; this was evidenced by the facts that (a) 6-hydroxy-8-azapurine was produced on gentle oxidation and (b) a methyl

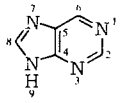
[16] *G. E. K. Branch* and *M. Calvin*: The Theory of Organic Chemistry. Prentice-Hall, New York 1944.

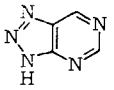
[17] *A. Albert*, *R. Goldacre*, and *J. Phillips*, J. chem. Soc. (London) *1948*, 2240.

[18] *F. Bergmann*, *H. Kwietny*, *G. Levin*, and *D. J. Brown*, J. Amer. chem. Soc. *82*, 598 (1960).

[19] *A. Albert*, J. chem. Soc. (London) *B 1966*, 438.

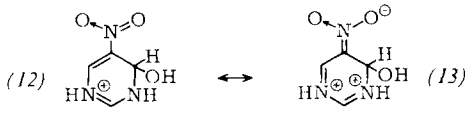
group in the 6-position (but not in 2-) restored normal pK_a and UV values [20]. An additional, and surprising, finding was that a methyl group in the 9-position prevented the cation from hydrating. This may be

(10) 

 (11)

ascribed to the antagonistic inductive effect of this group on the 8-nitrogen atom [21]. NMR spectroscopic studies of the azapurines also led to the same conclusions; equilibrium ratios and kinetics were also determined using the rapid-reaction apparatus [12].

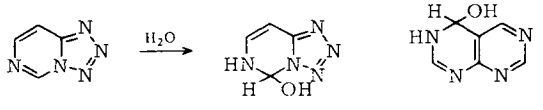
The first example of hydration in a single-ring heteroaromatic substance is the hydrated 5-nitropyrimidine cation [22]. In general, single-ring nuclei do not become hydrated because by doing so they would lose all benzenenoid resonance. However, the 5-nitropyridinium ion has access to the *p*-nitroaniline-type resonance *(12)* ↔ *(13)*. In spite of a general electronic



(12) (13)

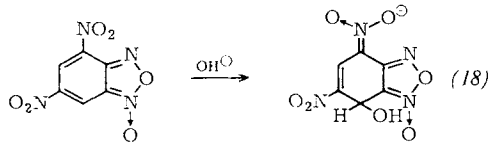
resemblance, this stabilization is not possible in 1,3,5-triazine which is immediately hydrolysed to formamide by cold water [23].

It has recently been found that the neutral species of tetrazolo[1,5-*c*]pyrimidine *(14)* absorbs atmospheric moisture to form 5-hydroxy-5,6-dihydrotetrazolo-[1,5-*c*]pyrimidine *(15)*, a reaction that is not easily reversible [24]. Hydration, *e.g.* to *(16)*, has also been detected in various derivatives of pyrimido[4,5-*d*]-pyrimidine [25].



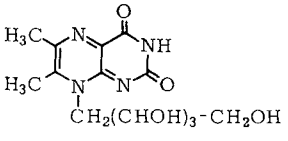
(14) (15) (16)

In spite of the frequency with which the pyrimidine ring occurs in hydrated compounds, its presence is not necessary for hydration as is shown by the ready hydration of 1,4,5- and 1,4,6-triazanaphthalenes [26] and of 3-nitro- and 8-nitro-1,6-naphthyridine [27] (cf. also 1,4,5,8-tetraazanaphthalene, below). It has now been shown that 4,6-dinitrobenzofuroxan *(17)*, usually considered to be a heteroaromatic compound, is converted into the hydrated anion *(18)* by alkali [28].

(17)  (18)

6. Recent Results for the 8-Substituted Pteridines

Ever since the time that *Masuda* [29] showed that 6,7-dimethyl-8-ribityllumazine *(19)* is an intermediate in the biosynthesis of the vitamin riboflavine, difficulties have been encountered in reconciling the UV spectrum of this important intermediate with the spectra of other 6,7,8-trialkyllumazines and the 3,6,7,8-tetra-alkyllumazines. Not only did the spectra of the neutral

 (19)

species of the models not agree with those of the intermediates but also they showed a surprising, variable hypsochromic shift when made alkaline [30]. When ionization constants were determined as a preliminary to confining the UV spectra to a single ionic species, it was found that these constants, too, differed widely among homologues [31]. These apparent contradictions were finally explained by studies of covalent hydration. First an account will be given of 8-alkylpteridines with only one polar substituent.

As early as 1956, *Brown* and *Mason* had indicated that 6,7,8-trimethyl-4-pteridone *(20)* (which is an acid of pK_a 9.5 and which shows hypsochromy in alkali) gives the anion *(21)* by 3,7-hydration followed by loss of a proton [2]. This work was recently followed up by *Jacobsen* who applied the complete range of diagnostic aids, including the rapid-reaction technique [32].

He studied 8-methylpteridines containing one oxo, thioxo, or imino substituent in the 2- or in the 4-position. In most cases it is impossible to obtain derivatives void of methyl groups in the 6- and 7-positions because such derivatives polymerize. The neutral species, *e.g.* 6,7,8-trimethyl-2-methylimino-2,8-dihydropteridine *(22)*, is analytically free from water

[20] *A. Albert*, J. chem. Soc. (London) *B 1966*, 427.

[21] This dehydrating effect does not occur with 7- or 8-methyl-8-azapurines, *A. Albert*, unpublished work.

[22] *D. J. Brown* and *T.-C. Lee*, personal communication (1966).

[23] *C. Grundmann* and *A. Kreutzberger*, J. Amer. chem. Soc. *76*, 5646 (1954).

[24] *C. Temple*, *R. McKee*, and *J. Montgomery*, J. org. Chemistry *30*, 829 (1965).

[25] *E. C. Taylor* in *W. Pfleiderer* and *E. C. Taylor*: Pteridine Chemistry. Pergamon Press, Oxford 1964, p. 126.

[26] *A. Albert* and *G. B. Barlin*, J. chem. Soc. (London) *1963*, 5156, 5737.

[27] *A. Albert* and *W. L. F. Armarego*, J. chem. Soc. (London) *1963*, 4237.

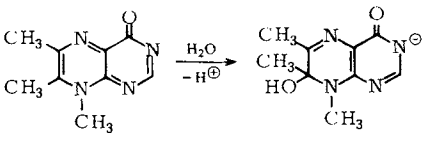
[28] *N. E. Brown* and *R. T. Keyes*, J. org. Chemistry *30*, 2452 (1965); *W. P. Norris* and *J. Osmundsen*, J. org. Chemistry *30*, 2407 (1965).

[29] *T. Masuda*, Chem. and pharmac. Bull. (Japan) *4*, 375 (1956).

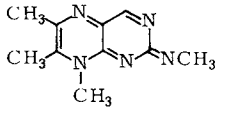
[30] *W. E. Fidler* and *H. C. S. Wood*, J. chem. Soc. (London) *1957*, 3980; *W. Pfleiderer* and *G. Nübel*, Chem. Ber. *93*, 1406 (1960); *C. H. Winestock* and *G. W. Plaut*, J. org. Chemistry *26*, 4456 (1961).

[31] *G. Nübel*, Dissertation, Technische Hochschule Stuttgart, 1960.

[32] *N. Jacobsen*, J. chem. Soc. (London) *C 1966*, 1065.

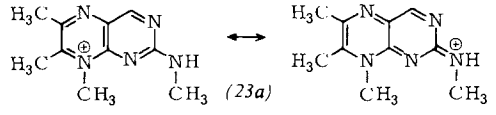


(20) (21)

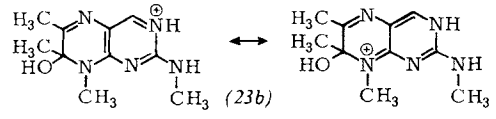


(22)

and gives the same UV spectrum in cyclohexane as in water, with a prominent peak at 350 nm. The anhydrous cation, formed by adding acid, has a similar spectrum in water (λ_{max} = 336 nm), which changes completely within 20 minutes. Peaks appear at lower wavelength, although not more than 75 per cent diminution in the height of the original peaks occurs at equilibrium. It was established that the cation *(23)* is hydrated to *(23b)* [*(23a)*:*(23b)* = 1:3]. The mixture of cations is shown in Scheme 4, together with the resonances that give almost equal stabilization to both. If this mixture of cations is made alkaline, the anhydrous neutral species is totally regenerated within 20 minutes. The UV spectrum of the anhydrous cation in a cyclohexane solution of dichloroacetic acid remains stable (at 336 nm) indefinitely. Ring opening was carefully excluded in this study.



(23a)

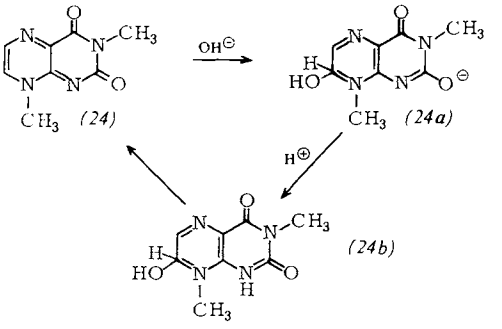


(23b)

Scheme 4. The two resonances that stabilize the 2-methylimino-6,7,8-trimethylpteridinium cation almost equally well in the anhydrous and hydrated states.

That the hydroxyl group has actually entered the 7-position, in spite of the steric hindrance offered by the methyl group, can be shown by oxidation with potassium permanganate in acetic acid at 20 °C. This reagent removes the methane, and affords 6,8-dimethyl-2-methylamino-7,8-dihydro-7-pteridone. The reaction was shown to be quite general for diagnosing the position of hydration in azanaphthalenes [32]; it is reminiscent of the oxidation of 1-methylcyclohexanol to cyclohexanone with potassium permanganate in water at room temperature [33].

W. Pfleiderer et al. of Stuttgart and our group in Canberra collaborated in a study of the hydrating properties of 28 examples of the 8-alkyllumazines [34]. The first series of investigations were carried out with lumazines in which the ionizable hydrogen atom on N-3 was replaced by a methyl group. It was found that 3,8-dimethyllumazine *(24)* (examined with or without further methyl groups in the 6- and 7-position) shows no anomalies of pK_a or UV spectra as the neutral species or cation. Alkali produces a mono-anion (p$K_a^{equil.}$ 10.4) which must necessarily come from a hydrated form. It has a lower UV maximum at shorter wavelengths, corresponding to the loss of a double bond (Scheme 5). A hydrated mono-anion of



Scheme 5. The anhydrous neutral species *(24)*, the hydrated neutral species *(24b)* and the hydrated anion *(24a)* of 3,8-dimethyllumazine. [*24*], λ_{max} = 394 nm; *(24a)*, λ_{max} = 306 nm; *(24b)*, λ_{max} = 308 nm].

this type had already, if not quite correctly (see below), been suggested for 8-methyllumazine [35]. Its relation to the anion (pK_a 11.2) which pteridine forms in alkali should be noted [1, 36]; this anion is stabilized by the resonance *(25)* ↔ *(26)*. In 3,8-dimethyllumazine, the electronegative oxygen accepts the negative charge more easily than does the nitrogen atom in the anion of pteridine.



When an alkaline solution of 3,8-dimethyllumazine is neutralized, an unstable form of the neutral species *(24b)* is produced; it has a UV maximum at 308 nm, an indication that it is the hydrated neutral species corresponding to the hydrated anion *(24a)*. On standing at room temperature, *(24b)* is soon converted into the anhydrous neutral species *(24)* (the starting material). Studies made with rapid reaction apparatus showed that, at equilibrium, there were 5360 molecules of the anhydrous neutral species to each one of the hydrated neutral species. That the anion was not dihydrated was confirmed by NMR spectroscopy.

Experiments were now directed to an investigation of 8-alkyllumazines, with a hydrogen atom on N-3. Here again the neutral species and cation presented no anomalies, but the spectra of solutions in alkali were wildly sensitive to small changes in the nature of alkyl groups in the 6-, 7-, or 8-positions. This variation was traced to the formation of equilibrium mixtures of two mono-anions (one of them hydrated) and a di-anion. According to its NMR and UV spectra, this di-anion corresponds to the mono-anion *(24a)*, but the pK_a (12.4) is higher (pK_a of *(24a)* = 6.7) because of the opera-

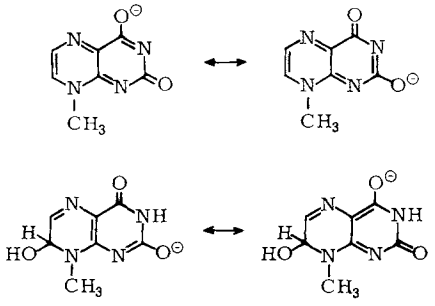
[33] *O. Philipow*, J. prakt. Chem. *93*, 162 (1916).

[34] *W. Pfleiderer, J. Bunting, D. D. Perrin*, and *G. Nübel*, Chem. Ber. *99*, 3503 (1966).

[35] *P. Hemmerich* in *W. Pfleiderer* and *E. C. Taylor*: Pteridine Chemistry. Pergamon Press, Oxford 1964, p. 143.

[36] *D. D. Perrin*, J. chem. Soc. (London) *1962*, 645.

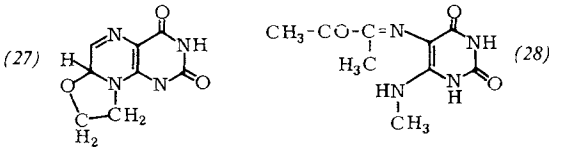
tion of Coulomb's Law. The two mono-anions of 8-methyllumazine exist in roughly equal proportions at equilibrium; each anion is stabilized by an effective resonance (see Scheme 6). The anhydrous anion (a reasonably strong acid of pK_a 10.1) can be obtained and its rate of hydration recorded by slightly basifying a solution of the neutral species in the rapid-reaction apparatus. The hydrated anions (pK_a values 6.4 and 12.4) are obtained in a similar manner by slightly lowering the pH of solutions of the di-anion [34].



Scheme 6. Resonance structures that stabilize the two mono-anions of 8-methyllumazine equally well in the anhydrous and hydrated states.

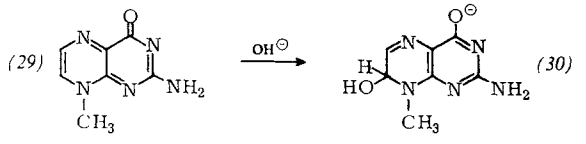
The proportion of hydrate in the neutral species of 8-methyllumazine was found to be 1 part in 5700. The presence of two methyl groups in the 6- and 7-positions decreases the hydration, whereas two isopropyl groups raises it to 1 in 86. These 6- and 7- isopropyl groups must interfere with each other's rotations, so that the normally flat pyrazine ring becomes distorted. This steric strain is relieved by hydration. Two phenyl-groups give rise to a similar, but slighter, effect [34]. Similar 6,7-steric effects have also been noted by *Jacobsen* [32]. Kinetic studies show that the neutral species of 6,7-diisopropyl-8-methyllumazine becomes hydrated about 20 000 times more slowly than the neutral species of 8-methyllumazine, although the former contains a higher proportion of hydrate when equilibrium is finally attained.

Lumazines with a β-hydroxyethyl group on N-8, of which the riboflavine precursor *(19)* is an example, were shown to be in equilibrium, not with a hydrate, but with a form in which the β-hydroxy group has attacked the 7-position, as in *(27)*. These substances give spectra similar to the hydrates, even though they are themselves anhydrous. The attack of the β-hydroxyethyl group on the 7-position is about 2000 times faster than the attack of water molecules on 8-methyl analogues. These β-hydroxyethyl compounds are much more stable to opening of the pyrazine ring on prolonged exposure to alkali than their analogues without the β-hydroxy group. The ring-opening products, *e.g. (28)*, are characterized as absorbing at 360 nm and can be identified by the dependence of ring-opening and -closing on the ionic strength of buffer solutions [34].



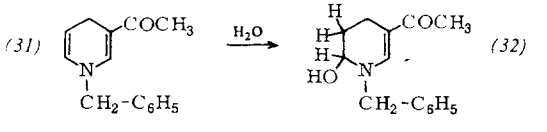
It can now be said that the problems posed by the riboflavine precursor *(19)* and the other 8-alkyllumazines have at last been solved.

The cations of the 8-alkyl-2-aminopteridin-4-ones, *e.g. (29)*, are stronger bases than the cations of the lumazines and, like them, are anhydrous. The neutral species are, in general, anhydrous; but a hydrated neutral species can be made by acidifying the anion *(30)*, which is necessarily hydrated, because the 2-aminopteridin-4-ones, unlike the lumazines, have no mobile hydrogen atom on the nitrogen. As with 8-alkyllumazines, the hydrated species show a UV peak at about 300 nm and the anhydrous species a peak at about 400 nm. The kinetics of hydration indicate first-order reactions, which are catalysed by both hydrogen ions and hydroxide ions. The kinetics of ring-opening and -closing of some 6,7-dimethyl derivatives (neutral species) have also been studied [37] and show salt catalysis.



7. Recent Results for Multiple Hydration and Shifting Hydration

In most of the examples discussed so far, only one molecule of water is added; but the hydration process need not stop there. Because monohydration gives the ring system an electron-releasing (–NH–) group, the drain on the π-electrons of the molecule is halted, and further hydration is not likely to occur in the remaining heteroaromatic ring. However, the ring that has already been hydrated now contains a highly polarized double bond which, while partly stabilized by conjugation with the heteroaromatic ring system, may be sufficiently activated to take up a second molecule of water. This is not surprising, for ethylenic (in contrast to aromatic) heterocycles readily form hydrates. For example, 3-acetyl-1-benzyl-1,4-dihydropyridine *(31)*, in dilute acid at 25 °C, adds water to give the crystalline 5,6-hydrate *(32)*, which can be isolated in 93 per cent yield [38].

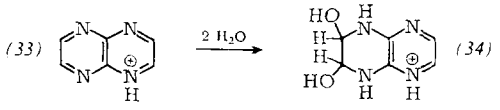


It has recently been found that the cation of 1,4,5,8-tetraazanaphthalene *(33)* can form a dihydrate *(34)* in this way. In anhydrous [D]-trifluoroacetic acid, the NMR-spectrum of the cation consists of only one peak – a sharp singlet at $\tau = 0.51$ (33 °C; 60 MHz), which can be ascribed to the four equivalent aromatic protons. A solution of the cation in 1 N DCl (in D_2O), on the other hand, shows two sharp singlets of equal intensity, one at $\tau = 2.48$ (aromatic protons) and one at $\tau = 4.63$ (aliphatic protons), *i.e.* a spectrum, which

[37] *W. Pfleiderer, J. Bunting, D. D. Perrin,* and *G. Nübel,* Chem. Ber. in press.

[38] *A. G. Anderson* and *G. Berkelhammer,* J. Amer. chem. Soc. *80,* 992 (1958).

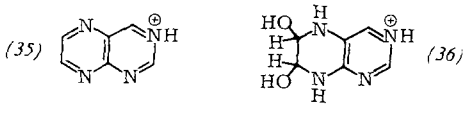
must arise from a symmetrical (time averaged) species. This dihydrate is stabilized by 2-aminopyridinium resonance. Gentle oxidation with acidic hydrogen peroxide gave 2,3-dihydroxy-1,4,5,8-tetraazanaphthalene [39].



The introduction of methyl groups hinders this hydration. Thus the cation of 2,3,6-trimethyl-1,4,5,8-tetraazanaphthalene [40] is not hydrated in aqueous solutions; in D_2O, H-7 shows a sharp NMR signal at $\tau = 0.78$. Similarly the cation of 1,4,6-triazanaphthalene was found to be dihydrated in the pyrazine ring, whereas that of 1,4,5-triazanaphthalene is almost anhydrous. These dihydrates are quickly converted by alkali into the anhydrous neutral species [39].

A few examples are known of a time-dependent intramolecular shift in the position of hydration of a substance. Thus the neutral species of 2,6-dihydroxypteridine initially takes up water in the 3,4-position, but after a lapse of about an hour, it is found to be hydrated exclusively in the 7,8-position. The 3,4-position has only a small affinity for water, but a low energy barrier, so that water is added there by a kinetic process. On the other hand, the 7,8-position has a high affinity for water but a high energy barrier, so that water is eventually transferred there by a thermodynamically controlled process [41]. It is noteworthy that both hydrates retain one heteroaromatic ring.

Recently it has been found that the cation *(35)* of pteridine transfers water in this way. The NMR spectrum of the neutral species of pteridine shows peaks for all four protons in the region $\tau = 0.2$ to 0.7. Acidifying a solution in D_2O with DCl to pH 2 quickly produces the 3,4-hydrate, in which the signal for H-4 has moved upfield to $\tau = 3.2$. Gentle oxidation at this stage gives 4-hydroxypteridine. If the acidic solution of *(35)* is allowed to stand at 33 °C, new peaks appear and the spectrum may be interpreted as being that of an equilibrium mixture of 3,4-monohydrate and 5,6,7,8-dihydrate *(36)* [42]. The UV spectrum of *(36)* is almost identical with that of the 5,6,7,8-tetrahydropteridine cation.



The near equivalence of the two resonances (4-aminopyridinium stabilization of 7,8-hydration, and amidinium stabilization of 3,4-hydration) in the pteridine cation prompted an investigation of the effect of substituents on this delicately balanced system. Only three other substances could be found in which 5,6,7,8-dihydration was preceded by 3,4-hydration, namely: 2-methyl-, 7-methyl-, and 2-amino-4-methylpteridine (note that 6,7-dimethyl-, 2-amino-, 2-amino-6-methyl-, and 2-amino-7-methyl-pteridine remain stably hydrated in the 3,4-position). Five cases of apparently direct 5,6,7,8-dihydration were also found: 4-methyl-, 2-methoxy-, 2-chloro-, 2-methylthio-, and 4-methylthio-pteridine. However, a detailed survey showed that the majority of pteridine cations are subject neither to dihydration nor to shifting hydration [42].

Two recent investigations have extended our understanding of 3,4-hydration of quinazoline and have more general significance. Although electron-attracting groups ($-NO_2$ or $-CF_3$) in the benzene ring of quinazoline assist hydration by their inductive (−I) effect [13], it has now been shown that this kind of substituent in the 2-position antagonizes hydration. This is to be expected because hydration requires a 3,4-double bond that is polarized as in *(37)*. When a −I substituent in the 2-position attracts an electron from N-3, the polarization conducive to hydration is diminished [43].

The effect of a 4-methyl group in preventing hydration of the quinazoline cation has usually been interpreted as being principally steric, acting in cooperation with a smaller inductive component. A kinetic study of 4-carbamoylquinazoline shows that this substituent exerts its steric effect by slowing the attainment of equilibrium (from less than a second to several hours). But since this molecule eventually becomes 3,4-hydrated, it is concluded that the inductive effect (−I) favors hydration. This suggests that the +I effect of the methyl group plays a more important part than had been thought in maintaining the cation of 4-methylquinazoline anhydrous at equilibrium [44]. The previous emphasis on the steric role of this methyl group was derived from the finding that 4-chloro- and 4-sulfo-quinazoline have anhydrous cations; but these could not be observed for more than a few minutes because of hydrolysis.



It has recently been shown that the mono-cation of 2-hydroxypteridine, when placed in strong alkali, forms the di-anion *(38)*; 6-hydroxypteridine also forms a di-anion. (The pK_a values and UV spectra of both have been recorded [45].) The anhydrous basic pK_a values of thirteen quinazolines and four triazanaphthalenes have been determined for the first time [12] by means of the fast-reaction oscilloscope apparatus. From the results, the anhydrous pK_a of pteridine was calculatedas −1.1. Such a negative value is, as yet, inaccessible experimentally because of the strong catalytic effect of the hydrogen ion at low pH values.

[39] *T. J. Batterham*, J. chem. Soc. (London) *C 1966*, 999.

[40] *W. L. F. Armarego*, J. chem. Soc. (London) *1963*, 4304.

[41] *A. Albert, Y. Inoue*, and *D. D. Perrin*, J. chem. Soc. (London) *1963*, 5151.

[42] *A. Albert, T. J. Batterham*, and *J. J. McCormack*, J. chem. Soc. (London) *B 1966*, 1105.

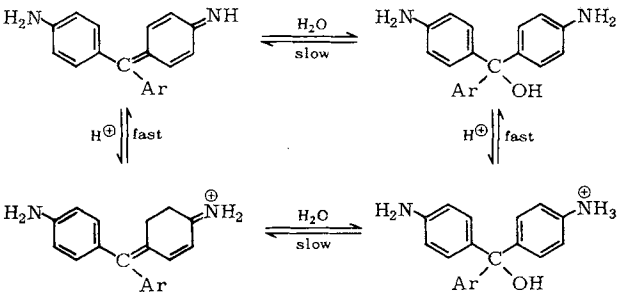
[43] *W. L. F. Armarego* and *J. I. C. Smith*, J. chem. Soc. (London) *C 1966*, 234.

[44] *W. L. F. Armarego* and *J. I. C. Smith*, J. chem. Soc. (London) *B 1967*, 449.

[45] *J. Bunting* and *D. D. Perrin*, Austral. J. Chem. *19*, 337 (1966).

8. Conclusion

The phenomenon of covalent hydration is not limited to heteroaromatic substances. That it is commonplace in heterocycles with olefinic double bonds was hinted in Section 7. The hydration of ethylene and the dehydration of ethanol involve such high energy barriers that they cannot be studied by the methods outlined in Sections 2 and 3. However these or similar methods have been employed for studying the hydration of aldehydes (to methylene glycols)[46], and the hydration equilibria of the aminotriphenylmethane dyes shown in Scheme 7[47]. These studies were carried out at room temperature and show interesting parallels with the results obtained for heteroaromatics.



Scheme 7. The hydration equilibria of amino triphenylmethane dyes.

The widespread occurrence of covalent hydration, which depends on a very small energy barrier, should encourage investigators in all fields of chemistry to look for this phenomenon in their own work.

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German version: Angew. Chem. 79, 913 (1967)

[46] *R. P. Bell* and *B. Darwent*, Trans. Faraday Soc. *46*, 34 (1950).

[47] *R. Cigén*, Acta chem. scand. *12*, 1456 (1958); *C. G. Ekström*, *ibid. 20*, 444 (1966).

The Concept of Hard and Soft Acids and Bases as Applied to Multi-Center Chemical Reactions[**]

BY B. SAVILLE [*]

Many chemical bonds of differing types and strengths have recently been regarded by Pearson[1] as representing partnerships between (Lewis) acids and (Lewis) bases. Most acceptor molecules or ions (acids) can be placed in one or other of two categories, graphically termed "Hard" and "Soft". There are also two broad categories of donor molecules or ions (bases) which can also be termed Hard and Soft. On the whole, strong chemical bonds are partnerships between either a Hard base and a Hard acid or a Soft base and Soft acid, whereas weaker bond types most usually result in cases of either Hard base-Soft acid or Soft base-Hard acid interactions. The present paper shows how this concept of acidity and basicity can be applied in the interpretation of multi-center chemical reactions involving interconnected acid-base relationships. In particular, four-center substitutions and additions involving cooperative attack by nucleophiles and electrophiles at various chemical bonds have been examined, and a conclusion is reached that especially reactive patterns of reactants can be developed if the substrates contain bonds between either a hard acid and a soft base, or a soft acid and a hard base. Indeed, the arguments can be elaborated to provide two distinct Rules which should be of interest in the interpretation of metal-ion assisted reactions and in the design of novel syntheses.

1. Introduction

In 1963 *Pearson* published a notable paper[1] on the concept of hard and soft acids and bases. In essence, the idea that *Pearson* succeeded in conveying so convincingly is that practically any type of chemical bond one cares to choose (be it either a strong σ or π bond of an organic molecule, a ligand-metal interaction, a bond between charge-transfer complex partners, or even a solvation bond) can be thought of as an acid bound to a base, this being true as long as one is prepared to adopt the view that there are two general classes of acids and two general classes of bases.

Pearson brought out powerfully the generalization that some bases, which can be termed hard, tend to form their strongest bonds with a fairly definite class of acids which he also called hard. On the other hand, hard bases interact rather weakly with a second class of acids which were termed soft. However, the latter

[*] Prof. B. Saville
Natural Rubber Producers' Research Association
Welwyn (England)
Present address:
Dept. of Chemistry, Oregon State University
Corvallis, Oregon 97331 (U.S.A.)

[**] Presented in part as lectures at Imperial College (London), Geneva (Cyanamid European Research Institute), and St. Andrews (Scotland).

[1] *R. G. Pearson*, J. Amer. chem. Soc. *85*, 3553 (1963); Science (Washington) *151*, 172 (1966).

form their strongest bonds with bases drawn from a second class, also labeled soft. The soft bases generally (but not always) fail to give strong bonds with hard acids.

acids		bases
hard	⇆	hard
soft	⇆	soft

How can one determine whether a molecule or an ion is hard or soft?

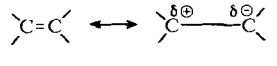
At an international symposium on this subject [2] it was generally agreed that hardness has to do with bonds which have high ionic character, whereas softness relates more directly to the current picture of covalent bonds. Thus, factors such as small atomic radius, high effective nuclear charge, low polarizability, and low ease of oxidation confer hard character. We find among hard acids the proton, cations of small size (Li^+, Be^{2+}), and cations or molecules in which substituents induce a high positive charge on the central atom (Mg^{2+}, Fe^{3+}, Co^{3+}, Th^{4+}, BF_3, $AlCl_3$, SiF_4).

These species give strong bonds with a restricted range of hard bases which are drawn from N, O, and F as donor atoms. It is interesting that carbanionoid systems ($R_3C^{\ominus}$ or $R_2C^{\delta\ominus}$), also containing a first row element, are not very hard as bases, especially in cases where the 2p electron density is low, as in an olefin. Indeed, saturated carbon as a base seems to be of hard-soft borderline character but falling, on the whole, into the wider group of soft bases.

Outstanding examples of soft bases are the hydride ion and ions derived from P(III), As(III), S(II), Se(II) (Cl(I)), Br(I), I(I), which form bonds of greater covalent character with soft acids.

Soft acids are usually characterized by low positive charge, large size, filled outer orbitals, and high polarizability and include derivatives of saturated C(IV), O(II) (surprisingly), S(II), P(III), Cl, Br, I (as cations or atoms) Hg(I), Hg(II), Ag(I), $B(Alk)_3$, Pt(II), Pt(IV), Pd(IV), as well as some electron-deficient π systems such as those in polynitroaromatics and tetrahalogenoquinones. A complete list and some explanation of these class divisions is provided in *Pearson*'s paper [1].

Although $R_3C^{\ominus}$ is not a very hard base it can still bond well with hard acid centers on account of its high charge density; nevertheless, a polarized olefin



is most decidedly a soft base [3]. A carbon radical is soft both as an acid and a base, whereas a carbonium ion must be regarded as a hard acid. Saturated carbon centers as acids (*e.g.* in nucleophilic substitutions) are definitely soft. Carbonyl and thiocarbonyl carbon centers which, as $>C^{\oplus}-O^{\ominus}$ and $>C^{\oplus}-S^{\ominus}$, resemble carbonium centers are hard like the proton [4,5], whereas aromatic carbon both as a donor and acceptor tends to be soft.

It will be seen that the above statements are in accord with the following well-known distinctions in simple organic reactions:

(i) It is much easier to make a soft acid such as Br^+ or Ag^+ react with an olefin than to convert the latter into a carbonium ion with a proton source (hard acid).

(ii) Carbon radicals add to soft oxygen π bonds or attack halogen compounds (soft acids) with great ease, or combine with themselves, but abstract hydrogen (hard acid) from activated methylene groups only slowly.

(iii) The t-butyl cation $(CH_3)_3C^{\oplus}$ in aqueous solution reacts preferentially with hard solvent molecules but not with added soft thio nucleophiles (bases), such as $S{=}C(NH_2)_2$ or $S_2O_3^{2\ominus}$.

(iv) The reagents generally used in attacking carbonyl groups, eliminating water, or displacing attached basic groups are $HO^{\ominus}$, $RO^{\ominus}$, $HOO^{\ominus}$, and a wide range of reagents containing amino groups; the latter are hard bases. Iodide ion and thiolate ions (soft bases) are less suitable reagents.

We shall now see how usefully the concept can be applied to aspects of chemical reactivity. We shall be concerned not only with equilibrium situations, but also with kinetic aspects – indeed, with hardness and softness seen in regard to the rate of interaction of acidic and basic centers. In the majority of situations it seems that the hard-soft disctinctions based on equilibrium properties may be applied to rate processes, but, as *Pearson* points out, acids and bases tend to exhibit soft character more in kinetic investigations than in equilibrium investigations [1]. This follows from the fact that bonds are longer in transition state configurations. Softness can in part be due to overlap between diffuse orbitals and thus can contribute to bonding at an earlier point along a reaction coordinate.

Notwithstanding such possible complications, the author is of the opinion that the concept may find major application when reactions are considered in which two or more pairs of atoms are at some stage involved in bond making and bond breaking processes, *i.e.* in the field of multi-center reactions. This article is devoted to developing a general picture of four-center reactions.

2. Four-Center Substitutions and Additions

Bimolecular nucleophilic substitution can be represented as follows:

$$Z{:} + A{-}X \rightarrow [Z{-}A]^{\oplus}\,[{:}X]^{\ominus} \qquad (1)$$

where Z: is a nucleophile which always carries an unshared pair of outer-shell electrons on the attacking atom; A is the electrophilic center, *i.e.* one which, after departure of the nucleophilic leaving group :X,

[2] For a summary of papers, see Chem. and Engng. News *43*, No. 22, p. 90 (1965).

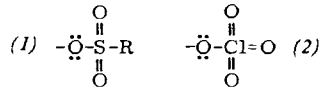
[3] *J. Chatt*, J. inorg. Nuclear Chem. *8*, 515 (1958).

[4] *J. O. Edwards* and *R. G. Pearson*, J. Amer. chem. Soc. *84*, 16 (1962).

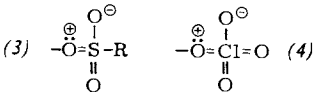
[5] *R. G. Pearson, D. N. Edgington*, and *F. Basolo*, J. Amer. chem. Soc. *84*, 3233 (1962).

can present a vacant orbital to the electron-pair of Z: for bonding purposes. Thus, as reaction proceeds, the center A changes its partnership with :X for a more satisfactory one with Z:.

Let us consider now the factors that influence the bimolecular substitution system. Clearly, the incipient development of a strong bond between Z: and A (particularly if this strength is maintained at the strained-bond lengths in transition states) will be of key importance in determining reaction rate, and may be of dominant importance if the new Z–A bond is nearly completely formed before the old A–X bond breaks. On the other hand, if in the transition state considerable stretching of the A–X bond has already occurred, the electron pair of the A–X σ bond begins to reside on X. The easier the pair can be accommodated on X the more rapidly will substitution proceed. Generally, the bonding pair of A–X is finally delocalized and stabilized if X is an electron-deficient π system spread over atoms of high effective positive charge. Thus *(1)* and *(2)* are two of the best leaving-groups because of the charge spreading contributions of the type *(3)* and *(4)*. By contrast, –ÖH and –ÖR



(1) *(2)*



(3) *(4)*

are much poorer leaving groups because the 2p electron pairs reside firmly on one oxygen atom.

The interaction of the developing species $[:X]^{\ominus}$ with the solvent can also be a stabilizing factor; however, the effect is complicated since it is often impossible to arrange for a solvent to bond well with $[:X]^{\ominus}$ and not with :Z. *Pearson*[1] has discussed *Parker*'s view[6] that solvation reduces basicity of small (hard) anions whilst having little effect on basicity of large (soft) anions. Selective assistance of substitutions is therefore possible on this basis.

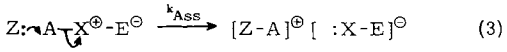
A greatly increased driving force for substitution (1) above can be provided by increasing the effective charge of the nucleophilic atom in the leaving group, a condition that can be achieved if :X carries at least two pairs of free p electrons. In this case, A–X (more correctly A–Ẍ) can coordinate with an added electrophilic acceptor molecule or ion E.

$$A\text{–}\ddot{X} + E \rightleftharpoons \underset{(5)}{A\text{–}\overset{\oplus}{X}\text{–}\overset{\ominus}{E}} \qquad (2)$$

A new reactive substrate *(5)* will develop in which X carries a higher effective nuclear charge than it does in A–Ẍ bond. The higher charge will now assist X in accepting and stabilizing the electron pair of the A–X bond in $A\text{–}X^{\oplus}\text{–}E^{\ominus}$ which we wish to break.

[6] *A. J. Parker*, Quart. Rev. (Chem. Soc., London) *14*, 163 (1962); *J. Miller* and *A. J. Parker*, J. Amer. chem. Soc. *83*, 117 (1961).

Adding the electrophile E thus causes a rate-enhancement of substitution (1). The rate constant k_{Ass} for the four-center electrophilic substitution (3),



(3)

should be greater than the second-order rate constant, k, of the normal substitution (1). Also, if reaction (1) were reversible, the final equilibrium position would be displaced well to the right in the presence of E. The species E would also serve to reduce the nucleophilicity of $[:X]^{\ominus}$.

This rather general statement is based on accepted orders of leaving group activity ($R_2O^{\oplus}$, $RHO^{\oplus}- \gg$ RÖ–, $R_3N^{\oplus}- \gg R_2\ddot{N}-$, $R_2{}^{\oplus}S- \gg R\ddot{S}$) given in textbooks dealing with reaction mechanisms[7].

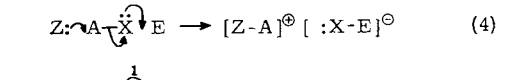
Although the above theme of electrophilic assistance of a bimolecular substitution has been developed having regard to a process in whose transition state considerable A–Ẍ bond stretching has occurred, it should be applicable also to the case where formation of a Z–A bond is well developed before the A–Ẍ bond begins to break. This follows from the idea that for Z–A bond formation to precede A–Ẍ bond breaking an initial vacant orbital must be available in A to receive the nucleophile Z:. However, if X carries an electron pair this will be involved in π bonding with the vacant orbital of A; thus the effect of adding E would be to uncouple the π bond, leaving the orbital on A vacant and ready to receive Z: more easily than before.

We therefore come to visualize a general form of four-center reaction (4) involving the cooperative action of a nucleophile (Z:) and an electrophile (E) on a substrate (A–Ẍ)[*].

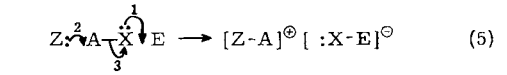
The arrows can be numbered to indicate the timing of the covalency changes. Equation (5) represents an electrophilically assisted nucleophilic substitution.

A nucleophilically assisted electrophilic substitution, in which the need for an unshared electron-pair on X is removed but in which a vacant orbital on A is mandatory, is depicted in eq. (6).

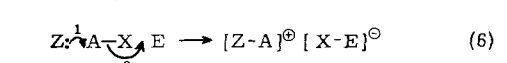
There will also be situations in which Z: and E are neighboring atoms or groups in the same molecule (eq. (7)).



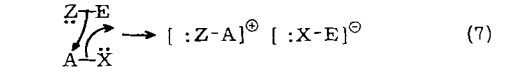
(4)



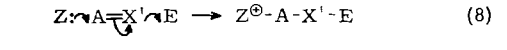
(5)



(6)



(7)



(8)

[7] *C.K.Ingold*: Structure and Mechanism in Organic Chemistry. Bell and Sons, London 1953, p. 338ff. *E. S. Gould*: Mechanism and Structure in Organic Chemistry. Holt, Rinehart and Winston, New York 1959, p. 261.

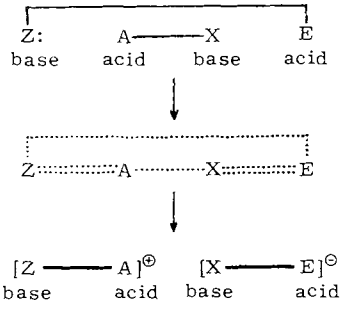
[*] *R. E. Dessy* [83] has approached the subject of multicenter substitutions from the standpoint of the conventional electrophilic substitution but has arrived at much the same picture.

These pictures of four-center substitutions in which A–X σ bonds become broken can be easily extended to the case of electrophilically assisted nucleophilic additions to π electron systems, in which π bonds are opened rather than σ bonds. Thus, if we consider A=X′ as substrate in place of A–Ẍ, then a four-center process can be written as eq. (8).

The rate of this process should again be greater than that of the corresponding process in the absence of the electrophile, E.

3. Two Rules Concerning Choice of Reactants

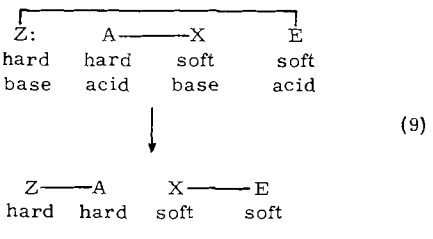
The above four-center reactions can be regarded as (i) formation of acid-base pairs and (ii) destruction of other pairs in the reactants (Scheme 1).



Scheme 1. —— denotes original acid-base pairs of reactants; ····· acid-base pairs being destroyed; ::::::: developing acid-base pairs; —— *final acid-base interactions of the products.*

How can the concept of hard and soft acids and bases be applied to the choice of reactants in four-center reactions? We believe that in order for reactions to proceed easily to afford thermodynamically well-stabilized products, the acid-base pairs[*] of the products Z–A and Ẍ–E must be bonded much more firmly than the acid-base pairs Z–E and A–Ẍ[**] present in the reactants. This condition will be best fulfilled when the substrate bond A–Ẍ possesses hard-soft dissymmetry, *i.e.* when A is hard and Ẍ is soft (1st case) or when A is soft and Ẍ is hard (2nd case).

For the first case, bearing in mind that it is important that Z–A, when developed, should be a strong bond it will be appropriate to make Z: a hard base. Also, as Ẍ is to bond strongly with E the latter should be a soft acid. A rational four-center reaction pattern can be written:



(9)

[*] From this point we omit overall charges in our representations of acid-base partnerships.

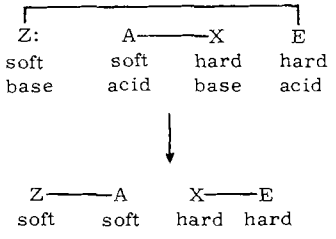
[**] Alternatively, here read the A = X′ π bond in the case of substrates undergoing nucleophilic addition.

It is only when the A–X bond possesses hard-soft dissymmetry that is it possible for the preferred Z: and E reagents to have a low mutual interaction energy, as required by the earlier deduction.

Equation (9) can now be formulated as the "first rule" for reagent choice in achieving particularly easy four-center substitutions. This is stated as follows:

If the electrophilic center A of a substrate A–Ẍ is a hard acid, then Ẍ should be a soft base. A–Ẍ will then react most easily with a nucleophile Z:, which is a hard base, together with an electrophile E, which is a soft acid.

In the second case of a substrate possessing hard-soft dissymmetry a second, complementary rule can be derived (eq. (10)).



(10)

Here, the weak Z——E and A——X bonds of the reactants are replaced by strong Z–A (soft-soft) and X–E (hard-hard) bonds in the products.

The above rules should apply equally well to the variants of four-center substitution (equations (4)–(7)) and also to four-center assisted nucleophilic additions eq. (8). (In the latter case, one has to decide whether the atoms terminating an opened π bond are hard or soft.)

If A–X is initially either a hard-hard or soft-soft partnership, Z: and E must be either both hard or both soft. In other words, Z: and E are no longer co-operative reagents, and one cannot expect easy forward reactions under such conditions.

It is now of interest to consider a selection of known four-center reactions to see if reagents used in these cases do indeed conform to the rules proposed above. To begin, we shall consider the first rule and note that here the electrophilic center is to be a hard acid. Examples of hard acid centers include those based on boron, carbon in R–CO- and R–CS–, phosphorus in R_2PO–, sulfur in R–SO_2– Al(III), Si(IV), Sn(IV), and of course $H^{\oplus}$.

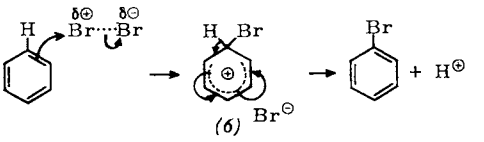
These provide a wide range of substrates when coupled to soft leaving-group centers Ẍ, such as RS–, R_2P–, halide, $H^{\ominus}$, and $R_3C^{\ominus}$.

4. Examples of the Operation of the First Rule

4.1. Cleavage of Aryl-Boron Bonds

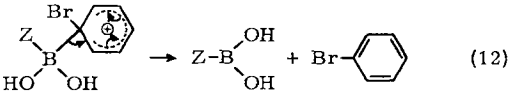
In the bromination of an aromatic compound it is generally assumed that the π electron system of the benzene ring attacks a bromine molecule (suitably activated in the sense $Br^{\delta\oplus}\cdots Br^{\delta\ominus}$) to provide an

intermediate *(6)* which then loses a proton in affording the observed substitution product:



(11)

It appears that a similar mechanism applies in the reaction of bromine with aryl-boron bonds. The ease of this process should be considerably enhanced if the vacant orbital on boron is first filled by the electrons of a suitable nucleophilic base (Z) to provide a four-center transition state, for example in the cleavage of benzeneboronic acid by means of bromine.



(12)

In acetic acid, the rate of this reaction is proportional to the product of concentration of substrate, bromine, and the added bases $OAc^{\ominus}$, or H_2O [8]. As the first rule predicts, the hard boron center responds to hard oxygenated bases, but not at all to soft $Br^{\ominus}$ species.

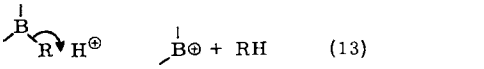
Clearly, also, the soft aromatic leaving group bonds well with the soft electrophilic $Br^{\oplus}$ center. Thus it seems that equation (12) furnishes excellent confirmation of the first rule:

Z:	A	X	E
oxygen	boron	benzene	bromine
base	center [*]	nucleus	(electrophilic acid)
hard	hard	soft	soft

If the first rule is to be useful, it must provide predictive information. It is therefore suggested that hypohalous acids, peracids, mercuric acetate, or bromine fluoride, *i.e.* reagents which all combine a soft electrophilic acid (E) [$Hal^{\delta\oplus}$, $HO^{\delta\oplus}$, $Hg^{\oplus}X$, $Br^{\delta\oplus}$] with a hard nucleophilic base [$HO^{\delta\ominus}$, $RCOO^{\delta\ominus}$, $F^{\ominus}$], would also be effective in cleaving aryl-boron bonds [**].

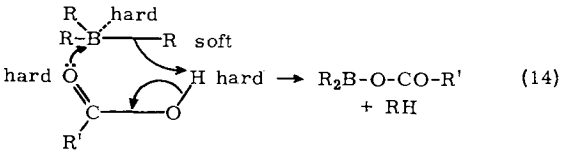
4.2. Cleavage of Boron Alkyls

The hydrolysis of trialkyl borons, even when catalysed by strong mineral acids, is remarkably slow [9,10]. This can be ascribed to the difficulty in producing the unusual "boronium" state (two vacant 2p orbitals on boron) demanded by the protolysis mechanism (eq. (13)).



(13)

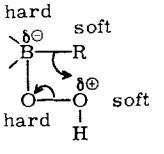
Even though the developing electron-deficiency at boron in such a process could be offset by prior coordination with a base, the bases available in solutions of strong mineral acids will be weak and relatively ineffectual. On the other hand, conventionally weak acids such as propionic acid, which supply a relatively potent hard carboxylate base, are far better reagents for the protolysis of boron alkyls [11–13]. The reaction can be visualized as a four-center substitution:



(14)

However, equation (14) does not conform with the requirements of the first rule; the hard proton has to be changed for a soft acid center *e.g.*, Hal^{+}, RS^{+}, or $HO^{\oplus}$ if rate enhancement is to occur. Indeed, perbenzoic acid (possessing the soft, electrophilic OH center) reacts with tri-n-butylborane at 0 °C in chloroform [1,17,57].

The use of alkaline hydrogen peroxide [14,15] as a general reagent for cleaving organoboranes is a similar example. The hard, electron-dense, oxygen base of hydroperoxide anion can coordinate with the vacant boron orbital to give an intermediate *(7)* (cf. [16]),



(7)

in which the soft alkyl group has enhanced nucleophilicity and, moreover, finds itself in close proximity to a soft electrophilic $OH^{\delta\oplus}$ center. Other reagents which could be suggested for the cleavages of boron alkyls, on the basis of the first rule, are hypochlorite ion and chloramine [*].

---

[8] *H. G. Kuivila* and *E. K. Easterbrook*, J. Amer. chem. Soc. *73*, 4629 (1951).

[*] Boron is a hard center in BF_3 (cf. $BF_4^{\ominus}$) but a soft one in BH_3 (cf. $BH_4^{\ominus}$) and BPh_3 (cf. $BPh_4^{\ominus}$). Hard ligands, such as $OH^{\ominus}$, confer hardness to boron.

[**] *A. D. Ainley* and *F. Challenger* (J. chem. Soc. (London) *1930*, 2171) have shown that hypoiodite ion, neutral hydrogen peroxide, and aqueous mercuric bromide are effective in cleaving aryl-boron bonds. Zinc and cadmium halides also serve as hydrolysis catalysts.

[9] *D. Ulmschneider* and *J. Goubeau*, Chem. Ber. *90*, 2733 (1957).

[10] *J. R. Johnson*, *H. R. Snyder*, and *M. G. Van Campen jr.*, J. Amer. chem. Soc. *60*, 115 (1938).

[11] *H. Meerwein*, *G. Hinz*, *H. Majert*, and *H. Sönke*, J. prakt. Chem. *147*, 226 (1936).

[12] *J. Coubeau*, *R. Epple*, *D. Ulmschneider*, and *H. Lehmann*, Angew. Chem. *67*, 710 (1955).

[13] *H. C. Brown* and *K. Murray*, J. Amer. chem. Soc. *81*, 4108 (1959).

[14] *H. C. Brown*: Hydroboration. Benjamin, New York 1962, p. 69.

[15] *H. C. Brown* and *B. C. Subba Rao*, J. Amer. chem. Soc. *78*, 5694 (1956).

[15a] *H. C. Brown*, *N. C. Herbert*, and *C. H. Snyder*, J. Amer. chem. Soc. *83*, 1001 (1961).

[16] *H. G. Kuivila*, J. Amer. chem. Soc. *76*, 870 (1954).

[17] *J. R. Johnson* and *M. G. Van Campen jr.*, J. Amer. chem. Soc. *60*, 121 (1938).

[*] Chloramine indeed cleaves trialkylboranes (*H. C. Brown*, *W. R. Heydkamp*, *E. Breuer*, and *W. S. Murphy*, J. Amer. chem. Soc. *86*, 3565 (1964) but in the opposite sense to the first rule, to afford alkylamines. *N*-chlorodialkylamines R_2NCl, however, give alkyl chlorides with trialkylboranes (*J. G. Sharefkin* and *H. D. Banks*, J. org. Chemistry *30*, 4313 (1965)). It is conceivable, in *Brown*'s reaction, that the alkyl attachments confer sufficient soft character on boron to attract soft $Cl^{\ominus}$. The $-NH_2$ group is left positively polarized and soft enough to attack the alkyl group.

$Cl-\!\!-\!\!-O^{\ominus}$ $Cl-\!\!-\!\!-\ddot{N}H_2$

soft hard soft hard

H. C. Brown[15a] has also described the reaction of silver, gold, and platinum oxides with triethylboron to furnish noble metal alkyls in accordance with the first rule.

In the intermediate *(7)* the leaving group R (alkyl) carries no lone pairs. On the other hand the center A (boron) has a vacant orbital. It thus seems that bond formation between boron and oxygen occurs first, and is followed by bond formation between R and OH; finally breakage of the R–B and O–O bonds takes place. The reactions are best thought of as nucleophilically assisted electrophilic substitutions.

4.3. Four-Center Systems in the Cleavage of Hydrogen Compounds

This field is less rich than might have been supposed because the conventionally weak acids (in which proton-transfer rates might be measurably slow) are often of the type $H^{\oplus}$ (hard acid) joined to a hard base, and are therefore not examples of an A–X substrate according to the first rule. Conversely, protons joined to soft-base centers (*e.g.* $Hal^{\ominus}$) give strong acids in the conventional sense in which proton transfer is too fast to study. However, we can consider thiols (eq. (15)), selenols, and phosphines as intermediate types.

$$\overset{\text{hard}}{\text{base}}\!\!\rightsquigarrow\!H\!\!\frown\!\!SR \longrightarrow [\text{base-H}]^{\oplus}\ SR^{\ominus} \qquad (15)$$

It would be of interest to know whether the forward dissociation rates of RSH, RSeH, and R_2PH can be enhanced by the presence of a suitable soft acid such as Ag(I), Hg(II), or I_2. The fact that equilibria are pushed well to the right in the presence of such agents forms the basis of analytical methods[18]. When the proton (A) is bonded to a very potent soft base (X) such as $H^{\ominus}$ and $R^{\ominus}$, proton transfer becomes slow and the system is suited to detailed kinetic studies. We ought then particularly to see the operation of the first rule in the nucleophilic cleavage of the hydrogen molecule, and in the cleavage of CH bonds in olefins and paraffins.

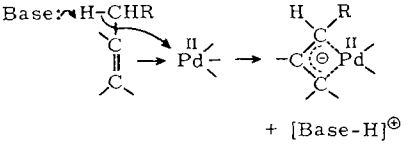
4.3.1. Cleavage of the Hydrogen Molecule

Halpern[19,20] has described an important form of homogeneous activation of molecular hydrogen (eq. (16)).

$$\text{Base:}\!\rightsquigarrow\!H\!\frown\!H\!\rightarrow\!M \longrightarrow [\text{Base-H}]^{\oplus}\,[\text{H-M}]^{\ominus} \qquad (16)$$

Here the preferred bases appear to be of the hard category (carboxylate ions, pyridine derivatives) and the entity M is a soft metal cation, notably Ag(I), Hg(I), or Hg(II), Cu(I), and Pt(II). A large range of reagent combinations were tested but only the above types were found to be effective. The pattern is seen to be completely consistent with the first rule. It is interesting to note that $F^{\ominus}$ (a very hard base according to *Pearson*) is particularly effective in promoting the silver ion-assisted heterolysis of the hydrogen molecule[21].

The author is unaware of an example that demonstrates the assisted ionisation of a paraffin in the sense $H\!\frown\!CR_3$. Recently, evidence has appeared that olefins form complexes with palladium-group metal centers according to eq. (17)[22].



(17)

The very soft palladium center can be thought of as assisting H–C ionization by supplying, within the initial π complex, a soft coordination position ready to acquire the electrons of the CH bond.

4.4. Cleavage of Bonds to Carbonyl Centers: Acyl Derivatives of Soft Bases

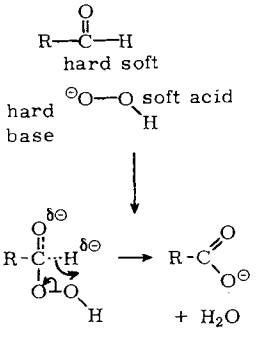
Pearson has firmly classified the carbonyl group as hard both on kinetic and equilibrium behavior[1]. In the well-known stable carbonyl[*] compounds (*e.g.* carboxylic acids, esters, and amides) the carbonyl center is bonded to hard basic groups (OH, OR, NHR, NR_2). Their reactions cannot be predicted in terms of the first rule. The acid fluorides RCOF may also be placed in this category.

However, in derivatives such as RCO–H, RCO–SH, RCO–SR, RCO–SeR, RCO–PR_2, and RCO–Hal (Cl, Br, I) the hard carbonyl center $R-CO^{\oplus}$ is bonded to the soft bases $H^{\ominus}$, $SH^{\ominus}$, *etc.*

Hence these acyl compounds should participate in four-center reactions and respond particularly to a combination of a hard nucleophilic base and a soft electrophilic acid.

4.4.1. Reactions of Aldehydes

In the Baeyer-Villiger oxidation[23] aldehydes are oxidized with alkaline hydrogen peroxide:



(18)

[18] *B. Saville*, Analyst *86*, 29 (1961).

[19] *J. Halpern*, Quart. Rev. (chem. Soc., London) *10*, 463 (1956).

[20] *J. Halpern*, Annu. Rev. physic. Chem. *16*, 103 (1965).

[21] *M.T. Beck*, *I. Gimesi*, and *J. Farkas*, Nature (London) *197*, 73 (1963).

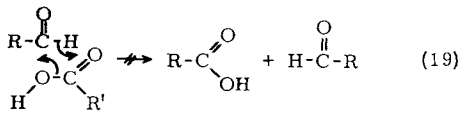
[22] *R. Hüttel*, *J. Kratzer*, and *M. Bechter*, Chem. Ber. *94*, 766 (1961); *G.W. Parshall* and *G. Wilkinson*, Inorg. Chem. *1*, 896 (1962).

[*] We here use carbonyl not in the sense of a derivative of carbon monoxide but rather to refer to the carbon center of R–CO–X.

[23] *C. H. Hassall*, Org. Reactions *9*, 73 (1957).

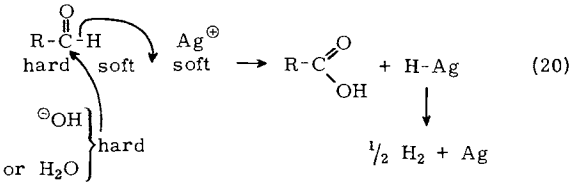
A hard oxyanion attacks carbonyl and the leaving soft hydride ion is removed by a sterically well-placed soft electrophilic O(II) center.

In distinction to this process, no report has been made of the conceptually similar reaction (19). Aldehyde-carboxylic exchange does not occur because the electrophilic R'CO center



(19)

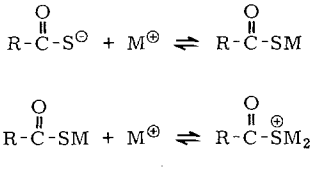
is hard and will therefore not bond easily with the potential hydride ion. Another example of the oxidation of aldehydes (conforming to the first rule) is the silver ion-assisted reaction in aqueous alkali [24–26].

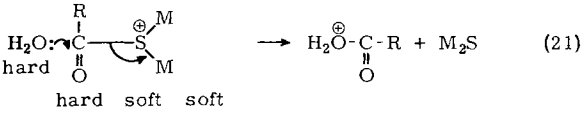


(20)

4.4.2. Thioacids and Thioesters

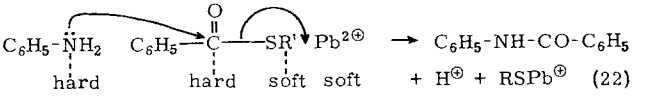
Thioacetic acid, and particularly thioacetamide, precipitate certain soft heavy-metal cations [27–30] as their sulfides. Since the hydrolysis of the carbonyl-sulfur bond is quite slow in the absence of heavy cations [31], and yet precipitation of the heavy metal sulfides can occur nearly instantaneously, it appears that the soft metal electrophile can actively assist hydrolysis (see eq. (21)), in accordance with predictions of the first rule.





(21)

It should be possible to add a hard base nucleophile to the above kind of reaction system in order to provide new acylation products at increased rates. In this regard it is known that thiolesters not only undergo hydrolysis assisted by the soft acids Ag^+, Hg^{2+}, and Pb^{2+}, but also undergo a faster, metal ion-assisted reaction with aniline or with amino groups of amino acids to afford amides in good yield [32, 33]:



(22)

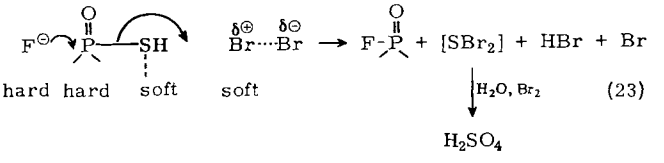
$R'SH$ = $HOCH_2-C(CH_3)_2-CHOH-CO-NH-(CH_2)_2-CO-NH-(CH_2)_2-SH$

(Pantetheine)

4.5. Phosphoryl and Sulfonyl Compounds

In reactions similar to that above, >P(O)–S bonds can be rapidly cleaved as follows:

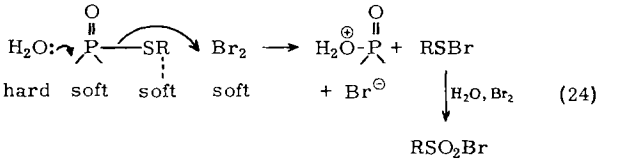
(a) A solution of fluoride ions in aqueous bromine [34] converts a phosphorothioic acid into a phosphorofluoridate instantly, whilst in the absence of fluoride



(23)

ions overall oxidative hydrolytic decomposition to a phosphoric acid and sulfate occurs with near equal ease (eq. (23)).

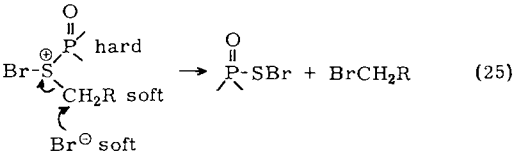
(b) Aqueous bromine or chlorine converts thiophosphate esters into acids and alkanesulfonyl halides [35,36]:



(24)

and mechanistically similar examples occur with thiolesters *etc.* [37].

In this reaction, the formation of alkyl bromides as well as sulfonyl bromides can be ascribed to high concentrations of bromide ions developing in preparative-scale reactions. The bromide ions (soft) prefer to attack the soft alkyl groups of the presumed *S*-bromosulfonium intermediate in preference to the hard phosphonyl center



(25)

[24] *I. A. Pearl*, US.-Pat. 2419158 (1947), Sulfite Products Corporation.

[25] *A. A. Goldberg* and *R. P. Linstead*, J. chem. Soc. (London) *1928*, 2343.

[26] *M. Délépine* and *P. Bonnet*, C. R. hebd. Séances Acad. Sci. *149*, 39 (1909).

[27] *A. R. Armstrong*, J. chem. Educat. *37*, 413 (1960).

[28] *L. M. Andreasov*, *E. I. Vall*, *V. A. Kremer*, and *V. A. Shelikovskli*, Z. analyt. Chim. *13*, 657 (1958).

[29] *G. C. Krijn*, *C. J. J. Rouws*, and *G. den Boef*, Analytica chim. Acta *23*, 186 (1960).

[30] *D. F. Bowersox*, *D. M. Smith*, and *E. H. Swift*, Talanta *2*, 142 (1959).

[31] *M. Cefola*, *S. Peter*, *P. S. Gentile*, and *A. V. Celiano*, Talanta *9*, 537 (1962).

[32] *R. Schwyzer* and *C. Hurlimann*, Helv. chim. Acta *37*, 155 (1954).

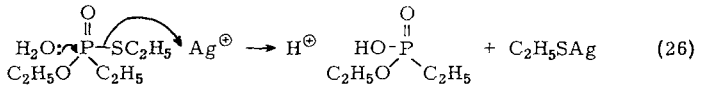
[33] *R. Schwyzer*, US.-Pat. 2786048 (1957), Ciba Pharmaceutical Products, Inc.

[34] *B. Saville*, unpublished.

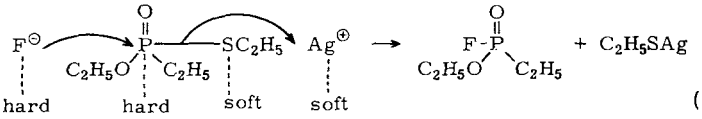
[35] *B. Saville*, Chem. and Ind. *1956*, 660.

[36] *C. J. M. Stirling*, J. chem. Soc. (London) *1957*, 3597.

[37] *I. B. Douglas* and *T. B. Johnson*, J. Amer. chem. Soc. *60*, 1486 (1938).



(26)



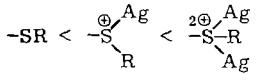
(27)

(c) A solution of fluoride and silver ions in water reacts with *O,S*-diethylethylthiophosphonate [38] rapidly giving the products of hydrolysis and substitution by fluoride ion (see equations (26) and (27)).

In the case of reactions (26) and (27), which proceed in accordance with the first rule, a detailed kinetic analysis [38] has revealed that the electrophile ($Ag^{\oplus}$)-modified substrate (that is susceptible to rapid attack by hard H_2O or $F^{\ominus}$ reagents) probably contains two silver ions per molecule (see also [39]).

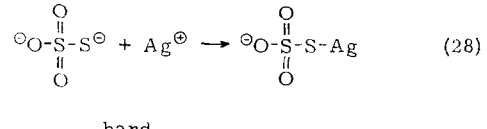
This contrasts with monoprotonation of oxygen or nitrogen derivatives in proton catalysed hydrolyses of esters or amides. The coordination of more than one silver ion to one atom of sulfur is most plausibly explained by the postulate that, in a silver-sulfur bond, metal to ligand electronic feed-back involving $d_{\pi}-d_{\pi}$ bonding has the effect of leaving the positivity of the sulfur atom only slightly enhanced. The sulfur is then able to use its remaining pair of 3p electrons to coordinate with yet another heavy-metal ion until high positive charge on sulfur precludes further coordination, and, moreover, produces a good leaving group (from the phosphonyl center).

Thus the leaving-group activities may be written:

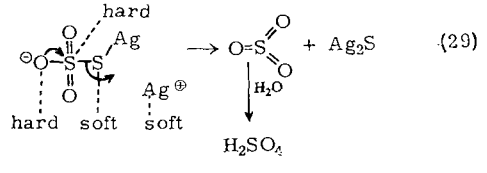


It may well be that this kind of multi-coordination is general for soft polarizable bases interacting with soft acids (being formally analogous to the multiplicity of oxidation numbers often characteristic of soft bases), so that many reactions in which assistance derives from soft leaving group/soft acid interaction will be of high kinetic order referred to the assisting acid. Recent work by *Schwarzenbach* and *Schellenberg* [40] on the binding of thio ligands to the methylmercuric cation is in accord with this picture, as is the recognition of species such as $Ag_3I^{2\oplus}$, $Ag_3S^{\oplus}$, 6 $AgNO_3 \cdot AgC \equiv CAg$ [41–43].

Similar activation of cleavage of bonds between sulfur(II) and sulfonyl sulfur – a hard acid center – has been observed in polythionate and thiosulfate chemistry [44]. Thus, in strong aqueous solutions of silver or mercury salts, thiosulfate ion breaks down readily according to eq. (28) and (29).



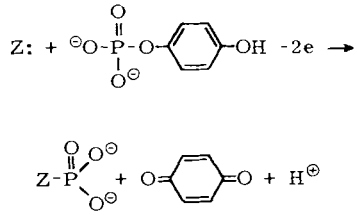
(28)



(29)

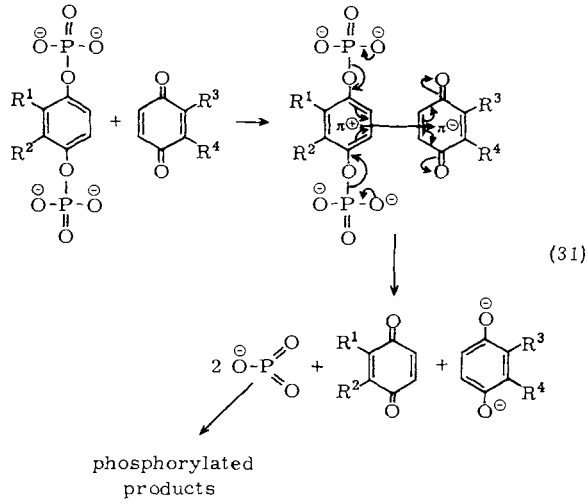
(d) Phosphorylations of biological importance are often geared to redox processes, and phosphorylated hydroquinone derivatives of the vitamin K, ubiquinone, and the vitamin E groups are known to be important intermediates [45–47].

Model studies [45] have shown the activation of *O*-phosphorylated quinols by oxidizing agents (air, Br_2, or Ce^{4+} ions) in the sense:



(30)

Hard nucleophiles (*e.g.* ADP, water, or inorganic phosphate) attack the hard phosphoryl center whilst the *p*-dihydroxyaryl system (a soft leaving group) is removed because of interaction with oxidizing agents, all of which can be regarded as soft electrophiles. It has been suggested [45] that certain *O,O'*-diphosphorylated quinols can become active phosphorylating agents in the presence of quinones. In this case the soft-soft interaction of partners in a charge-transfer complex, as envisaged by *Pearson* [1], becomes the driving force of assisted phosphorylation as depicted by eq. (31).



(31)

[38] *B. Saville*, J. chem. Soc. (London) *1961*, 4624.

[39] *B. Saville*, J. chem. Soc. (London) *1962*, 4062.

[40] *G. Schwarzenbach* and *M. Schellenberg*, Helv. chim. Acta *48*, 28 (1965).

[41] *B. Reuter* and *K. Hardel*, Angew. Chem. *72*, 138 (1960); Naturwissenschaften *48*, 161 (1961).

[42] *R. Vestin* and *E. Ralf*, Acta chem. scand. *3*, 101, 107 (1949).

[43] *I. Leden* and *C. Parck*, Acta chem. scand. *10*, 535 (1956).

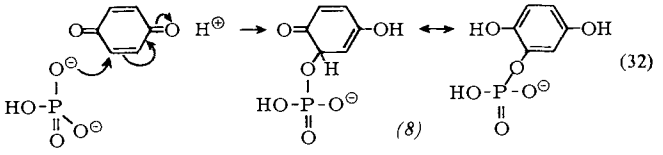
[44] *J. N. Friend*: Text-book of Inorganic Chemistry, Griffin, London 1931, Vol. 7, part 2, p. 199ff. and references quoted therein.

[45] *V. M. Clark*, *G. W. Kirby*, and *A. Todd*, Nature (London) *181*, 1131 (1958).

[46] *R. D. Dallam* and *J. F. Taylor*, Federat. Proc. *18*, 826 (1959).

[47] *V. C. Wessels*, Recueil Trav. chim. Pays-Bas *73*, 529 (1954).

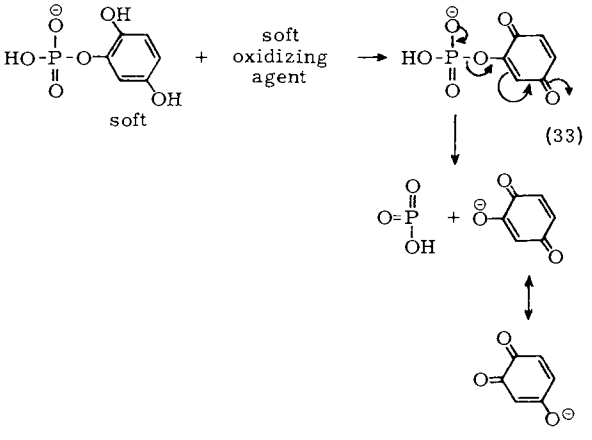
Hadler [48] has argued differently and suggests the intermediacy of enol phosphates in biological phosphorylations (eq. (32)).



(32)

(8)

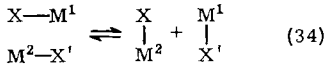
However, the oxidative activation of molecules such as *(8)* follows the same general pattern as that proposed in eq. (31).



(33)

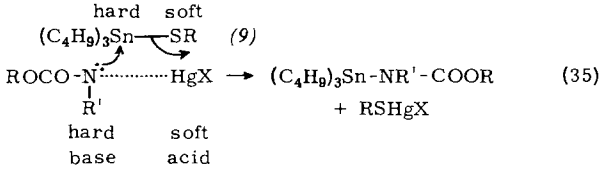
4.6. Other Examples of Substitutions Assisted According to the First Rule

The organometallic field contains numerous examples of exchange reactions of the type (34).



(34)

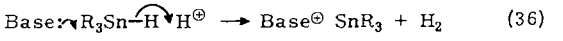
Clearly, the preferred equilibrium positions in these cases should be predictable from the first rule. Equation (35) represents a relevant reaction of organotin compounds [49].



(35)

(9)

Sn(IV) is usually regarded as a hard base [1]; however, we do not know the extent to which the three soft butyl groups confer softness on the tin center. Presumably, electron-attracting substituents on tin facilitate the above type of reaction. One can thus understand why *N*-halogenoamides also react with compounds such as *(9)* to furnish tin amides and sulfenyl halides. A further example of a multi-center reaction in organotin chemistry [51] is the decomposition of trialkyltin hydrides by acids in dimethylsulfoxide in the presence of basic substances [51] (eq. (36)).

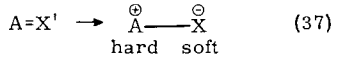


(36)

The activity of the assisting base is related roughly to its position in the spectrochemical series, which in turn is an approximate measure of hardness. According to the first rule, soft metal cations should be more effective than the proton as the electrophile in the above type of reaction.

4.7. Assisted Nucleophilic Additions

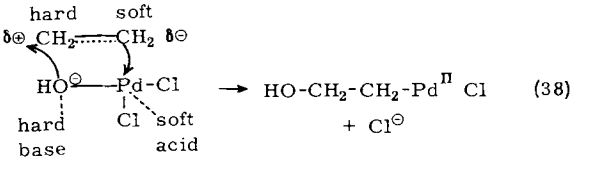
When, as in eq. (37), a π bond can be opened to provide a positively charged hard-acid center with a vacant orbital and simultaneously a negatively charged soft-base center, it is to be expected that such an



(37)

opening might best be brought about by the combined action of a hard nucleophile (Z:) and a soft electrophile (E).

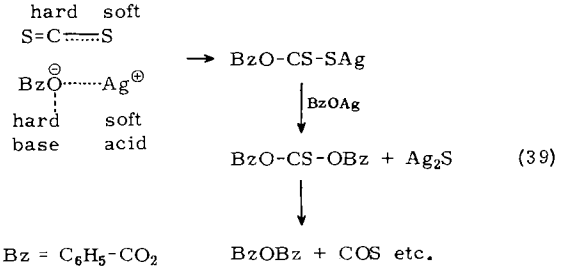
Olefins, $R^1R^2C{=}CR^3R^4$, where neither of the pairs R^1R^2 or R^3R^4 markedly stabilize the carbonium center, and thiocarbonyl compounds such as carbon disulfide, are therefore substrates to be considered in this regard. The reaction of alcoholic mercuric acetate solutions with olefins, and the oxidation of ethylene to a hydroxyethyl ligand under the action of $PdCl_2$ complexes [20,50], are good examples of such opening of olefinic π bonds.



(38)

The reaction of silver carboxylates with carbon disulphide gives acid anhydrides [52] (eq. (39)).

Finally, certain trialkylaluminums, trialkyl borons, and dialkylphosphines are spontaneously inflamma-



(39)

[48] *H. I. Hadler*, Experimentia *17*, 268 (1961).

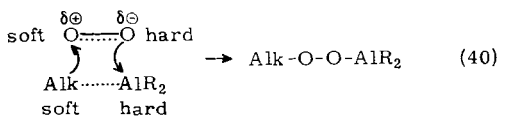
[49] *A. G. Davies* and *G. J. D. Peddle*, Chem. Commun. *5*, 96 (1965).

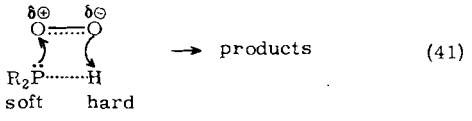
[50] *P. M. Henry*, J. Amer. chem. Soc. *86*, 3246 (1964).

[51] *R. E. Dessy*, *F. E. Paulik*, and *T. Hieber*, J. Amer. chem. Soc. *86*, 28 (1964).

[52] *D. Bryce-Smith*, Proc. chem. Soc. (London) *1957*, 20.

ble[53,54] (eq. (40) and (41)). Could this be a consequence of easy concerted acid-base activity?

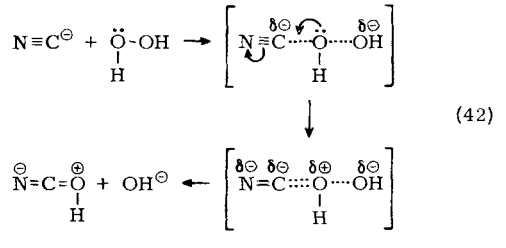




5. Examples of the Operation of the Second Rule

The saturated carbon center R_3C is a good example of a soft electrophilic center A of a substrate A–$\ddot{X}$ whose reactions should be interpretable in the light of the second rule. This center responds very directly to softness in the attacking nucleophile in the case of simple S_N2 displacements[4,55,56].

As other examples of a soft A center we have bivalent oxygen (as in peroxides and hypohalites)[4,57,58], sulfur[4,59,60], and probably trivalent nitrogen[61,62] in the rare cases of N attached to good leaving groups. The reason for the softness of these atoms as acids has not been made clear but may well concern the overlap of filled 2p or 3p orbitals on the oxygen or sulfur atom with empty p or d orbitals of the approaching soft nucleophile, a π-bonding effect which can strengthen the new bond both in the transition state and the final state (see, *e.g.*, eq. (42)).

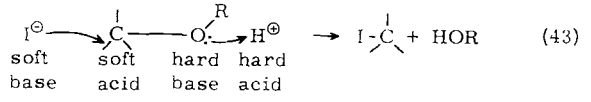


Softness in the case of saturated carbon is more difficult to rationalize; however, since most saturated carbon centers possess at least one C–H bond it is possible that in the transition state the σ electrons of this bond are somewhat delocalized across to the vacant orbital of the approaching soft nucleophile – in a manner similar to the current picture of hyperconjugation involving vacant carbon 2p orbitals.

Positive halogen compounds can also usefully be regarded as A–$\ddot{X}$ derivatives in which A is a soft-acid halogen atom.

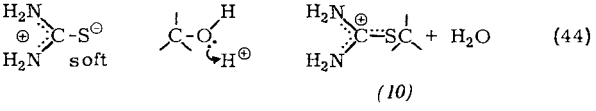
5.1. Cleavage of Carbon-Oxygen Bonds

The simple ethers are typical substrates involving soft saturated carbon and hard basic oxygen as leaving groups. The classical method, due to *Zeisel*[63,64], of cleaving ethers provides a good example of the operation of the second rule (see eq. (43)).



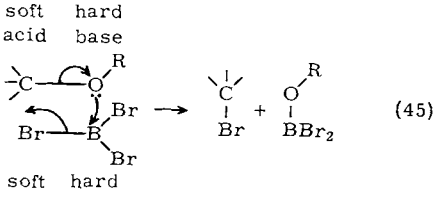
It is significant that if a weak hard nucleophile such as $HSO_4^{\ominus}$, is used in place of $I^{\ominus}$ or $Br^{\ominus}$ (soft) a much slower cleavage takes place[64]. Also, replacement of the hard ether oxygen atom by a soft sulfur atom (thus violating the conditions of the second rule) gives an almost unreactive system[65].

The reaction of halogen acids with n-alkanols to yield alkyl halides, and the reaction of thiourea with n-alkanols and mineral acids (eq. (44))[66] likewise obey the second rule.



(10)

A more recent reagent for the cleavage of ethers is boron tribromide[67,68], in which a hard boron center (E) is present in the same molecule as an incipient soft nucleophilic bromide ion (Z). With this reagent, cleavage (eq. (45)) may occur at temperatures as low as $-60\,^{\circ}C$. Violation of the second rule pattern by changing from BBr_3 to BF_3 (F is hard) leads to nonreactive addition compounds, at least one of which can be distilled unchanged[69]. The many examples given



[53] *G. E. Coates*: Organo-metallic Compounds. Methuen, London 1956, Chapter III.

[54] *G. M. Kosolapoff*: Organophosphorus Compounds. Chapman and Hall, London 1958, Chapter II.

[55] *C. G. Swain* and *C. B. Scott*, J. Amer. chem. Soc. *75*, 141 (1953).

[56] *J. O. Edwards*, J. Amer. chem. Soc. *76*, 1540 (1954); *78*, 1819 (1956).

[57] *J. O. Edwards*, paper given at Peroxide Reaction Mechanism Conference. Brown University, Providence, R.I. (USA), June 1960.

[58] *M. C. R. Symons*, Chem. and Ind. *48*, 1480 (1960).

[59] *A. J. Parker* and *N. Kharasch*, Chem. Reviews *59*, 583(1959).

[60] *P. D. Bartlett*, *A. K. Colter*, *R. E. Davis*, and *W. R. Roderick*, J. Amer. chem. Soc. *83*, 109 (1961).

[61] *H. H. Sisler*, *A. Sarkis*, *H. S. Ahuja*, *R. J. Grage*, and *N. L. Smith*, J. Amer. chem. Soc. *81*, 2982 (1959).

[62] *F. N. Collier jr.*, *H. H. Sisler*, *J. G. Calvert*, and *F. R. Hurley*, J. Amer. chem. Soc. *81*, 6177 (1959).

[63] *S. Zeisel*, Mh. Chem. *6*, 989 (1885).

[64] *R. L. Burwell jr.*, Chem. Reviews *54*, 615 (1954).

[65] *G. K. Hughes* and *E. O. P. Thompson*, J. Proc. Roy. Soc. New South Wales *83*, 269 (1950).

[66] *R. L. Frank* and *P. V. Smith*, J. Amer. chem. Soc. *68*, 2103 (1946).

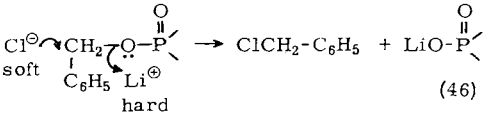
[67] *J. F. W. McOmie* and *M. L. Watts*, Chem. and Ind. *1963*, 1658.

[68] *F. L. Benton* and *T. E. Dillon*, J. Amer. chem. Soc. *64*, 1128 (1942).

[69] *H. C. Brown* and *R. M. Adams*, J. Amer. chem. Soc. *64*, 2557 (1942).

in *Gerrard*'s papers on the reaction of alcohols with boron halides involving carbon-oxygen bond cleavage would similarly fit into the second category of four-center assisted substitutions [70, 71].

Further examples of a saturated carbon center joined to a hard oxygen undergoing reactions according to the second rule appear in the chemistry of phosphate esters. Lord *Todd* and his co-workers [72, 73] noted that lithium chloride is a valuable reagent for the dealkylation of phosphate and pyrophosphate esters (eq. (46)).



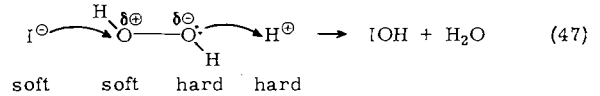
(46)

Since $Cl^{\ominus}$ is not an outstandingly potent soft nucleophile it seems possible that the lithium ion (which *Pearson* clearly classifies as hard [1]) may render electrophilic assistance.

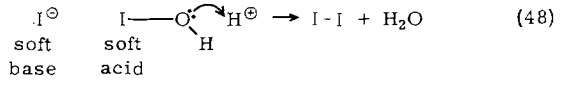
Lithium salts are frequently used in studies of salt effects in organic reactions. The question now occurs whether catalysis by salts, in appropriate cases, should be re-interpreted to include specific electrophilic assistance, in addition to ion-atmosphere effects.

5.2. Substitutions at Oxygen and Sulfur Atoms

Substitutions at O and S centers tend to require soft nucleophilic reagents (Z:) [57, 58] and hence we should again expect to find examples of assistance by hard acids when the leaving-group is hard, as required by the second rule. Such a case is exemplified by the acid-catalysed reaction of hydrogen peroxide with iodide ion [74, 75] (eq. (47) and (48)).



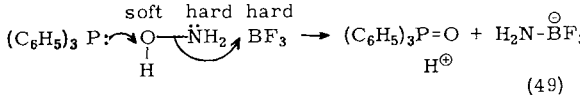
(47)



(48)

Indeed, practically every known proton-catalysed reaction of hydrogen peroxide involves attack by a soft nucleophile on oxygen (*e.g.* epoxidation of olefins, oxidation of sulfides to sulfoxides and sulfones). Iodide ion attack on hydrogen peroxide is also strongly catalysed by molybdic acid [76], and, although the mechanism is unknown, the reaction classifies this acid as hard.

Outside these examples, however, little use seems to have been made of behavior conforming to the second rule in connection with the cleavage of O–O or O–N bonds. It is here considered that soft nucleophiles such as RSR′, R_3P:, and R_3As: used in conjunction with BX_3, SnX_4, or AlX_3 could become interesting reagents; for example, equation (49) represents a proposed cleavage of hydroxylamine. (This reaction is

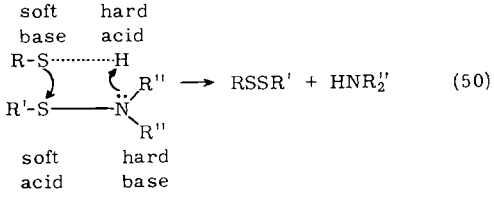


(49)

similar in principle to the reaction of sulfurous acid [$HO\ddot{S}O_2^{\ominus}$: soft, $H^{\oplus}$: hard] with hydroxylamine [77] [*].)

For substitutions at bivalent sulfur centers, the second rule demands that those centers be attached to hard leaving groups. Hence the sulfenic acids and esters (RS–OH, RS–OR′) and sulfenamides (RS–NR′R″) are suitable substrates. The sulfenic esters readily react with soft base/hard acid combinations (*e.g.* HX [X = Hal], HSR) as also do the sulfenamides [78, 79].

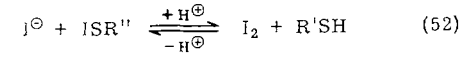
Thiols, as well as hydrogen sulfide, generally react with sulfenamides according to equation (50), and with halogen acids according to equations (51) and (52) [78].



(50)

Dialkylphosphites and sulfenamides also react by the same principle [80], as also do thiosulfuric acid and sulfenamides [80a].

(51)



(52)

The soft base and hard acid (Z: and E) requirements of the reagents for assistance under the second rule can sometimes be provided through the opening of a suitable π bond. For example, π bond opening of a C=S bond in carbon disulfide leads to the state

[70] *W. Gerrard* and *M. F. Lappert*, J. chem. Soc. (London) *1951*, 1020.

[71] *W. Gerrard* and *M. F. Lappert*, J. chem. Soc. (London) *1952*, 1486.

[72] *V. M. Clark* and *A. Todd*, J. chem. Soc. (London) *1950*, 2031.

[73] *J. Lecocq* and *A. Todd*, J. chem. Soc. (London) *1954*, 2381.

[74] *P. Rumpf*, C. R. hebd. Acad. Sci. *198*, 256 (1934).

[75] *H. A. Liebhafsky* and *A. Mohammad*, J. physic. Chem. *38*, 857 (1934).

[76] *A. I. Vogel*: Quantitative Inorganic Analysis. 3rd Edit., Longmans, London 1961, p. 363.

[77] *D. S. Brackman* and *W. C. E. Higginson*, J. chem. Soc. (London) *1953*, 3896.

[*] Actually, hydroxylamine tends to react in the form $NH_2^{\delta\oplus}$ (soft)···$OH^{\delta\ominus}$ (hard) in this case giving sulfamic acid as the main product. However, arsenite (soft nucleophile) combines with the $OH^{\delta\oplus}$ (soft) pole and displaces ammonia.

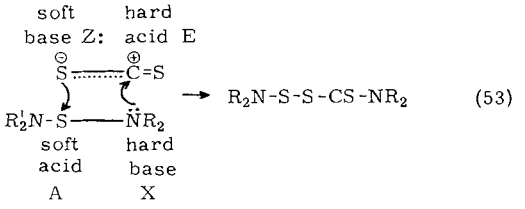
[78] *P.-L. Hu* and *W. Scheele*, Kautschuk u. Gummi *18*, 290 (1965).

[79] *M. R. Porter* and *B. Saville*, unpublished; see also *W. Scheele* and *J. Helberg*, Kautschuk u. Gummi *15*, S.WT 400, (1962).

[80] *K. A. Petrov*, *N. K. Bliznyuk*, and *V. A. Saostenok*, Ž. Obšč. Chim. *31*, 1361 (1961).

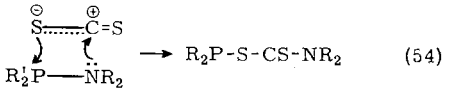
[80a] *O. Foss*, Acta chem. scand. *1*, 307 (1947).

$S{=}C^{\oplus}{-}S^{\ominus}$ in which $C^{\oplus}$ is a hard acid and $S^{\ominus}$ is a soft base. Hence certain "insertion" reactions of carbon disulfide can be interpreted; an example [81] is given in equation (53).



(53)

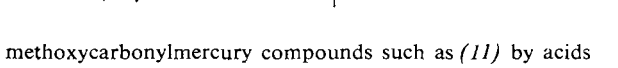
An analogous reaction takes place with tervalent phosphorus [82] (eq. (54)), thus indicating that P(III) in its rather unusual role of an electrophilic center is soft.



(54)

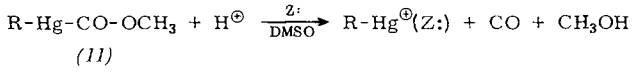
5.3. The Reaction of Methoxycarbonylmercury Complexes

Dessy discovered an analogue of the α-elimination mechanism [83] (equation (55)) which involves the decomposition of



(55)

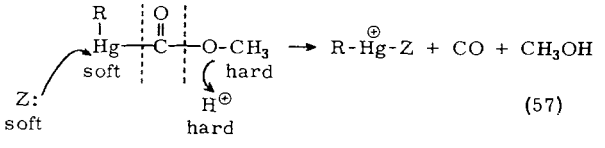
methoxycarbonylmercury compounds such as *(11)* by acids in the presence of anionic and neutral "assistors" (equation (56)). The "assistor"-bases are of the polarizable soft type



(56)

(11)

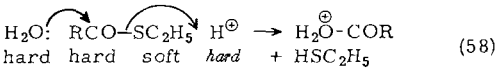
(RSH, $I^{\ominus}$, $Br^{\ominus}$, *etc.*). This pseudo-four-center substitution conforms well with the requirements of the second rule.



(57)

6. Final Remarks

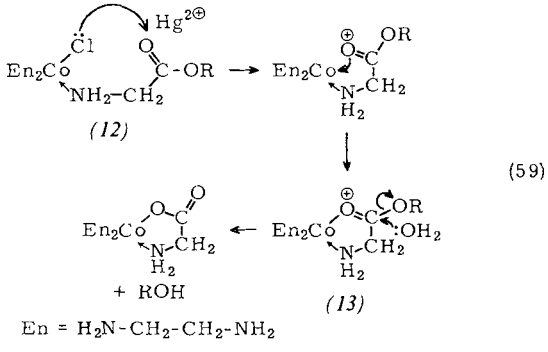
How may the "Rules" outlined be best applied in practice? If a given reagent assembly being used in a four-center reaction does not conform to the patterns of the first or second rules it should be of interest to study the effect of changing the assembly to conform with one or other of these cooperative patterns. As a final illustration it is noted that the hydrolysis of a thiol ester is weakly catalysed by protons (see equation (58)). In this case the hard proton does not



(58)

"match" with the soft SC_2H_5 group. However, if the catalysing proton is changed for a soft acid, such as silver ion, then the thiol ester is hydrolysed far more rapidly.

It is hoped that the principles arrived at here may further prove useful in interpreting metal-ion assisted reactions of biochemical (*e.g.* enzymic processes) and industrial (*e.g.* heterogeneous metal catalysis) importance. In concluding this section mention may be made of the elegant use of the hard-soft principle by *D. H. Busch* [84] in his studies of the cobalt-complex assisted hydrolysis of glycine esters (eq. (59)).



(59)

The chloro derivative *(12)* is stable until a chloride ion is removed by Hg^{2+} ions (soft base interacting with soft acid). This leaves a hard vacant acid center on Co^{3+} that can coordinate with the hard oxygen atom of the glycine moiety thereby leaving a hard carboxyl carbon center in *(13)*. This compound is now suitably activated for attack by a hard water molecule.

The Author acknowledges with sincere thanks the encouraging interest shown in these ideas by Professor R. F. Hudson (in particular), by his colleagues Dr. A. A. Watson and Mr. G. M. C. Higgins, and by Professors R. G. Pearson, Sir Ronald Nyholm, F. R. S., G. Wilkinson, F. R. S., and J. I. G. Cadogan.

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German version: Angew. Chem. 79, 966 (1967)

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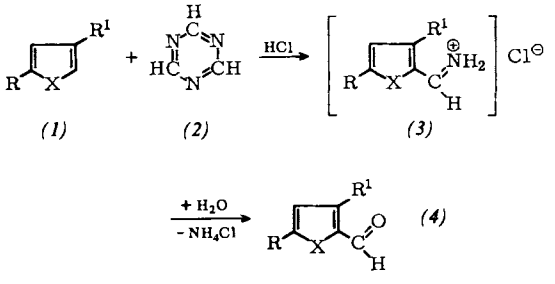
[84] *D. H. Busch*, Chem. Engng. News *43*, No. 10, p. 58 (1965).

Gattermann Aldehyde Syntheses with *s*-Triazine in Place of Hydrogen Cyanide[1]

By *A. Kreutzberger*[*]

In syntheses of polymethine dyes by treatment of *s*-triazine *(2)* with quaternary five- or six-membered heterocycles[2], aldimines have been postulated – but not isolated – as intermediates[3].

We have succeeded in preparing the hydrochlorides of such aldimines in the furan and pyrrole series by treating *(2)* with 2-methylfuran *(1a)* or the pyrrole derivatives *(1b)* to *(1d)*. The reaction takes place at room temperature when anhydrous hydrogen chloride is passed into a solution of *(2)* and one of the compounds *(1a)* to *(1d)*. In order to prepare the aldehyde *(4)*, the aldimine hydrochloride *(3)* is hydrolysed by water or dilute acids or bases without prior isolation.

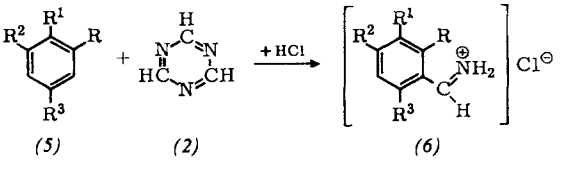


(1) *(2)* *(3)*

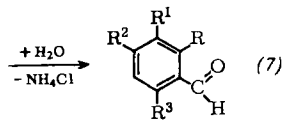
(4)

	X	R	R^1	Solvent	*(4)*, b.p. (°C/mm) or m.p. (°C)	Yield (%)	IR bands (cm^{-1})
(a)	O	CH_3	H	$(C_2H_5)_2O$	72–73/12	56	$\nu_{C=O}$ 1710, 1680
(b)	NH	CH_3	CH_3	$(C_2H_5)_2O/HCCl_3$ (5:7)	90–91	86	ν_{N-H} 3450
(c)	NCH_3	H	H	$HCCl_3$	71–72/12	31	$\nu_{C=O}$ 1670
(d)	NC_4H_9	H	H	$(C_2H_5)_2O$	85–86/6	66	$\nu_{C=O}$ 1660

Reactive aromatic compounds including those of the carbocyclic series, such as phloroglucinol *(5a)* and orcinol *(5b)*, undergo this aldehyde synthesis without a Friedel-Crafts catalyst. Even in cases where the Gattermann synthesis with hydrogen cyanide depends on the presence of aluminum chloride, as with pyrogallol *(5c)*, the synthesis can be effected with *s*-triazine without a catalyst. However, phenol ethers and aromatic compounds lacking an activating substituent undergo the aldehyde synthesis with *(2)* only at elevated temperature and then only in the presence of a Friedel-Crafts catalyst.



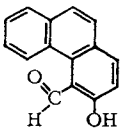
(5) *(2)* *(6)*



(7)

	R	R^1	R^2	R^3	Solvent	Temp. (°C)	Catalyst	*(7)*, m.p. (°C) or b.p. (°C/mm)	Yield (%)
(a)	OH	H	OH	OH	$(C_2H_5)_2O$	25	–	292–295 (decomp.)	77
(b)	OH	H	OH	CH_3	$(C_2H_5)_2O$	25	–	179–180	86
(c)	OH	OH	OH	H	$(C_2H_5)_2O$	25	–	158–159	61
(d)	H	H	OCH_3	H	Anisole	40	$AlCl_3$	137–138/18	67
(e)	H	H	OC_6H_5	H	Benzene	40	$AlCl_3$	158–159/4	78
(f)	H	H	H	H	Benzene	100	$AlCl_3$	86–87/40	31

The Gattermann aldehyde synthesis with *(2)* can also be effected with condensed aromatic ring systems. Thus 3-hydroxyphenanthrene-4-carbaldehyde *(8)* can be prepared in 64% yield by the action of *(2)* on 3-phenanthrol in benzene at 45 °C in the presence of $AlCl_3$.



(8)

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[*] Doz. Dr. A. Kreutzberger
Institut für pharmazeutische Chemie der Universität
Hittorfstrasse 58–62
44 Münster (Germany)

[1] This work was supported by the Verband der Chemischen Industrie.

[2] *A. Kreutzberger* in: Berichte – XXIII. Internationaler Kongress der Pharmazeutischen Wissenschaften. Govi-Verlag GmbH, Frankfurt/Main 1963, p. 311; Angew. Chem. *77*, 1086 (1965); Angew. Chem. internat. Edit. *4*, 1090 (1965); Arch. Pharmaz. *299*, 984 (1966).

[3] *A. Kreutzberger*, Arch. Pharmaz. *299*, 897 (1966).

Fluorothiocarbonyl Isothiocyanate

By *A. Haas* and *W. Klug*[*]

The presumed bifunctional behavior of Cl–CO–SCl *(1)* in its reaction with silver pseudohalides[1] led us to study whether the C–Cl bond in chlorofluorothiocarbonyl S=CClF *(2)* is susceptible to attack by silver salts. In this compound, as in compound *(1)*, the carbon is sp^2 hybridized.

There was no reaction when compound *(2)* was treated with silver cyanate at room temperature; similarly, reaction of *(1)* with AgCNO involves replacement of only the Cl atom attached to sulfur by a NCO group.

However, when *(2)* is treated with AgSCN (molar ratio 1:1.15) in a bomb tube at –25 °C, fluorothiocarbonyl isothiocyanate S=CF–NCS *(3)* is obtained in 50 to 60% yield (calculated on the amount of *(2)* used). This product is an orange liquid of b.p. 35 °C/40 mm and has an extremely pungent odor. At room temperature it slowly becomes red, and at higher temperatures it decomposes rapidly to dark solids. It was characterized by elemental analysis and by IR, ^{19}N–NMR, and mass spectra.

The IR spectrum measured in the NaCl and KBr regions shows strong absorptions at 1208, 1298, and 1972 cm^{-1} and bands of medium strength at 511, 843, 930, 956, 2043, 2395, 2500, 2633, and 2930 cm^{-1}.

The ^{19}F-NMR spectrum at 30 °C contains one very broad signal, which becomes narrower with decrease in the temperature. At −60 °C the chemical shift amounts to −55.1 ppm referred to CCl_3F as internal standard.

The mass spectrum of *(3)* contains the typical fragments SC−NCS (*m/e* = 102), CNCS (70), SCF (63), CS (44), and FC (31), as well as the molecule ion at *m/e* = 121.

An equimolar mixture of *(3)* and chlorine reacts at −70 °C in a bomb tube in an extremely short time, the color becoming paler and the chlorine being consumed quantitatively. Elemental analysis and the IR, ^{19}F-NMR, and mass spectra of the yellow liquid product showed that FCl(SCN)C−SCl *(4)* is formed quantitatively in this reaction; this compound boils at 53 °C/10 mm and has the typical odor of sulfenyl chlorides. The IR spectrum contains a strong absorption band at 1958 cm^{-1} and bands of medium strength at 530, 575, 811, 1040, and 1165 cm^{-1}. The ^{19}F-NMR spectrum of *(4)* at 30 °C contains a single signal with chemical shift +44.7 ppm referred to CCl_3F as internal standard. The mass spectrum shows, *inter alia*, fragments FCl(S)C−NCS (*m/e* = 156), FClC−NCS (124), F(S)C−NCS (121), and SCClF (98).

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*] Dozent Dr. A. Haas and Dipl.-Chem. W. Klug
Anorganisch-Chemisches Institut der Universität
Hospitalstr. 8–9
34 Göttingen (Germany)

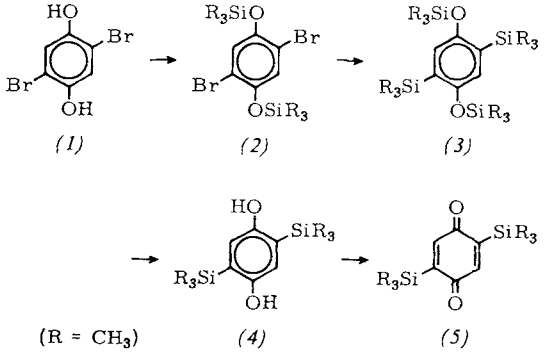
[1] *A. Haas* and *H. Reinke*, Angew. Chem. *79*, 687 (1967); Angew. Chem. internat. Edit. *6*, 705 (1967).

Half-wave Reduction Potentials of 2,5-Bis(trimethylsilyl)- and 2,5-Di-t-butyl-1,4-benzoquinone [**]

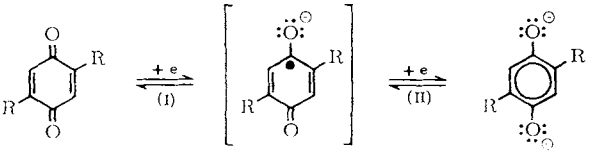
By *H. Bock* and *H. Alt* [*]

The interpretation of d-orbital effects [1] is made difficult in the case of phosphorus-nitrogen compounds according to the oxidation state and coordination number of phosphorus by the presence of free electron pairs, positive charges, or partial double bonds. However, the d-π and d-π* interactions and their differences can be investigated by comparing silicon-substituted π-electron systems with the corresponding alkyl derivatives using suitable methods of measurement [2]. Thus the half-wave reduction potentials $E_{1/2}$ are related to the eigenvalues of the lowest unoccupied levels of π-electron systems into which the electron is inserted on reduction [3]. The prerequisite of a reversible redox equilibrium is fulfilled for alkylated *p*-benzoquinones [4].

The 2,5-bis(trimethylsilyl)-1,4-benzoquinone *(5)* needed for comparison with the 2,5-di-t-butyl derivative was obtained as follows: *(1)* is converted with trimethylchlorosilane/pyridine in boiling toluene into the ether *(2)* (m.p. 58–59 °C) which reacts with sodium/trimethylchlorosilane in boiling toluene to form *(3)* (m.p. 121 °C). Cleavage of the O−SiR_3 bonds with 4 M sodium methoxide in methanol at 20 °C leads after neutralization with diluted acetic acid to *(4)* (m.p. 183 to 186 °C), which can be oxidized with silver(I) oxide in benzene at 20 °C to *(5)*.



The 2,5-bis(trimethylsilyl)-1,4-benzoquinone (n→π*: ν^m = 19999 cm^{-1}; ε_m = 25 l $mole^{-1}$ cm^{-1}) is orange in contrast to the yellow 2,5-di-t-butyl compound (n→π*: ν_m = 21900 cm^{-1}; ε_m = 36 l $mole^{-1}$ cm^{-1}); it melts a 188 °C and gives two NMR singlets at τ = 3.24 and 9.77 in the required ratio 2:18. The half-wave reduction potentials for the two steps (I) and (II) in acetonitrile were measured with tetra-n-butylammonium iodide as conducting electrolyte against the constant [5] mercury anode.



R	$E_{1/2}^{(I)}$ (V)	$E_{1/2}^{(II)}$ (V)
H	+0.04	−0.47
$C(CH_3)_3$	−0.15	−0.71
$Si(CH_3)_3$	+0.04	−0.51

The results show that the silicon-substituted quinone and semiquinone have higher oxidation potentials than the alkyl derivatives, *i.e.* they are stronger electron-acceptors. This is inexplicable if one assumes exclusively an inductive effect ($+I_{SiR_3} > +I_{CR_3}$) [6] and indicates an additional d-π* interaction between the vacant 3d levels of the silicon and the lowest unoccupied or singly occupied molecular orbitals of the *p*-benzoquinone π-system.

This type of model, already postulated several times [7], for the Si−C_{sp^2} bond, which requires $Si_d \leftarrow C_\pi$ back-donation of electrons alongside the $^{\delta+}Si \rightarrow C^{\delta-}$ inductively polarized σ skeleton, is in accord with the results of further polarographic measurements on silyl- and alkyl-butadienes, -styrenes, -naphthalenes, and -phenyl ketones [2].

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[*] Priv.-Doz. Dr. H. Bock and Dipl.-Chem. H. Alt
Institut für Anorganische Chemie der Universität
Meiserstr. 1
8 München 2 (Germany)

[**] Part I of d-Orbital Effects in Silicon-substituted π-Electron Systems.

[1] Cf. *H. Bock*, Chimia *21*, 35 (1967).

[2] *H. Bock, H. Alt, U. Krynitz*, and *H. Seidl*, unpublished.

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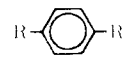
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UV and ESR Studies of *p*-Bis(trimethylsilyl)- and *p*-Dialkylbenzenes [**]

By *H. Alt, H. Bock, F. Gerson*, and *J. Heinzer* [*]

A notable feature of the UV spectrum of *p*-bis(trimethylsilyl)benzene *(1a)*, when compared with the UV spectrum of *p*-di-t-butylbenzene, is that the ^1L_a band ($^1B_{1u} \leftarrow {}^1A_{1g}$)

which is polarized along the substituent axis is shifted bathochromically and considerably intensified.

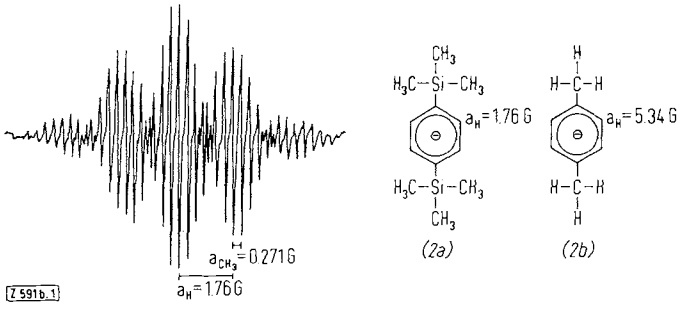


(1a), R = $Si(CH_3)_3$
(1b), R = $C(CH_3)_3$

	^1L_b		^1L_a	
	ν_m (cm^{-1})	ε_m (l $mole^{-1}$ cm^{-1})	ν_m (cm^{-1})	ε_m (l $mole^{-1}$ cm^{-1})
(1a)	36250	390		
	37050	480	43500	14700 (shoulder)
	37900	460	44250	16850
	38750	340		
(1b)	36900	310		
	38000	340	45850	8850
	39050	240	46950	9400
	40000	160		

The difference in ^1L_a transition energies amounts to 2700 cm^{-1} = 7.7 kcal/mole and can be interpreted as the difference between the d-π^* and d-π interactions in *(1a)* if the varying inductive effects are neglected.

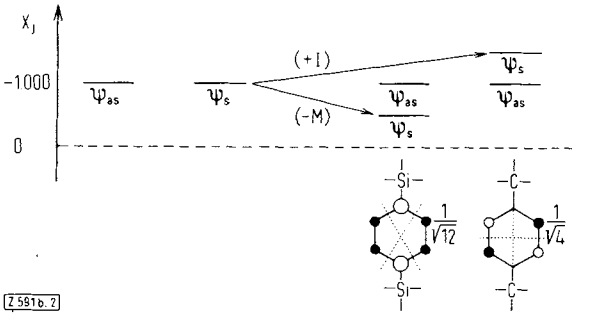
In general[1], electron spin resonance measurements for radical anions permit conclusions to be drawn about the unoccupied non-bonding or antibonding states of the original neutral molecule and thus about the electronic effects of substituents. For instance, from a comparison of the ESR spectra of silyl- and alkyl-substituted benzene[2] and biphenyl radical anions[3] it was concluded that a $Si_d \rightarrow C_\pi$ back-donation of electrons counteracts the inductive $^{\delta+}Si \rightarrow C^{\delta-}$ polarization[4]. In the case of *p*-bis(trimethylsilyl)benzene *(1a)* such a –M effect of the R_3Si groups, which is already indicated by differences in the electron spectra of *(1a)* and *(1b)*, should be demonstrable for the monoanion *(2a)* by ESR spectroscopy. For biphenyl derivatives[3] interpretation is made difficult by twisting effects, and for monosubstituted benzene derivatives[2] splitting of the initially degenerate antibonding e_{2u} orbitals ψ_s and ψ_{as} may be too small to exclude vibrationally induced mixing with energy-richer states; but *p*-disubstituted benzene derivatives are planar and show a considerable energy difference between ψ_s and ψ_{as} orbitals[5]. Owing to participation of unoccupied Si-3d states in the π-system of the benzene radical anions the ψ_s molecular orbital that takes up the unpaired electron should thus be more strongly depressed, in this way increasing the stability of the radical. In accordance with expectation, a solution of *p*-di-t-butylbenzene *(1b)* in potassium/1,2-dimethoxyethane at –70 °C shows the ESR signal of only the solvated electron, whereas the ESR spectrum of the *p*-bis(trimethylsilyl)benzene radical anion *(2a)* (Fig. 1) can be observed up to more than 0 °C.



Z 591b. 1

Fig. 1. ESR spectrum of *p*-bis(trimethylsilyl)benzene, measured in K-1,2-dimethoxyethane at –70 °C. Coupling constants of the ring protons of *p*-disilyl- and *p*-dialkyl-benzene.

As can be calculated from the simple 5-group spectrum the coupling constants of the four equivalent nuclear protons of *(2a)* amount to 1.76 gauss, whereas those of the *p*-xylene radical anion *(2b)*[6] selected as reference substance amount to 5.34 gauss. These values can be reproduced quantitatively by use of the McConnell equation $a_H = Q \cdot \rho_H$ with a *Q* value of 21.2 gauss and Hückel spin densities $(c_{J\mu})^2$ of 1/12 and 1/4, respectively; this proves the occupation of ψ_s in *(2a)* as required by the –M effect of the R_3Si group, and the occupation of ψ_{as} of *(2b)* as required by the +I effect of the H_3C group. The d-π^* splitting thus demonstrated for the radical anion *(2a)* follows – although different electron interactions have to be considered – for the neutral *p*-bis(trimethylsilyl)benzene *(1a)* from the electron spectra too.



Z 591b. 2

Fig. 2. MO scheme of inductive and mesomeric substituent effects on the antibonding molecular orbitals (e_{2u}) of *p*-disubstituted benzene derivatives. Hückel coefficients c_{J2} of the symmetrical (s) and the antisymmetrical (as) molecular orbitals.

However, experimental verification of a d-π interaction in *p*-bis(trimethylsilyl)benzene encounters difficulties. Attempts to determine approximately the ionization potentials of *(1a)* and *(1b)* from the longer-wavelength band of the charge-transfer complexes failed because this band was always overlapped by the shorter-wavelength band of the charge transfer complex to give a single band of large half-width. The –M effect of R_3Si groups in the ground state can, however, be proved by means of charge-transfer complexes of mono- or di-substituted benzene and naphthalene derivatives[7].

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[*] Dipl.-Chem. H. Alt and Priv.-Doz. Dr. H. Bock
Institut für Anorganische Chemie der Universität
Meiserstr. 1
8 München 2 (Germany)
Priv.-Doz. Dr. F. Gerson and Dipl.-Chem. J. Heinzer
Laboratorium für Organische Chemie der Eidgenössischen
Technischen Hochschule
Universitätsstr. 6
Zürich 6 (Switzerland)

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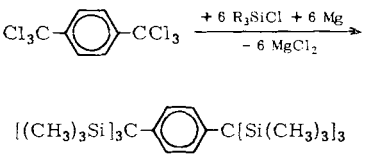
Substituent Effects of β-Trimethylsilyl Groups in Bis-, Tetrakis-, and Hexakis-(trimethylsilyl)-*p*-xylenes [**]

By *H. Bock* and *H. Alt* [*]

An interaction between unoccupied Si-3d orbitals and antibonding states of neighboring π-electron systems can be demonstrated by comparing the UV and ESR spectra of

R_3Si- and R_3C-substituted benzene derivatives[1]. For the substituents R_3Si-CH_2- and R_3C-CH_2-[2] it remains to be decided whether the group R_3Si exerts a–M effect in spite of the insulating action of the CH_2 group or whether it acts mainly inductively.

α,α′-Poly(trimethylsilyl)-*p*-xylenes were chosen as model compounds, since, in order to increase the desired effect, up to six R_3Si groups can be introduced in the β-positions to the aromatic system by *in-situ* Grignard reactions[3]:



(1)

Experimental: 0.2 mole of α,α,α,α′,α′,α′-hexachloro-*p*-xylene was added dropwise to 2.4 moles each of trimethylsilyl chloride and magnesium (100 % excess) in tetrahydrofuran. After the strongly exothermic reaction had ceased, the mixture was heated for 2 days under reflux, then hydrolysed cautiously with 1 N HCl. The ether phase was concentrated and chromatographed on Al_2O_3 (neutral, activity grade I) with benzene, and the crude product was recrystallized from 2-butanol and purified by sublimation (yield 3 %). α,α,α′,α′-Tetrakis(trimethylsilyl)-*p*-xylene *(2)* was obtained in 2 % yield analogously from the tetrabromo derivative.

The structures of the new compounds follow from molecular weight determinations and ^1H–NMR spectra [*(1)*, singlets in the ratio 4:54 at τ = 2.85 and 9.79; *(2)*, singlets in the ratio 4:2:36 at τ = 3.27, 8.65, and 10.05; tetramethylsilane as internal standard]. The dumbbell-shaped compound *(1)* sublimes at 280 °C and liquifies in a closed tube only at 332 °C, whereas the tetrakis(trimethylsilyl) derivative *(2)* melts at 125 °C.

of the donor, it is possible to correlate these maxima with the energies of the highest bonding states of the donor[5].

It can be seen that the TCNE complex of trimethylsilylbenzene absorbs at shorter wavelength than does that of t-butylbenzene, a finding that can be ascribed to a d-π interaction[1,6] opposing the +I effect of the R_3Si group. If, however, the $C(CH_3)_3$ group of neopentylbenzene is replaced by $Si(CH_3)_3$, one of the two CT bands lying at longer wavelength[7] is shifted so strongly bathochromically that two distinctly separated CT maxima can be observed for the benzyltrimethylsilane/TCNE complex, in contrast to complexes of all other monoalkylbenzenes. This CT doublet is derived from the considerable splitting of the degenerate e_{1g} molecular orbitals of the benzene ψ_s and ψ_{as} by the

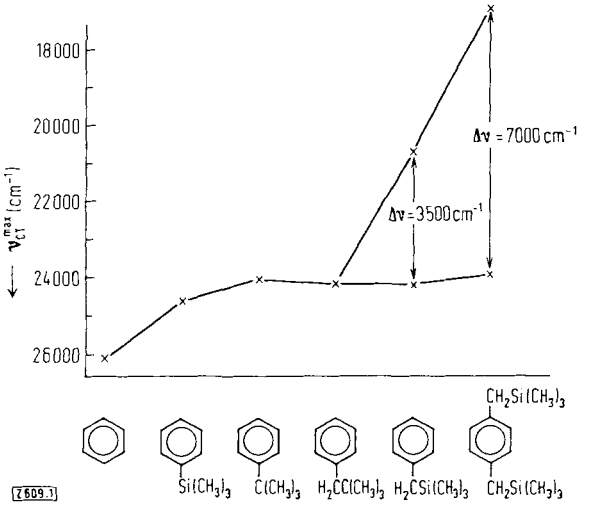


Fig. 1. Charge-transfer maxima of TCNE complexes of alkyl-, silyl, and silylalkyl-benzenes.

	p-R–C_6H_4–R							
	(4), R = $C(CH_3)_3$		*(3)*, R = $CH_2Si(CH_3)_3$		*(2)*, R = $CH[Si(CH_3)_3]_2$		*(1)*, R = $C[Si(CH_3)_3]_3$	
	ν_{max} (cm^{-1})	ε [a]	ν_{max} (cm^{-1})	ε [a]	ν_{max} (cm^{-1})	ε [a]	ν_{max} (cm^{-1})	ε [a]
^1L_b	36900	310	34950	725	34300	720	34600	640
	38000	340	35800	765	35600	960	35750	1050
	39050	240	36100	800	36200	810		
	40000	160	36950	635				
^1L_a	45850	8850	42800	16150	41600	21600	40300	27500
	46950	9400						
^1B	> 50000		[49250] [b]	48700	49400	63800	48100	37150
			50250	54500				

[a] In n-hexane. Dimensions of ε: l mol^{-1} cm^{-1}. [b] Shoulder.

The absorption bands of the α,α′-poly(trimethylsilyl)-*p*-xylenes *(1)*, *(2)*, and *(3)*[4] lie at unexpectedly long wavelengths in comparison with those of the hexamethyl compound *(4)*[1] (see Table).

According to Pariser-Pople-Parr calculations, energies for the ^1L_b, ^1L_a, and $^1B_{a,b}$ transitions are in general lowered by simulated positive inductive effects at centers 1 and 4 of the benzene ring; yet, in the absence of conjugative interactions, the bathochromic shifts listed in the Table – for the ^1L_a band maxima up to 6650 cm^{-1} = 19 kcal/mole – correspond to a considerable +I effect of the β R_3Si groups. That this is actually true can be demonstrated by the charge-transfer maxima ν_{CT}^{max} of the tetracyanoethylene (TCNE) complexes of the compounds listed in Fig. 1: for any one acceptor, an approximately constant equilibrium distance between the components of the complex, and a high ionization potential

$-CH_2Si(CH_3)_3$ group and establishes the presence of a notable +I effect of β R_3Si groups, as previously postulated from electronic spectra. For bis(trimethylsilyl)-*p*-xylene *(3)* the position of band II ($c_{as,1} = c_{as,4} = 0$) remains approximately constant but its distance Δν from band I increases to twice the value for the mono(trimethylsilyl) compound. Within the framework of the HMO theory, this additivity of the perturbations indicates an exclusively inductive influence on the ground state by R_3Si-CH_2 substituents where the R_3Si group is insulated from the π-electron system by a tetrahedral C atom.

Thus, for aromatic compounds in which a R_3Si group is directly attached to a ring carbon atom, an inductive polarization $^{\delta+}Si-C^{\delta-}$ should also strongly lower the transition energy of the CT band I. In fact, however, the CT bands[7] of trimethylsilylbenzene lie at shorter wavelengths than do

those of other monoalkylbenzenes, which again indicates a considerable conjugative $Si_d \leftarrow C_\pi$ electron back-donation [1,6] to the Si/C_{sp^2} bond.

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[*] Dr. H. Bock and H. Alt
Institut für Anorganische Chemie der Universität
Meiserstr. 1
8 München 2 (Germany)

[**] Part III of *d*-Orbital Effects in Silicon-substituted π-Electron Systems. – Part II: [1].

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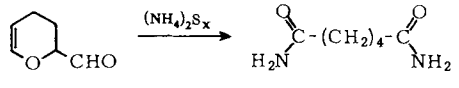
[7] Substituted benzenes should in general show two CT bands due to removal of the degeneracy of the e_{1g} orbitals. The half-band widths for trimethylsilyl- ($\Delta\nu_{1/2} = 6050\ cm^{-1}$) and for t-butyl-benzene ($\Delta\nu_{1/2} = 6750\ cm^{-1}$) are greater than that for benzene ($\Delta\nu_{1/2} = 5800\ cm^{-1}$) and indicate overlapping of the two expected CT bands, the position of the maximum being determined largely by the more intense, longer-wavelength, substituent-dependent CT absorption.

Synthesis of Dicarboxylic Acids by the Willgerodt-Kindler Reaction

By *H. Feichtinger* and *W. Konkol* [*]

Carboxylic acids and their derivatives are accessible by the Willgerodt-Kindler reaction [1]. Oxalic and malonic acids can also be obtained in this way from vinyl and propenyl ethers [2] *i.e.* from compounds containing two functional groups.

Ring cleavage under the conditions of this reaction appeared to us as a possibility for synthesis of dicarboxylic acids, and their derivatives, containing acid groups that are widely separated from one another. We have now found the first example of this principle: 2,3-Dihydro-4*H*-pyran-2-carbaldehyde *(1)* reacts under the usual conditions (5 h at 160 °C in pyridine) to yield adipdiamide *(2)* directly in 25–30 % yield.



(1) *(2)*

Adipic acid monoamide (5–10 %) and small amounts of oxidative degradation products, such as glutardiamide (6–8 % and succindiamide (1–2 %), were also detected.

We can contribute the following findings towards elucidation of the reaction mechanism. Under the conditions stated, 2-hydroxyhexanedial *(3)* [3] affords very little diamide *(2)*. The cyclic trimeric aldimine *(4)* [4] of 2-formyl-2,3-dihydropyran obtained from the aldehyde *(1)* and aqueous ammonia, as well as the 2-hydroxythiohexanedial *(5)* of formula $(C_6H_{10}O_2S)_x$ (m.p. 133–143 °C), give lower yields of adipdiamide than are obtained from *(1)*. Thus occurrence of compounds *(3)* to *(5)* as intermediates is unlikely.

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[*] Dr. H. Feichtinger and Dr. W. Konkol
Ruhrchemie AG.
42 Oberhausen-Holten (Germany)

[1] *M. Carmack* and *M. A. Spielman,* Org. Reactions *3,* 83 (1949).

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Preparation of Phosphorin Derivatives from Pyrylium Salts and Phosphine

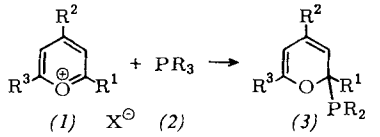
By *G. Märkl, F. Lieb,* and *A. Merz* [*]

For steric reasons, the synthesis of phosphorins from pyrylium salts *(1)* and tris(hydroxymethyl)phosphine *(2a)* [1] or tris(trimethylsilyl)phosphine *(2b)* [2] is limited to the 2,4,6-triaryl and tri-t-butyl derivatives [3]. Nucleophilic attack by *(2a)* or *(2b)*, which could occur at either C-2 or C-4 of *(1)*, is rendered irreversible by the loss of formaldehyde or $X–Si(CH_3)_3$; α-pyrans *(3)* or their γ-isomers are formed.

If R^2 is smaller than R^1 and R^3, the phosphines *(2a)* and *(2b)* react with *(1)* exclusively at C-4: 2,6-diphenylpyrylium perchlorate is quantitatively dimerized to 2,2',6,6'-tetraphenyldipyrylene, m.p. 313 °C [4]. Compound *(1)*, $R^2 = CH_3$, $R^1 = R^3 = C_6H_5$, does not give a phosphorin.

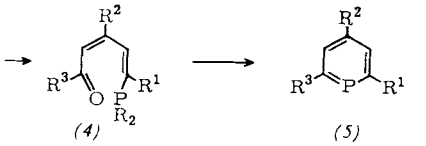
If R in *(2a)* or *(2b)* is larger than, or equal in size to, R^1 and R^3 and if these are smaller than R^2, then nucleophilic attack occurs preferentially at C-2. In contrast to the reaction of 2,4,6-triarylpyrylium salts (in which R is smaller than $R^1–R^3$), the α-pyran *(3a)* or *(3b)* appears to open, yielding the ketone that is isomeric with *(4)* by virtue of containing a *trans*-phosphine group. Compound *(1)*, $R^2 = CH_3$, $R^1 = R^3 = C_6H_5$, does not react to give *(5)*.

These difficulties would be overcome if one could make the phosphine *(2c)* react with *(1)*. Nucleophilic attack on *(1)* would then be reversible, and the smaller steric requirements of PH_3 should then always favor the opening of the α-pyran ring *(3c)* to give *(4c)* which is required for ring closure. The low nucleophilicity of PH_3, however, made this reaction unlikely. 2,4,6-Triphenylpyrylium salts do in fact react with phosphine but the compound *(5)*, $R^1 = R^2 = R_3 = C_6H_5$, could not be detected in the complex mixture of products, even when ethyldicyclohexylamine was used as auxiliary base.



(1) $X^\ominus$ *(2)* *(3)*

(a), R = $-CH_2OH$
(b), R = $-Si(CH_3)_3$
(c), R = $-H$



(4) *(5)*

R^1	R^2	R^3	(5) M.p. (°C)	(5) Yield (%)	(5) λ_{max} (nm) and (ε) in CH_3CH_2OH	^1H—NMR Spectrum (in $CDCl_3$):
C_6H_5	C_6H_5	C_6H_5	172—174	61	see [1]	
p-CH_3—C_6H_4	C_6H_5	p-CH_3—C_6H_4	134	81	see [2]	
C_6H_5	p-CH_3O—C_6H_4	C_6H_5	107	63	see [2]	
2,3,4,5,6-pentaphenyl-			253—255	67	see [2]	
CH_3	C_6H_5	C_6H_5	79—81	61	267 (25300); shoulder at 296 (13400)	τCH_3 = 7.55; doublet, $^5J_{P-H}$ = 3.5 Hz; $\tau H_3,H_5$ = 2.24; doublet, $^2J_{P-H}$ = 6 Hz; τPhenyl—H = 2.3—2.8, multiplet
C_6H_5	CH_3	C_6H_5	118—120	63	276 (27700)	τCH_3 = 7.32; doublet, $^2J_{P-H}$ = 15 Hz; $\tau H_3,H_5$ = 2.02; doublet, $^2J_{P-H}$ = 6 Hz; τPhenyl—H = 2.15—2.85, multiplet

The primary phosphine *(4c)* must be assumed to be an intermediate in the synthesis and, like primary and secondary phosphines in general[5], should be able to react with the carbonyl group under proton catalysis. In fact, the pyrylium salt *(1)*, $R^1 = R^2 = R^3 = C_6H_5$, reacts smoothly with phosphine in 1-butanol at 120—130 °C within 48 h yielding 2,4,6-triphenylphosphorin without side reactions. As shown in the table, 2- and 4-methylphosphorins could thus be prepared for the first time. Phosphabenzenes substituted by alkyl groups are thus accessible without limitation.

2-Methyl-4,6-diphenylphosphorin:

A suspension of 2.1 g (6.3 mmoles) of 2-methyl-4,6-diphenylpyrylium fluoroborate in 50 ml n-butanol and 2.6 g (16 mmoles) phosphonium iodide are heated for 24 h at 110—120 °C. After removal of the solvent, the residue is taken up in benzene; the benzene solution is washed several times with water, dried over $CaCl_2$ and finally concentrated. The residue crystallizes from a cold ethanol solution on scratching. Colorless crystals (m.p. 79—81 °C, yield 945 mg) are obtained on recrystallization from a little ethanol.

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[*] Priv.-Doz. Dr. G. Märkl, cand. chem. F. Lieb, and cand. chem. A. Merz
Institut für Organische Chemie der Universität
Röntgenring 11
87 Würzburg (Germany)

[1] *G. Märkl*, Angew. Chem. *78*, 907 (1966); Angew. Chem. internat. Edit. *5*, 846 (1966).

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Linear Relation between Chemical Shifts of the ^{31}P Resonance and Hammett Constants [1]

By *A. Schmidpeter* and *H. Brecht* [*]

It is still uncertain how the influence of substituents on the chemical shift of the ^{31}P resonance of tetracovalent phosphorus should be interpreted. We are therefore studying possible relations between the shift $\delta^{31}P$ and values that characterize a known substituent effect. For several series of phosphinyl derivatives we found $\delta^{31}P$ to lie in the same order as the Hammett constants $\sigma_{(para)}$ [3] of the substituents, the shielding increasing with increasing efficiency of the substituent as electron donor.

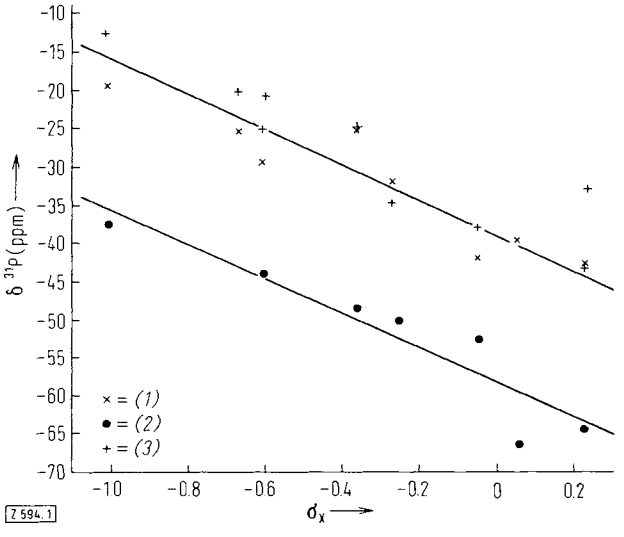


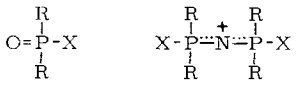
Fig. 1. Relation between chemical shifts $\delta^{31}P$ and Hammett constants σ_X for compounds *(1)* to *(3)*.

Table 1. Experimental values of the chemical shifts $\delta^{31}P$ (figures in ppm referred to 85 % H_3PO_4; negative values denote shifts to lower field strengths) for compounds *(1)* to *(3)*, together with the values calculated according to the equations given in the text.

X	σ_X	δ(1) exp.	δ(3) exp.	δ(1), (3) calc.	δ(2) exp.	δ(2) calc.
$-O^{\ominus}$	−1.0	−19.5 [a]	−12.7 [c]	−15.5	−37.5 [c]	−35.3
$-NH_2$	−0.660	−25.5 [5]	−20.3 [8]	−23.6		−43.1
$-N(CH_3)_2$	−0.600	−29.6 [b]	−25.4 [d]	−25.1	−44.1 [11]	−44.5
$-NHCH_3$	−0.592		−20.9 [b]	−25.2		−44.8
−OH	−0.357	−25.5 [b]	−25.1 [e]	−30.8	−48.6 [6]	−50.1
$-OCH_3$	−0.268	−32.2 [b]	−35.0 [b]	−33.0		−52.3
$-OC_2H_5$	−0.250			−33.8	−50.3 [12]	−52.7
$-S^{\ominus}$	[g]		−35.6 [9]			
$-SCH_3$	−0.047	−42.3 [b]	−38.4 [2]	−38.2	−52.7 [11] [f]	−57.4
−F	+0.062	−40.0 [7]		−40.8	−66.3 [7]	−60.3
−Cl	+0.226	−42.7 [6]	−43.3 [9,10]	−44.7	−64.3 [13]	−64.8
−Br	+0.232		−33.2 [9] [b]	−44.9		−64.9

Our own, hitherto unpublished, measurements: [a] in ethylene glycol (−23.6 was given in [5]); [b] in CH_2Cl_2; [c] in CH_3OH; [d] in $C_6H_5NO_2$; [e] tetra-*P*-phenylimidodiphosphinic acid in glacial acetic acid; [f] value for $(CH_3)_2PO(SC_3H_7)$; [g] unknown.

If the shifts measured for all available diphenylphosphinyl derivatives *(1)* are plotted against σ_X, a linear relation is obtained (Fig. 1). The same is true for the tetra-*P*-phenylimidodiphosphinyl derivatives *(3)*, which are formally derived from *(1)* when O is replaced by $N^+/2$.



(1) R = C_6H_5 *(3)* R = C_6H_5
(2) R = CH_3

For both *(1)* and *(3)* the relation

$$\delta_{(1),(3)}\ (\text{ppm}) = -39.4 - 23.8\ \sigma_X$$

holds approximately (correlation coefficient = −0.96). The shifts calculated in this way are compared with the experimental values in Table 1; further, plotting the shifts for the dimethylphosphinyl derivatives *(2)* against σ_X (Fig. 1) gives a parallel line:

$$\delta_{(2)}\ (\text{ppm}) = -58.4 - 23.2\ \sigma_X$$

(correlation coefficient = −0.94). The difference of 19.0 ppm in the position where the axis is cut is in agreement with the average shift of 10.8 ppm found previously [4] for replacement of one methyl by a phenyl group in phosphinyl chlorides. This value is not, however, generally valid, as was previously assumed.

The relation found between $\delta^{31}P$ and σ_X is remarkable in that the influence of a substituent on the shift should certainly not be characterized solely by the Hammett constant. Clearly, in the examples given above, other changes must have a small influence compared to the increase in diamagnetic shielding that results from increased electron density. The large deviation observed for *(3)*, X = Br, can be ascribed to an anisotropy effect of the substituent.

Phosphine oxides *(1)* and *(2)* in which X is an organic group cannot be included in the above considerations. Their shifts are always to higher field strengths than are calculated from the equations given.

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[*] Dr. A. Schmidpeter and Dipl.-Chem. H. Brecht
Institut für Anorganische Chemie der Universität
Meiserstr. 1
8 München 2 (Germany)

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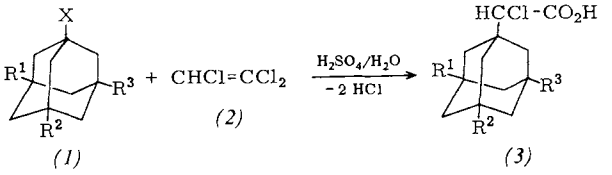
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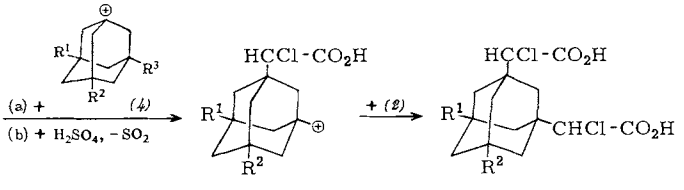
Synthesis of α-Chloro-1-adamantaneacetic Acids and α-Chloro-2-norbornaneacetic Acid by means of Trichloroethylene

By *K. Bott* [*]

The method of carboxylic-acid synthesis by means of 1,1-dichloroethylene [1] can be applied to trichloroethylene *(2)*. However, at the high temperatures (80–115 °C) required, only the carbonium ions from the adamantane and norbornane series are sufficiently stable in concentrated sulfuric acid to permit addition to *(2)*.



(1) *(3)*



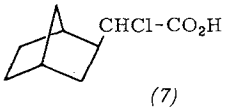
(5) *(6)*

R^1	R^2	R^3	X	Yield (%) *(3)*	Yield (%) *(6)*	*(3)*, m.p. (°C)	CH_3 ester of *(6)* b.p. (°C/mm)
H	H	H	Br	20	65 [a]	141–142	174–176/0.5
CH_3	H	H	Br	26	55 [a]	118–119	174–176/0.4
CH_3	CH_3	H	Br	28	37 [a]	130–131	160–162/0.1
CH_3	CH_3	Br	Br	—	88		160–162/0.1
CH_3	CH_3	CH_3	Br	94	—	175–176	
H	H	CH_2CO_2H	H	86	—	162–164	
CH_3	CH_3	CH_2CO_2H	OAc	95	—	209–211	
CH_3	CH_3	CH_2CO_2H	H	86	—	209–211	

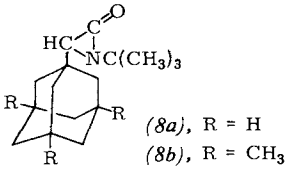
[a] In the calculation of the yields no attention was paid to loss of *(1)* by hydride exchange [route (a)]. The actual yields in the synthesis are thus higher than those given.

The primary products, α-chloro-1-adamantaneacetic acids *(3)* with hydrogen atoms at the bridgehead position, lead (a) by hydride transfer from *(3)* to *(4)* or (b) on oxidation by sulfuric acid to new carbonium ions *(5)* which react in a further synthetic step to give α,α'-dichloro-1,3-adamantanediacetic acids *(6)*. The mixture of *(3)* and *(6)* obtained can be separated into its components by esterification with methanol and subsequent fractional distillation. Heating the 1-adamantaneacetic acids with *(2)* and sulfuric acid gives α-chloro-1,3-adamantanediacetic acids.

Treating norbornene with *(2)* affords α-chloro-2-*exo*-norbornaneacetic acid *(7)*, m.p. 46–50 °C, in 66 % yield.



(7)



(8a), R = H
(8b), R = CH_3

In aqueous sodium hydroxide, even at 90 °C, α-chloro-1-adamantaneacetic acids exchange the chlorine atom for hydroxyl. The reaction presumably goes through an α-lactone stage since the rate of hydrolysis is independent of the hydroxide ion concentration. Also, like the t-butylamides of α-bromocarboxylic acids [2], t-butylamides of *(3)* are con-

verted into the stable α-lactams *(8a)* (m.p. 58–59 °) and *(8b)* (m.p. 85–86 °) by potassium t-butoxide. The IR spectra (KBr discs) contain the absorption maxima for carbonyl groups at 1820 cm^{-1} characteristic of aziridinones.

Preparation of α-Chloro-3,5,7-trimethyl-1-adamantaneacetic Acid:

A mixture of 1-bromo-3,5,7-trimethyladamantane (30 g) and trichloroethylene (90 g) is added dropwise over 4 h, with stirring, to 90 % sulfuric acid (240 ml) at 103–106 °C. Stirring is continued for a further 2 h at the stated temperature, then the mixture is cooled and hydrolysed with crushed ice. The product that separates can be freed from the neutral fraction by dissolution in dilute aqueous sodium hydroxide and extraction with ether. Acidification of the alkaline layer with dilute hydrochloric acid precipitates the carboxylic acid (29.5 g; m.p. 173–175 °C). The product melts at 175–176 °C after recrystallization from cyclohexane.

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[*] Dr. K. Bott
Forschungslaboratorium, Chemische Werke Hüls AG.
437 Marl (Germany)

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Diethylmetal Thiocyanates of Aluminum, Gallium, and Indium

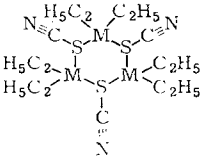
By *K. Dehnicke* [*]

Reaction of equivalent amounts of triethyl-aluminum, -gallium, and -indium with thiocyanogen occurs exothermally and quantitatively according to the equation:

$$M(C_2H_5)_3 + (SCN)_2 \rightarrow (C_2H_5)_2MSCN + C_2H_5SCN$$

When the solvent and ethyl thiocyanate are distilled off, there remain the diethylmetal thiocyanates (M = Al, Ga, or In) as yellow hygroscopic oils that are very reactive and are sensitive to oxygen. Whereas the compounds with M = Al or In decompose at 180 °C on distillation in a vacuum, diethylgallium thiocyanate distils without decomposition at 145 °C/10^{-3} mm. When pure, the gallium compound is inert to water. When kept for some time in the cold the indium compound forms crystals having m.p. 51 °C.

Cryoscopic determination of the molecular weight in benzene shows that the diethylmetal thiocyanates are trimeric. The IR spectra indicate planar six-membered metal-sulfur



(M = Al, Ga, In)

rings (symmetry D_{3h}). Evidence for this is the high-frequency CN stretching vibration, which corresponds to a C≡N triple bond, the long-wave absorption due to the CS stretching vibration, which corresponds to a C–S bond [1], and the strictly single occurrence of these bands, which is to be found, for point group D_{3h}, only with antisymmetrical vibrations (class E′) whereas for a non-planar six-membered ring (symmetry C_{3v}) the symmetrical vibrations (class A_1) must also appear. The diethylmetal thiocyanates are thus analogous to the diethylmetal azides $[(C_2H_5)_2MN_3]_3$ (M = Al [2] or Ga [3]).

Heating $[(C_2H_5)_2AlSCN]_3$ at 180 °C in a vacuum yields ethylaluminum dithiocyanate as a pale yellow crystalline powder that is insoluble in benzene:

$$2\ (C_2H_5)_2AlSCN \rightarrow C_2H_5Al(SCN)_2 + Al(C_2H_5)_3$$

This reaction is explosive at 210 °C. According to the solubility relations and the IR spectrum, the dithiocyanate is to be regarded as a coordination polymer in which the aluminum atoms are linked through the sulfur atoms of the SCN groups. Characteristic IR bands are at 2050 cm^{-1} (s, νCN), 619 cm^{-1} (s, νCS), 601 cm^{-1} (vs, νCS, νAl–C), 458 cm^{-1} (vs, δSCN), and 393 cm^{-1} (vs, δSCN).

Table 1. Characteristic IR absorptions of the compounds $[(C_2H_5)_2MSCN]_3$.

Class	Vibration	M = Al	M = Ga [a]	M = In [a]
E′	ν CN	2075 vs [b]	2150 vs	2128 vs
E′	ν CS	627 vs	665 vs	649 vs
A_2''	ν_{as} MC_2	627 vs	578 s	522 s
E′	ν_s MC_2	555 m	534 s	468 s
E′	δ SCN	501 s	476 ms	468 s
A_2''	δ SCN	438 vs	454 ms	450 sh

[a] Assignment of stretching vibrations after consideration of the vibrational spectrum of $Ga(CH_3)_3$ and $In(CH_3)_3$ [4].

[b] Values in cm^{-1}; vs = very strong, s = strong, m = medium, sh = shoulder.

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[*] Priv.-Doz. Dr. K. Dehnicke
Laboratorium für anorganische Chemie
der Technischen Hochschule
Schellingstr. 26
7 Stuttgart-N (Germany)

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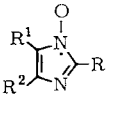
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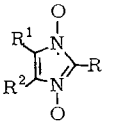
N-Oxides of Imidazolyls

By *K. Volkamer*, *H. Baumgärtel*, and *H. Zimmermann* [*]

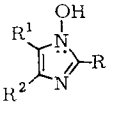
During our work on imidazolyls [1] we took an interest in the *N*-oxides of these radicals and their ESR spectra. Imidazolyl *N*-oxides *(1)* and *N,N′*-dioxides *(2)* are to be considered as dehydrogenation products of imidazol-1-ol *(3)* and its *N*-oxide *(4)*.



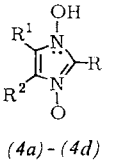
(1a)-(1b)



(2a)-(2d)



(3a)-(3b)



(4a)-(4d)

	R	R^1	R^2
(a)	C_6H_5	2,2′-Biphenylylene	
(b)	C_6H_5	C_6H_5	C_6H_5
(c)	CH_3	CH_3	CH_3
(d)	C_6H_5	CH_3	CH_3

The radicals *(1a)* and *(2a)–(2c)* are formed on treatment of the alkali salts of *(3a)* and *(4a)–(4c)* with halogen in polar organic solvents, and *(2c)–(2d)* by dehydrogenation of *(4c)–(4d)* with lead dioxide. Short-lived radicals *(1a)* and *(2a)–(2b)* were detected at room temperature by ESR spectroscopy when a streaming technique was used.

The spectrum of *(1a)* shows three equidistant lines in the intensity ratio 1:1:1, corresponding to coupling of the radical electron with the nitrogen nucleus of the NO group. Coupling constants and g factors are, in benzonitrile, J_N = 3.59 gauss and g = 2.0059.

In contrast to the formation of *(1a)*, that of *(1b)* could not be effected by treatment of the alkali salt with halogen. On dehydrogenation of *(3b)* with lead dioxide in dioxane a radical was formed, which gave an ESR spectrum with seven equidistant lines having an intensity ratio 1:1:2:1:2:1:1. The fine structure can be interpreted as due to coupling of the unpaired electron with two non-equivalent nitrogen nuclei. J_{N1} = 7.98; J_{N2} = 3.99 gauss; g = 2.0062 (in dioxane). On oxidizing lophine with *p*-nitroperbenzoic acid, *Rassat et al.*[2], also obtained a radical whose ESR spectrum contains a signal with seven lines (intensity ratio 1:1:2:1:2:1:1); they ascribed structure *(1b)* to this signal. J_{N1} = 8.4 gauss; J_{N2} = 4.2 gauss (in methylene chloride). In contrast to *(1a)*, the radical obtained by dehydrogenation of *(3b)* with lead dioxide has an unusually long life. Although its ESR spectrum is compatible with structure *(1b)*, it seems to us that identification of the radical *(1b)* is not beyond question.

Imidazolyl *N,N'*-dioxide *(2a)* gives an ESR spectrum with five equidistant lines in the intensity ratio 1:2:3:2:1, corresponding to coupling of the unpaired electron with the equivalent nitrogen nuclei of the two NO groups. J_N = 3.89 gauss, g = 2.007; λ_{max} = 613 nm (in dimethylformamide).

(2a) is the most stable radical of the series under study. Its decomposition, as followed by ESR spectroscopy, can be described by the equation $(dc/dt) = -kc^{2.5}$ (c = radical concentration) where $k = 3.6\times10^3$ $l^{1.5}$ mole$^{-1.5}$ sec^{-1}.

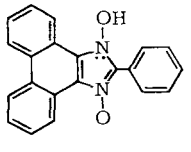
The ESR spectrum of *(2b)* is similar to that of *(2a)* in number of lines and intensity ratios. J_N = 3.61 gauss, g = 2.0071; λ_{max} = 548 nm (in dimethylformamide).

The ESR spectrum of *(2c)* consists of twelve equidistant lines (intensities in the ratios 1:3:5:7:9:11:11:9:7:5:3:1). The multiplet can be interpreted as due to coupling of the radical electron with the two equivalent nitrogen nuclei and the three equivalent protons of the 2-methyl group. J_N = 6.92 gauss, J_H = 3.46 gauss, g = 2.0067 (in dioxane).

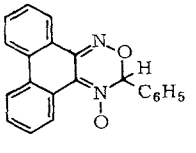
Replacing the 2-methyl group of *(2c)* by phenyl gives the radical *(2d)* whose ESR spectrum, as expected, also contains five lines at equal distance with intensity ratios 1:2:3:2:1, corresponding to coupling of the radical electron with the two nitrogen nuclei. J_N = 7.24 gauss, g = 2.0068 (in dioxane).

The imidazol-ols *(3a)* and *(3b)* used as starting materials were prepared by condensing phenanthraquinone monoxime or benzil monoxime, respectively, with concentrated ammonia solution and benzaldehyde in ethanol. *(3a)*: colorless crystals, m.p. 232–235 °C (solidifies, after melting, to a substance of m.p. 285–290 °C). *(3b)*: colorless crystals, m.p. 240–241 °C (decomp.).

Imidazol-1-ol *N*-oxides *(4c)* and *(4d)* were prepared as described in the literature[3,4]. *(4b)* was synthesized by *Bodendorf* and *Towliati*[5], and similarly but independently by us, by condensation of benzil α-monoxime and α-benzaldoxime. *(4b)*: colorless crystals, m.p. 231–232 °C (decomp.).



(4a)



(5)

We obtained compound *(4a)* by condensing phenanthraquinone dioxime and benzaldehyde at 5–10 °C in ethanol that was saturated with hydrogen chloride. Colorless crystals, m.p. 188–189 °C (decomp.); at 60–65 °C the isomer *(5)* is formed as main product alongside *(4a)*. *(5)*: yellow crystals, m.p. 184–185 °C.

The structures of compounds *(3a)*, *(3b)*, *(4a)*, *(4b)*, and *(5)* were proved by the IR, NMR, and mass spectra, as well as by reduction with hydrogen and Raney nickel in ethanol. This reduction gave the corresponding imidazoles from *(3a)* and *(3b)* and *(4a)* and *(4b)* with consumption of one and two molecular equivalents, respectively, of hydrogen. Benzyl alcohol and 9,10-phenanthrenediamine were formed from *(5)* on consumption of four molecular equivalents of hydrogen.

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[*] Dipl.-Chem. K. Volkamer, Dr. H. Baumgärtel, and Prof. Dr. H. Zimmermann
Institut für Organische Chemie der Universität
Karlstr. 23
8 München 2 (Germany)

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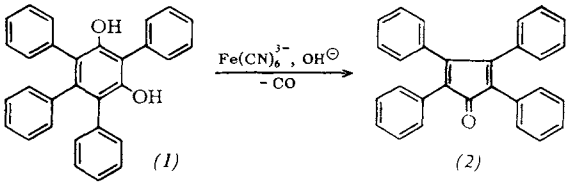
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Ring Contraction on Oxidation of Phenyl-substituted Resorcinols

By *H. Güsten, G. Kirsch*, and *D. Schulte-Frohlinde*[*]

Oxidation of 2,4,5,6-tetraphenylresorcinol *(1)* in benzene with alkaline $K_3[Fe(CN)_6]$ solution affords deep red crystals of tetraphenylcyclopentadienone (tetracyclone) *(2)* in 47% yield.



(1) *(2)*

The tetracyclone was identified by elemental composition, molecular weight, mixed melting point, UV spectrum (512 nm, ε = 1300; 342 nm, ε = 6700 in benzene)[1], and IR spectrum (C=O band at 1718 cm^{-1})[2]. The 100 MHz NMR spectrum in $CDCl_3$ at 30 °C contains a sharp singlet at τ = 2.76 and two groups of multiplets centered at approximately τ = 2.81 and 3.04[3]. The CO evolved can be detected by means of an aqueous $PdCl_2$ solution. The oxidation has also been effected with PbO_2 and tetrachloro-*o*-benzoquinone[4], but yields are poorer.

Oxidation of 2,4,6-triphenylresorcinol gives 2,3,5-triphenylcyclopentadienone, and that of 2,4-diphenylnaphthoresorcinol gives 2,3-diphenyl-1-indenone.

The deeply colored solutions obtained on oxidation give strong ESR signals.

Experimental: A solution of tetraphenylresorcinol (1 g, 2.4 mmoles) in benzene (80 ml) is added dropwise to solution of $K_3[Fe(CN)_6]$ (4 g, 12 mmoles) and KOH (0.6 g) in water (15 ml) at room temperature and with vigorous stirring. The deep-red benzene solution is separated off after 3 h, washed with water, and, after drying, chromatographed on an Al_2O_3

(II, standard) column. Deep-red crystals of *(2)* are obtained; m.p. 217–218 °C (from petroleum ether), yield 0.44 g (47 %).

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[*] Dr. H. Güsten, G. Kirsch, and
Priv.-Doz. Dr. D. Schulte-Frohlinde
Kernforschungszentrum Karlsruhe,
Institut für Strahlenchemie
Postfach 947
75 Karlsruhe (Germany)

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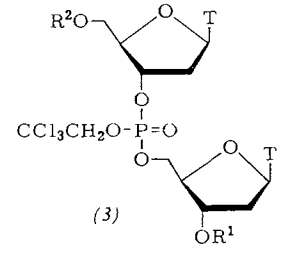
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Oligonucleotide Syntheses by means of 2,2,2-Trichloroethyl Phosphorodichoridate [1]

By *F. Eckstein* and *I. Rizk* [*]

Although phenyl phosphorodichloridate has proved useful in phosphatide chemistry for the preparation of unsymmetrical phosphoric acid esters, monoesters of phosphorodichloridic acid have been applied successfully in nucleotide chemistry only for the synthesis of symmetrical esters, *e.g.* diuridine 5′→5′-phosphate [2].

We have found that the 2,2,2-trichloroethyl phosphorodichloridate *(1)* [3] can be used for the step-wise preparation of oligonucleotides with the desired 3′ → 5′-linkage. 5′-Tritylthymidine (1 equiv.) in chloroform was added dropwise over a period of 6 h, with stirring, to a solution of *(1)* (1.2 equiv.) and pyridine (2.5 equiv.) in chloroform. The mixture was stirred for a further 24 h. The tritylthymidine was thus phosphorylated to 5′-tritylthymidine 3′-[2,2,2-trichloroethyl phosphorochloridate] *(2)* which was neither characterized nor isolated; bis(5′-tritylthymidine-3′) tris(2-chloroethyl) phosphate was formed only in traces. The solution was evaporated with exclusion of moisture and the resulting residue was dissolved in anhydrous pyridine. This solution was treated with 3′-*O*-acetylthymidine (0.7 equiv.) and, after the mixture had been kept for 48 h at room temperature, the pyridine was evaporated off and the reaction mixture was separated by preparative thin-layer chromatography (Merck Kieselgel PF 254, chloroform/methanol = 93:7). The triester *(3a)* [4], m.p. 127–130 °C, was obtained in 56 % yield (calculated on acetylthymidine).



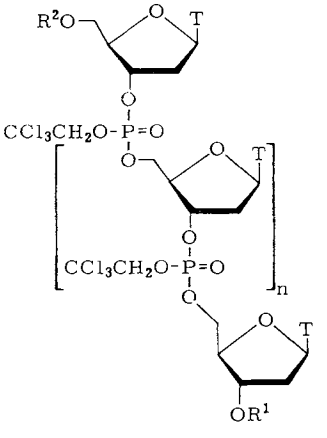
(3)

(3a), R^1 = Acetyl
R^2 = Trityl

(3b), R^1 = Acetyl
R^2 = H

(3c), R^1 = H
R^2 = Trityl

(3d), R^1 = $-PCl(O)OCH_2CCl_3$
R^2 = Trityl



(4), n = 1
R^1 = Acetyl
R^2 = Trityl

(5), n = 2
R^1 = Acetyl
R^2 = Trityl

	R_F [a]		R_F [a]
5′-Tritylthymidine	0.70	*(3c)*	0.40
3′-Acetylthymidine	0.61	*(4)*	0.51
(3a)	0.83	*(5)*	0.48
(3b)	0.43		

[a] On Merck DC-Fertigplatten Kieselgel F_{254}, chloroform/methanol = 93:7.

Removing the trityl group by treatment with 80 % acetic acid at 100 °C for 15 min affords *(3b)*. If *(3b)* is used in place of 3′-*O*-acetylthymidine in the reaction described, the product *(4)* [4] is obtained in 40 % yield after the same working up procedure.

We also tried to prepare a tetranucleotide from two dinucleotides in this way. Removing the acetyl group from *(3a)* (12 % ammonia solution, 1 h, room temperature) gives *(3c)* in quantitative yield. The triester is not hydrolysed under these conditions. Compound *(3c)* is phosphorylated by *(1)* to give *(3d)*, in a similar manner to that described for *(3a)*. After evaporation of the solution, the residue is taken up in anhydrous pyridine, and a solution of *(3b)* in pyridine is added. The mixture is kept for 12 h at 50 °C, then worked up by preparative thin-layer chromatography. Compound *(5)* is thus obtained in poor yield (3 %).

Removal of the trichloroethyl groups (Zn dust in 80 % acetic acid, 10 min, room temperature), the trityl (80 % acetic acid, 100 °C, 15 min), and the acetyl groups (concentrated ammonia solution, 2 h, room temperature) from compounds *(3a)*, *(4)*, and *(5)*, gives the nucleotides TpT, TpTpT, and TpTpTpT, respectively, in about 80 % yield. We were able to degrade these products by means of phosphodiesterase from spleen to thymidine and thymidine 3′-phosphoric acid in the expected proportions.

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[*] Dr. F. Eckstein and Dipl.-Chem. I. Rizk
Max-Planck-Institut für experimentelle Medizin,
Abteilung Chemie
Hermann-Rein-Str. 3
34 Göttingen (Germany)

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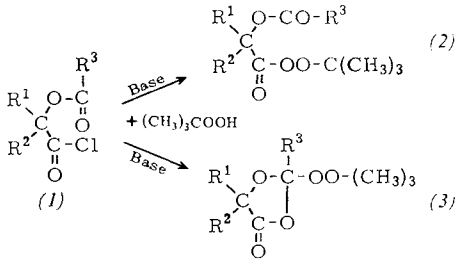
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New High-temperature Initiators [1]

By *Ch. Rüchardt* and *G. Hamprecht* [*]

t-Butyl α-acyloxypercarboxylates *(2)* have been obtained from acid chlorides *(1)* and t-butyl hydroperoxide in pyridine. They belong to a new class of active low-temperature initiators [2]. We have now found that 2,5,5-trisubstituted 2-t-alkylperoxy-1,3-dioxolan-4-ones *(3)* are formed from the same components *(1)* and t-alkyl hydroperoxides under certain conditions [3]. These are more stable than most of the known peroxides [*e.g.* *(3)*, $R^1 = CH_3$, $R^2 = C_2H_5$, R^3 = iso-C_3H_7: $t_{1/2}$ = 40 min in decalin at 172 °C] and form a new class of readily accessible, very reactive, high-temperature initiators. A new type of neighboring group participation of the α-acyloxy group during the acylation [4] is responsible for the ring closure.



R^1	R^2	R^3	Base	(3), Yield[a]
CH_3	CH_3	CH_3	Pyridine	0
CH_3	CH_3	CH_3	2,6-Lutidine	100
CH_3	C_2H_5	CH_3	Pyridine	20
CH_3	C_2H_5	CH_3	None	100
C_2H_5	C_2H_5	CH_3	Pyridine	100 [b]
C_2H_5	C_2H_5	CH_3	2,6-Lutidine	100
CH_3	iso-C_3H_7	CH_3	Pyridine	80
C_2H_5	C_2H_5	C_2H_5	Pyridine	70
C_2H_5	C_2H_5	C_6H_5	Pyridine	40
$-(CH_2)_4-$		CH_3	$NaOH/H_2O$	100
$-(CH_2)_5-$		CH_3	Pyridine	72
$-(CH_2)_5-$		CH_3	2,6-Lutidine	100 [c]
CH_3	C_2H_5	p-$CH_3O-C_6H_4-CH_2-$	None	100

[a] Given as % of *(3)* in the mixture of *(2)* and *(3)*; total yields were usually greater than 60%.

[b] Same result with t-pentyl hydroperoxide.

[c] Same result with aqueous sodium hydroxide as base.

If in *(1)* neither R^1 nor R^2 is hydrogen, then ring closure is favored by increase in size of R^1 and R^2, by a smaller group R^3, and by a bulky base (*e.g.* 2,6-lutidine or triethylamine). The ring closure is kinetically controlled. *(1)*, $R^1 = R^3 = CH_3$, $R^2 = C_2H_5$, and *(1)*, $R^1 = R^2 = CH_3$, $R^3 = S\text{-}C_6H_4\text{-}CH_2$, in absence of a base, give *(3)* almost exclusively.

Acid chlorides *(1)* in which R^1 or R^2 is hydrogen, even with the bulky base ethyldiisopropylamine, afford only a little *(3)*. On the other hand, even in the absence of base, *O*-acetyllactoyl chloride *(1)*, $R^1 = H$, $R^2 = R^3 = CH_3$, and *O*-acetylglycoloyl chloride *(1)*, $R^1 = R^2 = H$, $R^3 = CH_3$, give *(3)* almost exclusively[5].

The composition and the active-oxygen content of the oily peroxides were determined. The dioxolane derivatives *(3)* can be quantitatively and qualitatively analysed by means of the carbonyl bands near 1800 cm^{-1} [*(2)*, C=O at 1735 and 1775 cm^{-1}] and the NMR signal of the methyl group R^3 at $\tau = 8.33$ [*(2)*, $R^3 = CH_3$, $\tau = 7.96$].

Experimental: 4.11 g (25.0 mmole) of α-acetoxyisobutyryl chloride in 15 ml of petrol ether (b.p. 40 °C) or methylene chloride was added dropwise over 15 min to a stirred solution of 3.22 g (30.0 mmole) of 2,6-lutidine and 3.60 g (40.0 mmole) of t-butyl hydroperoxide in 45 ml of the same solvent at 0 °C. After having been stirred for two hours the solution was filtered and subsequently washed neutral with dilute sulfuric acid, aqueous sodium bicarbonate, and water and dried over magnesium sulfate. It was quickly chromatographed on a 10 cm column of neutral Al_2O_3 (activity I) in order to remove residual hydroperoxide and was then concentrated in vacuum. 3.31 g (60%) of colorless, oily 2,5,5-trimethyl-2-t-butylperoxy-1,3-dioxolan-4-one (3 $R_1=R_2=R_3=CH_3$) was isolated having $n_D^{20} = 1.4189$ and containing 7.2% active oxygen (calc. 7.3%); IR spectrum showed C=O band at 1808 cm^{-1}; molecular weight (osmometric) = 243 (calc. 232). The same material was obtained when no base was present and the HCl formed was removed in a stream of nitrogen.

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[*] Priv.-Doz. Dr. Ch. Rüchardt and Dipl.-Chem. G. Hamprecht
Institut für Organische Chemie der Universität
Karlstr. 23
8 München 2 (Germany)

[1] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

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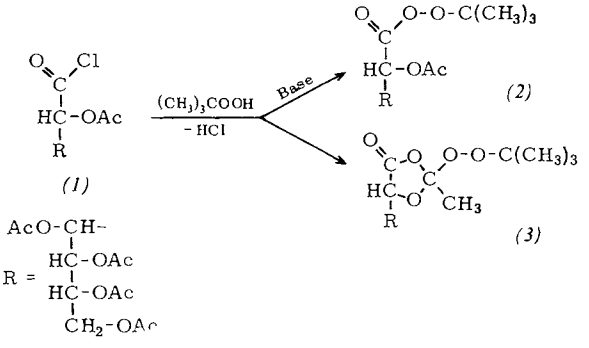
[4] Neighboring group participation of α-acyloxy groups in esterifications was observed also independently by *A. R. Mattocks*, J. chem. Soc. (London) *1964*, 1918, 4840. See also *E. E. Blaise*, Bull. Soc. chim. France (4) *1914*, 728.

[5] These investigations were stimulated by *H. Schulz*'s results in the sugar series [3]; we thank Frau *I. Mayer-Ruthardt* for carrying out the experiments.

Isomeric Peroxy Esters of Sugar Carboxylic Acids

By *Manfred Schulz* and *P. Berlin*[*]

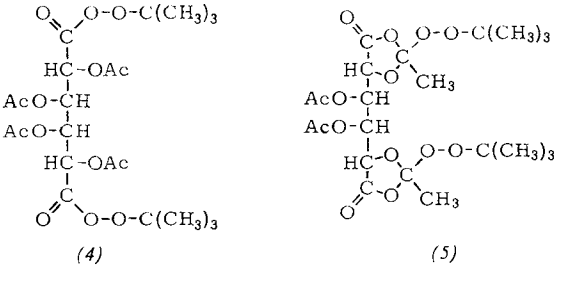
Reaction of penta-*O*-acetyl-D-gluconoyl chloride *(1)* with t-butyl hydroperoxide gives two isomeric peroxy esters. In the presence of bases such as 2,4,6-collidine, pyridine, or triethylamine in benzene at room temperature, t-butyl 2,3,4,5,6-penta-*O*-acetyl-D-peroxygluconate *(2)* is formed in 80% yield. M.p. 70–72 °C, $[\alpha]_D^{22} = +6.53°$ ($c = 3.5$ in $CHCl_3$), IR band of the perester-carbonyl at 1779 cm^{-1}.



However, in the absence of a base, reaction of the acid chloride *(1)* with t-butyl hydroperoxide gives exclusively the isomeric "anomalous perester" *(3)*[1]. 2-t-Butylperoxy-2-methyl-5-(D-*arabino*-1,2,3,4-tetracetoxybutyl)-1,3-dioxolan-4-one *(3)* is isolated in 90% yield after *(1)* has been heated with an excess of t-butyl hydroperoxide at *ca.* 70 °C for 4 h; it has m.p. 162–163 °C and $[\alpha]_D^{22} = -8.0°$ ($c = 3.7$ in $CHCl_3$). Ring closure to the 1,3-dioxolanone system, which occurs here under acid conditions, is caused by neighboring group participation of the α-acetyl group of *(1)*[2].

The structure of *(3)* was proved by elemental analysis, IR spectrum (acetyl-carbonyl 1747 cm^{-1}, dioxolanone-carbonyl 1813 cm^{-1}), and NMR data (t-butyl protons, $\tau = 8.77$; acetyl-CH_3 protons, $\tau = 7.94$; CH_3 protons of the methyl group on the dioxolanone ring, $\tau = 8.30$).

Reaction of tetra-*O*-acetylmucoyl dichloride with t-butyl hydroperoxide in the presence of pyridine gives the bisperoxy ester *(4)*, m.p. 126 °C (decomp.), in 91% yield. Warming the acid chloride with an excess of t-butyl hydro-

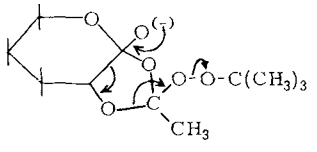


peroxide *without* a base gives exclusively *(5)*, m.p. 211 to 213 °C (90 % yield).

Treatment of *(2)* or *(3)* with methanolic 0.01 N $NaOCH_3$ solution causes a sugar degradation by a new type of perester degradation. The anomalous peroxy ester *(3)* is completely decomposed within 5 h at room temperature, yielding 70 % of D-arabinose (crystalline, paper-chromatographically pure), 66 % of carbon dioxide, t-butyl alcohol, and methyl acetate, with 30 % of methyl D-gluconate as by-product (percentages calculated with respect to compound *(3)*). Complete decomposition of the normal peroxy ester *(2)* requires more energetic conditions: after 8 hours' warming at 60 °C, D-arabinose was isolated in 51 % yield.

The diperoxy compounds *(4)* and *(5)* are not degraded with C–C cleavage by sodium methoxide solution; only transesterification and deacetylation occur, yielding dimethyl mucate (90 %).

We interpret the decomposition of *(3)* as fragmentation[3] of an intermediate pyranoid compound *(6)*. Presumably, *(2)* also decomposes by way of a cyclic intermediate.



(6)

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[*] Dr. Manfred Schulz and Dipl.-Chem. P. Berlin
Institut für Organische Chemie der Deutschen Akademie der Wissenschaften zu Berlin
An der Rudower Chaussee
DDR 1199 Berlin-Adlershof (Germany)

[1] An analogous synthesis of 5,5-disubstituted 2-t-butylperoxy-1,3-dioxolan-4-ones was recently discovered independently by *Ch. Rüchardt* and *G. Hamprecht*, Angew. Chem. 79, 939 (1967); Angew. Chem. internat. Edit. 6, 949 (1967).

[2] For neighboring group participation of α-acetoxy groups in esterifications compare *A. R. Mattocks*, J. chem. Soc. (London) *1964*, 1918, 4840.

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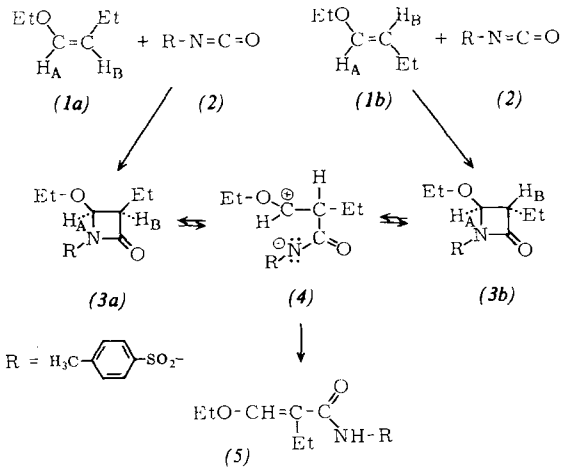
Stereochemistry of the Cycloaddition of Sulfonyl Isocyanates and *N*-Sulfinylsulfonamides to Enol Ethers [1]

By *F. Effenberger* and *G. Kiefer* [*]

4-Alkoxyazetidin-2-ones *(3)* are formed on cycloaddition of sulfonyl isocyanates to enol ethers under mild conditions[2]. We have now studied the stereochemistry of this reaction in order to decide between a synchronous mechanism, as proposed by *Huisgen et al.*[3] for the cycloaddition of ketenes to enol ethers, and a two-stage reaction involving an intermediate compound of type *(4)*.

The *cis*- and *trans*-1-butenyl ethyl ethers *(1a)* and *(1b)*, which are separable by preparative gas chromatography, were treated separately in $DCCl_3$ with *p*-tosyl isocyanate *(2)* in the molar proportions 1:1, and the progress of the reaction was followed by NMR spectroscopy (Table).

One minute after the reactants had been mixed the signals of *(1a)* (H_A = doublet at τ = 4.18, H_B = quadruplet at τ = 5.74; J_{AB} = 6.3 Hz) and *(1b)* (H_A = doublet at τ = 3.82, H_B = 2 triplets at τ = 5.32; J_{AB} = 12.6 Hz) had disappeared, whence it is concluded that there is very rapid reaction with *(2)*.



Reaction of *(2)*

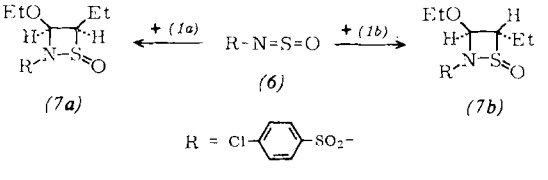
with *(1a)*			with *(1b)*		
Reaction time (min)	*(3a)* (%)	*(3b)* (%)	Reaction time (min)	*(3a)* (%)	*(3b)* (%)
1	95	—	1	10	90
3	90	10			
7	80	20	5	15	85
10.5	75	25			
18	65	36			
23	54	46	24	20	80
62	30	70	63	23	77
1440	27	73	1440	27	73

The proportions of the β-lactams *(3a)* and *(3b)* formed (see table) can be obtained from the newly appearing resonance signals of the proton H_A in *(3a)* or *(3b)* with an accuracy of about ± 4 %. *(3a)*: H_A gives a doublet at τ = 4.5, J_{AB} 5.3 Hz; *(3b)*: H_A gives a doublet at τ = 4.81, J_{AB} = 2 Hz. The structures *(3a)* and *(3b)* are assigned on the basis of the coupling constants J_{AB}[4].

From the table it can be seen that *(1a)* reacts stereospecifically with *(2)* and that *(1b)* reacts stereoselectively, but that after somewhat more than an hour an equilibrium mixture containing 27 % of *(3a)* and 73 % of *(3b)* is formed from either pure *(1a)* or pure *(1b)*. The isomerization *(3a)* ⇄ *(3b)* is formulated as occurring by way of a resonance-stabilized polar intermediate *(4)*.

When kept for several days in $DCCl_3$ the equilibrium mixture of *(3a)* and *(3b)* rearranges to the thermodynamically more stable compound *(5)*, the compound *(4)* being again assumed as intermediate.

Enol ethers combine with *N*-sulfinylsulfonamides to give 1,2-thiazetidine 1-oxides *(7)*[5]. NMR spectroscopic studies conducted during this cycloaddition in $DCCl_3$ show a stereospecific reaction of both *(1a)* and *(1b)*. The products *(7a)* and *(7b)* do not isomerize and do not rearrange on long storage in $DCCl_3$.



(7a) *(6)* *(7b)*

The results show that in the reaction of enol ethers with polar reagents the kinetically controlled cycloaddition occurs largely synchronously. Quite possibly, different bond lengths are to be considered for the transition state[6]. Depending on the ring strain, isomerization and removal of a proton occur,

both under thermodynamical control, to give a stable substitution product.

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[*] Doz. Dr. F. Effenberger and Dipl.-Chem. G. Kiefer
Institut für Organische Chemie der Universität
Azenbergstr. 14/16
7 Stuttgart (Germany)

[1] This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

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Derivatives of Imidobissulfamide [1]

By *R. Appel* and *R. Helwerth* [*]

Sulfimide, $HNSO_2$, has been assumed to be a reactive intermediate in the reaction of sulfamoyl chloride with nitrogenous bases. Hitherto, however, it has been isolated only as the pyridinium salts of the oligomers, tri- and tetra-sulfimide [2]. *Atkins* and *Burgess* [3] proved the formation of *N*-substituted derivatives of sulfimide, $RNSO_2$ (*N*-sulfonylamines), on treatment of *N*-substituted sulfamoyl chlorides with tertiary amines at −78 °C.

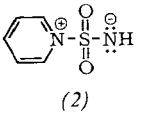
We have found that sulfamoyl(trialkylammonio)sulfonyl imides *(1)* are formed when a solution of sulfamoyl chloride in acetonitrile is treated at −40 °C with tertiary nitrogenous bases such as trimethyl- or triethyl-amine or pyridine in the molar ratio 2:3. They are nitrogen analogues of the mesylsulfenamine adducts recently described by *Opitz* and *Bücher* [4].

$$2\ H_2NSO_2Cl + 3\ NR_3 \longrightarrow H_2N\text{-}SO_2\text{-}\ddot{\underset{\ddot{}}{N}}^{\ominus}\text{-}SO_2\text{-}\overset{\oplus}{N}R_3 \quad (1)$$
$$+$$
$$2\left[HNR_3\right]^{\oplus}Cl^{\ominus}$$

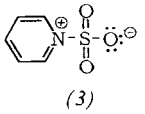
	R	M.p. (°C)	Yield (%)
(1a)	CH_3	154–156	90
(1b)	C_2H_5	94–96	47
(1c)	$NR_3 = C_5H_5N$	Rearrangement above 105 °C	68

The compounds *(1)* are precipitated, sometimes with the amine hydrochlorides, from which they can be separated readily by utilizing their poor solubility in cold water.

When sulfamoyl chloride is treated with pyridine below −80 °C, a very reactive intermediate (m.p. 57–65 °C) can be isolated, which dissolves in water to an acid solution. Within a few seconds this clear solution deposits the neutral compound *(1c)*. Slow heating of the reactive intermediate affords first this product *(1c)*, which, when further heated, resolidifies and is converted into the known pyridinium salts of tri- and tetra-sulfimide [2]. Further experiments are to be performed to decide whether the reactive intermediate is the pyridine adduct *(2)* of monomeric $HNSO_2$, which is isoelectronic with the known pyridine-SO_3 adduct *(3)*.



(2)



(3)

The structure of compounds *(1a)* to *(1c)* follows from their elemental analysis, IR and ^1H–NMR spectra, and the lack of conductivity of freshly prepared solutions.

The behavior of the compounds is similar to that of the SO_3-amine adducts, *e.g.* stronger bases replace weaker ones from their linkage to the S atom. With liquid ammonia they give a quantitative yield of the NH_4^+ salt of imidobissulfamide, which was identified by conversion into free imidobissulfamide *(7a)* [5].

The action of primary or secondary amines on compounds *(1a)* to *(1c)* provides a synthesis of trialkylammonium salts of monosubstituted *(4)* and asymmetrically di-*N*-substituted imidobissulfamides *(5)*. They can be converted by ion-exchangers or by treatment of their silver salts with the calculated amounts of hydrochloric acid into the free, hitherto unknown asymmetrically substituted imidobissulfamides *(6)* and *(7)* in yields exceeding 90 %.

$$H_2N\text{-}SO_2\text{-}\ddot{\underset{\ddot{}}{N}}^{\ominus}\text{-}SO_2\text{-}\overset{\oplus}{N}R_3 + HNR_2' \longrightarrow [H_2N\text{-}SO_2\text{-}\ddot{\underset{\ddot{}}{N}}\text{-}SO_2\text{-}NR_2']^{\ominus}[HNR_3]^{\oplus} \quad (4)$$

$$H_2NR' \longrightarrow [H_2N\text{-}SO_2\text{-}\ddot{\underset{\ddot{}}{N}}\text{-}SO_2\text{-}NHR']^{\ominus}[HNR_3]^{\oplus} \quad (5)$$

$H_2N\text{-}SO_2\text{-}NH\text{-}SO_2\text{-}NR_2'$ *(6)*

$H_2N\text{-}SO_2\text{-}NH\text{-}SO_2\text{-}NHR'$ *(7)*

	R'	M.p. (°C)
(6a)	C_2H_5	Liquid
(6b)	NR'_2 = piperidine	110–111
(7a)	H	167–168
(7b)	C_6H_{11}	124–125
(7c)	C_6H_5	154–155
(7d)	iso-C_3H_7	97–100

Compounds *(6)* and *(7)* dissolve readily in water, giving strongly acid solutions. Sulfate ions can be detected therein only after addition of sodium nitrite. These well-crystalline materials are stable in air.

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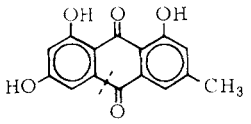
[*] Prof. Dr. R. Appel and Dipl.-Chem. R. Helwerth
Anorganisch-Chemisches Institut der Universität
Meckenheimer Allee 168
53 Bonn (Germany)

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[2] *R. Appel* and *G. Berger*, Z. anorg. allg. Chem. *327*, 114 (1964).
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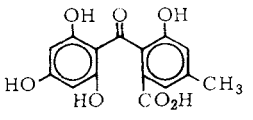
Model Reactions for Biological Ring Opening of Anthraquinones [1]

By *B. Franck, V. Radtke*, and *U. Zeidler* [*]

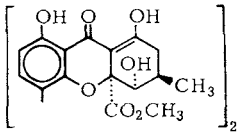
Although the biosynthesis of more than 100 natural anthraquinone pigments is largely clarified [3,4], very little is known about their biological degradation. This must begin with an oxidative opening of the quinonoid ring. We have previously reported the detection of such a ring opening as a metabolic reaction [2]. It was shown by feeding experiments with radioactively labeled precursors that ergochromes [5], *e.g.* secalonic acid A *(3)*, are formed from emodin *(1)* by way of the acid *(2)*. We have now found a reaction sequence that may serve to explain this oxidative ring opening *(1)* → *(2)* that was previously unknown in anthraquinone chemistry.



(1)

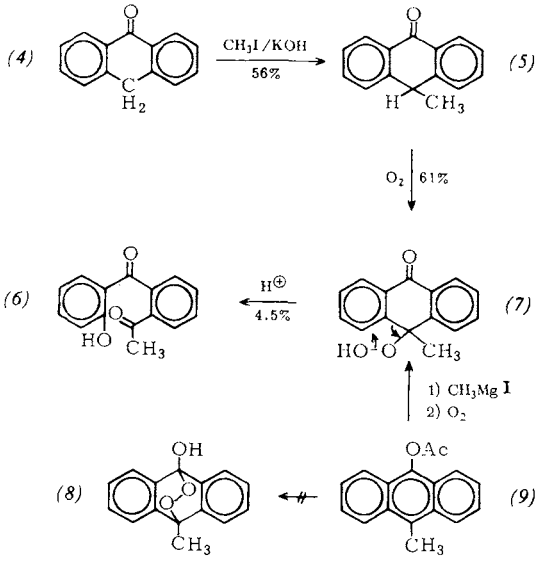


(2)



(3)

We first ascertained that 19 systematically selected hydroxyanthraquinones, including emodin *(1)*, were stable to peracids (perbenzoic acid, peracetic acid, and trifluoroperacetic acid) which seemed most likely to effect ring opening, whereas benzophenone was cleaved smoothly thereby. Thus it is unlikely that anthraquinones themselves are liable to biological ring opening. Anthrones *(4)*, on the other hand, which are biogenetic precursors or reduction products of anthraquinones, can be considered as starting products for the ring cleavage.



10-Methylanthrone *(5)*, which was prepared from anthrone *(4)*, gave on reaction with O_2/azobisisobutyronitrile in benzene the hitherto unrecorded 10-methylanthronyl hydroperoxide *(7)* [m.p. 159–161 °C (decomp.)]. This was rearranged by CH_3CO_2H/4 N H_2SO_4 (4:3), with ring opening, to 2-acetyl-2′-hydroxybenzophenone *(6)* (m.p. 108 °C); an approximately equal yield of anthraquinone, formed by elimination of methanol, was also obtained. The structure of *(6)* was confirmed by elemental analysis, UV spectrum in CH_3OH (λ_{max} = 253, 328 nm), IR spectrum in KBr ($\nu_{C=O}$, chelated = 1635, $\nu_{C=O}$ = 1685 cm^{-1}), and mass spectrum [*m/e* = 240 ($M^{\ominus}$, 100%) 197 (M − CH_3CO), 147 (M − C_6H_4OH), 121 (M − C_6H_4CO–CH_3)]. The proton-catalysed rearrangement of *(7)* is analogous to the rearrangement of cumyl hydroperoxide and may follow the same mechanistic route. Attempts by *Money*[6] and by us to effect this ring opening with anthrone *(4)* or anthranol in place of *(5)* failed because of the instability of the corresponding hydroperoxides.

10-Methylanthronyl hydroperoxide *(7)* was obtained, not only by autoxidation of 10-methylanthrone *(5)*, but also by another route which was stated by *Julian, Cole*, and *Diemer*[7] to lead to 9,10-epidioxy-10-methylanthranol *(8)*. The action of CH_3MgI on 10-methylanthryl acetate *(9)* and subsequent autoxidation gave a product $C_{15}H_{12}O_3$ that agreed in m.p. and other properties with the hydroperoxide *(7)* and with the material previously described as *(8)*[7]. There is no doubt that its structure is that of *(7)*[8], as is shown by, *inter alia*, its anthrone-like UV spectrum in cyclohexane (λ_{max} = 219, 271 nm) and its IR spectrum in KBr ($\nu_{C=O}$ = 1640 cm^{-1}); further, mass and NMR spectra support structure *(7)*.

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[*] Prof. Dr. B. Franck, Dipl.-Chem. V. Radtke, and
Dipl.-Chem. U. Zeidler
Institut für Organische Chemie der Universität
Neue Universität
Olshausenstr. 40–60
23 Kiel (Germany)

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Bis(triphenylphosphine)triazenium Tetrachloroantimonate(III) [1]

By *N. Wiberg* and *K. H. Schmid*[*]

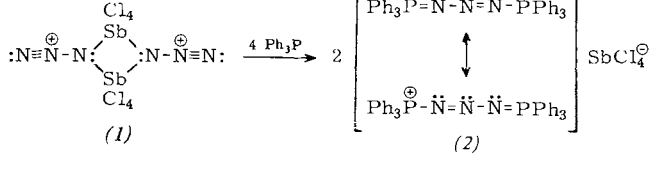
Antimony azide tetrachloride *(1)* contains[2] *N*-diazenium groups. An ability to add bases is typical of diazenium groups attached to carbon. In order to see whether this ability is possessed by azenium groups bonded to nitrogen we treated the salt *(1)* with triphenylphosphine.

This reaction, however, did not lead to the adduct containing the group $\overset{\oplus}{N}=N-N=PPh_3$. The adduct is probably formed as intermediate but at once decomposes to other products. The course of the reaction is determined by the redox reaction:

$$Sb(V) + P(III) \rightarrow Sb(III) + P(V)$$

When *(1)* is treated in benzene with PPh_3 in the molar ratio 1:4 (2 h at 20 °C), the antimony is reduced, the phosphorus is oxidized, and a quantitative yield of bis(triphenylphosphine)-triazenium tetrachloroantimonate(III) *(2)* is obtained as insoluble product[3].

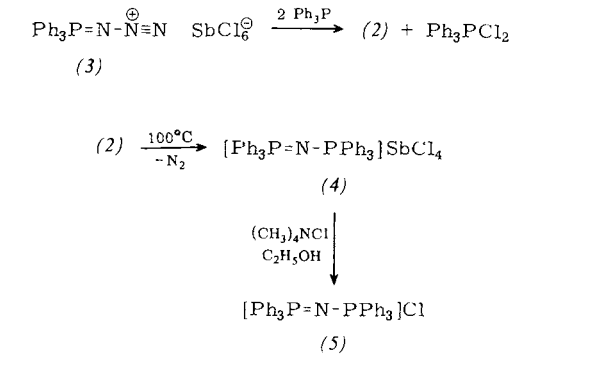
The cation *(2)*, an aza vinylogue of the known cation $Ph_3PNPPh_3^+$[4], is the first example of a compound containing a PNNNP group. The salt *(2)* forms yellow crystals,



(1) (2)

which melt at 90 °C with decomposition and are insoluble in apolar solvents but soluble in CH_2Cl_2. The charge on the cation is spread equally over the PNNNP group, since only one signal appears in the ^{31}P–NMR spectrum.

The structure given is supported, not only by the composition, molecular weight, solubility relations, and IR and ^{31}P–NMR spectra, but also by the following facts: (i) Compound *(2)* can also be prepared from *(3)*[5] and triphenylphosphine, and (ii) *(2)* is converted quantitatively at 100 °C, with evolution of nitrogen, into the compound *(4)* (m.p. 168 to 169 °C) which can then be transformed into the known chloride *(5)* (m.p. 268 °C; lit.[4], m.p. 269–271 °C).



Treatment of tellurium azide trichloride, $TeCl_3N_3$[6], with Ph_3P in CH_2Cl_2 apparently causes simultaneous formation and thermal decomposition of the cation *(2)*, since the reaction occurs quantitatively, even at room temperature, in accord with the equation:

$$2\ Cl_3TeN_3 + 4\ Ph_3P \rightarrow [Ph_3P{=}N{-}PPh_3]_2TeCl_6 + 2\ N_2 + Te$$

Decomposition of the cation *(2)* may be catalysed by the tellurium produced.

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[*] Priv.-Doz. Dr. N. Wiberg and Dr. K. H. Schmid
Institut für Anorganische Chemie der Universität
Meiserstr. 1
8 München 2 (Germany)

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[2] *N. Wiberg* and *K. H. Schmid*, Chem. Ber. *100*, 741 (1967).

[3] Reaction of *(1)* with Ph_3P in the molar ratio 1:(1 to 2) gives, *inter alia*, $[Ph_3P{=}N{-}\overset{\oplus}{N}{\equiv}N]SbCl_5N_3^-$ [5].

[4] *R. Appel* and *G. Büchler*, Z. Naturforsch. *17b*, 422 (1962).

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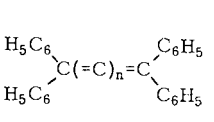
[6] Preparation:
$Cl_4Te + (CH_3)_3SiN_3 \rightarrow Cl_3TeN_3 + (CH_3)_3SiCl$.

UV-Absorption of α,α,ω,ω-Tetraphenylcumulenes with Coplanar Benzene Rings [1]

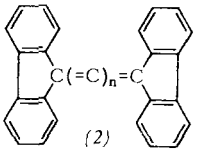
By *H. Fischer* and *W. D. Hell*[*]

Cumulenes containing an odd number of cumulated double bonds mostly give very intense long-wave bands in their UV spectra and are thus suitable for a study of the influence of substituents on the spectrum. If the positions of the longest-wavelength bands for tetraphenylcumulenes *(1)* and bis-biphenylenecumulenes *(2)* are calculated by HMO methods (all $\alpha_i = 0$, all β_{ik} for bonded centres $= \beta$) it transpires that corresponding compounds of the two series should differ only slightly from one another. Experimentally, however, cumulenes of type *(2)* absorb at longer wavelengths, by *ca.* 60 nm (2000 to 3000 cm^{-1}), than do the corresponding cumulenes of type *(1)*[2]. This discrepancy is apparently due to a non-planar arrangement of the geminal benzene rings of *(1)*. Cumulenes in which the positions of the phenyl groups are exactly known would therefore be of interest.

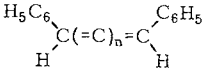
In the series of α,ω-diphenylcumulenes *(3)* the spectrum of 1,6-diphenylhexapentaene is known[3]. Starting from 9,9-dimethyl-10-anthrone[4], we have prepared the butatriene, hexapentaene, and octaheptaene of the series *(4)* by standard methods[2]. In these cumulenes the geminal "benzene" rings should be essentially coplanar.



(1)

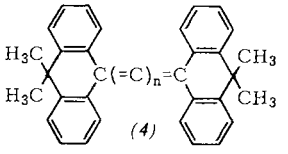


(2)



(3)

n = 2, 4, 6



(4)

Table 1.

n in *(4)*	M.p. (°C)	Color of soln. in $CHCl_3$	λ_{max} (mμ) [log ε] in $CHCl_3$
2	260	Orange-yellow	481 [4.68], 295 [4.46], 284 [4.49]
4	>360 (dec.)	Red-violet	555 [5.04], 520 [4.68], 437 [3.78], 382 [3.96], 311 [4.43], 293 [4.45]
6 [a]		Blue	610 [5.2], 560 [4.7], 472 [4.6]

[a] Not yet isolated in crystalline form; extinction estimated.

As expected, the cumulenes *(4)* absorb at appreciably longer wavelengths than do the corresponding cumulenes *(1)*. The non-planarity of the benzene rings in *(1)* can be taken into account in the HMO calculations by reducing the resonance integrals for the bonds from the benzene rings to the cumulene chain. The best results are obtained by taking a resonance integral of 0.85 β for these bonds. Table 2 shows a comparison of the positions of the longest-wavelength UV bands for the cumulenes *(1)* to *(4)* as calculated by HMO methods (least squares refinement) with the values found experimentally. The deviations are within reasonable limits.

Table 2. Comparison of the calculated and experimental values (in eV) of the positions of the longest-wavelength UV bands for the cumulenes *(1)* to *(4)*.

n	*(1)*		*(2)*		*(3)*		*(4)*	
	HMO	exp.	HMO	exp.	HMO	exp.	HMO	exp.
2	2.95	2.95	2.52	2.58	3.28		2.64	2.58
4	2.53	2.55	2.24	2.27	2.76	2.75	2.31	2.23
6	2.24	2.22	2.03	2.09	2.41		2.07	2.04

If the resonance integral is set proportional to the cosine of the angle formed by the two neighboring π-orbitals then the benzene rings of the cumulenes *(1)* would have to be twisted out of plane by about 30°. On the basis of dipole moment measurements for 1,1-diphenylethylene, *Coates* and *Sutton*[5] also deduced an angle of twist of 30°; and a similar result was obtained from MO calculations for 1,1-diarylethylenes by *Simonetta* and *Carrà*[6].

It is remarkable that introduction of conjugation between the benzene rings [transition from the cumulenes *(4)* to *(2)*] leads to a small hypsochromic shift of the longest-wavelength

band (cf. Table 2). This result is not intelligible within the framework of the HMO theory.

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[*] Priv.-Doz. Dr. H. Fischer and W. D. Hell
Max-Planck-Institut für Medizinische Forschung,
Institut für Chemie
Jahnstr. 29
69 Heidelberg (Germany)

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Chemical Shifts of NMR Signals of the Acetyl Protons of β-Penta-*O*-acetylglucose

By *K. Heyns*, *W.-P. Trautwein*, and *F. Garrido Espinosa* [*]

The NMR signals of the acetoxyl groups of acetylated carbohydrates are often used for configurational and conformational analysis [1], a use that depends on the fact that the methyl protons of equatorial acetoxyl groups in general absorb at higher field than do such axial groups. Whereas this rule has proved its value for countless partially or completely acetylated pyranoses [2], halogeno sugars [3], amino hexoses [4], and inositols [5], there are only a few, and partially contradictory, indications as to how to assign the individual signals within each of these groups. It is sometimes assumed that acetoxyl groups on the primary C atom 6 of hexopyranoses absorb at highest field [1,6] and that acetoxyl groups above the plane of the ring are less shielded than those under the pyranose ring [7,8].

We have studied, by NMR spectroscopy, 2,3,4,6-, 1,3,4,6-, 1,2,3,6-, and 1,2,3,4-tetra-*O*-acetyl-β-D-glucopyranose that have been acetylated on the unsubstituted OH group by hexadeuterioacetic anhydride in pyridine. Whereas the NMR spectrum of unlabeled β-penta-*O*-acetylglucose shows four

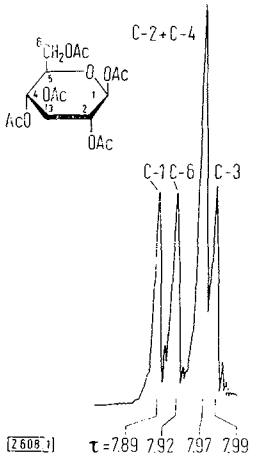


Fig. 1. ^{1}H—NMR spectrum of 1,2,3,4-penta-*O*-acetyl-β-D-glucose at 100 MHz in $CDCl_3$.

signals for the acetyl protons (one of these signals has double intensity), the spectra of all the labeled compounds lack one line, namely, that of the trideuterioacetyl group (Fig. 1). By selective labeling of individual acetyl groups it is possible to assign each line in the spectrum to a definite acetyl group. It was thus shown that the two signals at lowest field refer to groups on C-1 and C-6, whereas the line of relative intensity 2 is caused by the groups on C-2 and C-4; the signal at highest field was present in all the spectra and thus is to be ascribed to the group on C-3.

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[*] Prof. Dr. K. Heyns, Dr. W.-P. Trautwein, and
Dr. F. Garrido Espinosa
Chemisches Staatsinstitut,
Institut für Organische Chemie der Universität
Papendamm 6
2 Hamburg 13 (Germany)

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Occurrence of Cyclododecasulfur in Sulfur Melts

By *M. Schmidt* and *H.-D. Block* [*]

The physical properties of liquid sulfur have long been the subject of study [1], but it was only the theoretical propositions by *Powell* and *Eyring* [2], *Gee* [3], and in particular *Tobolsky* and *Eisenberg* [4] that made it possible to interpret satisfactorily its unusual behavior over the whole liquid range. Fundamental to the theory that is currently recognized is the assumption of temperature-dependent equilibria between cyclooctasulfur and catenaoctasulfur as "monomers" and of polycatenaoctasulfur as "polymer".

We now report experiments which throw doubt on this principle and at least necessitate refinement of, if not a change in, the theoretical interpretation. Working up sulfur that has been melted at 120 °C, 140 °C, 165 °C, 190 °C, 220 °C, 290 °C, 340 °C, 350 °C, or 370 °C and then brought quickly to the solid state by cooling in air, cold water, or liquid air leads in each case, reproducibly, to crystalline cyclododecasulfur [5], S_{12}, even if only in a "yield" of *ca.* 0.1 %. The sulfur used as starting material was free from S_{12}, as also from S_6 and S_8 that are formed by chain-building on decomposition of thiosulfate by acid [6]. Slow cooling of the melt (during 10 hours) leads, however, to pure S_8. This result shows that in sulfur melts there are also S_{12} rings in the equilibrium mixture alongside S_8, and it is certain that only a small part of the S_{12} rings survive transition, on cooling, into the S_8 rings that constitute the only thermodynamically stable form. It is, however, also probable that other, hitherto unisolated, rings S_x ($x < 12$ and in particular $x > 12$ – perhaps even $x \gg 12$) are present in the equilibrium of the melt, as previously postulated by *Krebs* [7]. It remains an open question to what extent the S_{12} content, already shown to be present slightly above the melting point, is responsible for the decrease of the "ideal" to the "natural" melting point.

Experimental Example: 20 g of sulfur is heated at 200 °C for 10 min. The vessel is cooled with tap water and the sulfur is divided as finely as possible and stirred for 12 hours with

100 ml of pure CS_2 at room temperature. The clear yellow solution, obtained by filtration from insoluble polymer, is concentrated to 20 ml in a vacuum and then cooled at −30 °C for 12 h. The mother liquor is decanted from precipitated sulfur, and the latter is treated dropwise, with careful shaking, with sufficient pure CS_2 (*ca.* 10 ml) to dissolve all the yellow S_8 and leave behind only the characteristic four-cornered platelets of S_{12}. After decantation of the solution, these platelets are washed with 1 ml of CS_2 and the remaining suspension of crystals is finally dried on filter paper. In this way 20 mg of S_{12} ("yield" *ca.* 0.1 %) of S_{12} is isolated, having m.p. 140–142 °C (146–148 °C after recrystallization from benzene).

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[*] Prof. Dr. M. Schmidt and Dipl.-Chem. H.-D. Block
Institut für Anorganische Chemie der Universität
Röntgenring 11
87 Würzburg (Germany)

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Photodimerization of Uracil Sensitized by Acetone

By *C. H. Krauch, D. M. Krämer, P. Chandra, P. Mildner, H. Feller*, and *A. Wacker* [*]

When a 10^{-3} M solution of uracil in acetone/water (1:3) is irradiated with light of wavelength 315 nm (1×10^6 erg/mm^2), four products are formed quantitatively, of which we have identified one as the *syn* head-to-head dimer of uracil by means of its R_F value [1]. Use of more than 50 % acetone as solvent during the irradiation leads to addition of about 5 % of acetone. This photosensitized dimerization of uracil may be more useful for molecular-biological studies than is the dimerization by UV light [2], since in the latter the uracil also adds water at the 5,6-double bond [3]. When cytosine is irradiated in aqueous acetone, a change in the molecule (including addition of acetone) can be observed only after radiation doses that have caused total reaction of uracil. Acetone-sensitized photodimerization of thymine has already been reported [4].

The effect of the reaction on the template activity of nucleic acids is shown by the following observations. When poly-A, poly-C, and poly-U [5] (1 mg/ml) in 23 % acetone are irradiated with light of wavelength 315 nm (3×10^5 erg/mm^2, grating monochromator, Bausch and Lomb, Rochester, USA; mercury high-pressure lamp HBO 200, Osram), the extinction at λ_{max} falls by 1 % for poly-A, by 6 % for poly-C, and by 61 % for poly-U. In cell-free protein synthesis (the reaction mixture contained, after *Nirenberg* and *Matthaei* [6], 80 μg/ml of poly-U or 120 μg/ml of poly-A or poly-C; specific activity of the [^{14}C]-amino acids = 3.6 mCi/mmole), the irradiation affects only the phenylalanine incorporation that is poly-U-dependent, this being inhibited to the extent of more than 80 %. If homopolynucleotides are used as templates for the synthesis of RNA with a polymerase from *Micrococcus lysodeikticus* [7], then again it is only the poly-U-dependent incorporation of AMP that is inhibited (by about 40 %). Thus photodimerization of uracil sensitized by acetone provides a further, mild method of specifically altering nucleic acids by photochemical methods.

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[*] Dr. C. H. Krauch
Max-Planck-Institut für Kohlenforschung
Abteilung Strahlenchemie
Stiftstr. 34–36
433 Mülheim, Ruhr (Germany)

Dr. D. M. Krämer, Dr. P. Chandra, Prof. Dr. P. Mildner, Frau H. Feller, and Prof. Dr. A. Wacker
Institut für Therapeutische Biochemie der Universität
Ludwig-Rehn-Str. 14
6 Frankfurt/Main (Germany)

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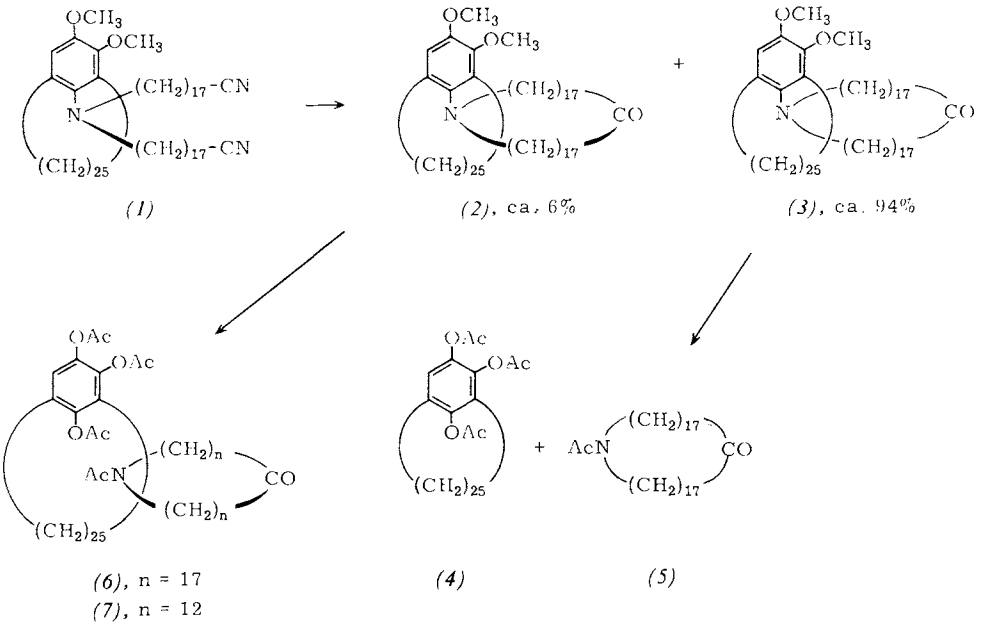
Synthesis of a Catena Compound by the Semistatistical Principle

By *A. Lüttringhaus* and *G. Isele* [*]

Cyclization of the dinitrile *(1)* [1] by Ziegler's method [2] affords the isomers *(2)* and *(3)* as viscous oils that are separable chromatographically on silica gel but give identical IR and NMR spectra. Since these products also give identical mass spectra (the same molecular ion and similar fragments), they are stereomers or topological isomers [3], differing only in that the macrocycles of *(2)* are intraannularly, and of *(3)* extraannularly, combined by the N atom.

The total yield from the cyclization amounted to 57 %. Of this, 5–8 % consisted of *(2)* and 92–95 % of *(3)*. Proof that only *(2)* is a pre-catena compound was provided by cleavage of the nitrogen-phenyl bond by way of the *o*-quinone according to the pattern established by *Schill* [4]. Compound *(3)* was cleaved into compounds *(4)* and *(5)*, but compound *(2)* was converted into the catena-compound *(6)*. The product *(6)* was shown to be homogeneous by thin-layer chromatography; its IR spectrum contains the expected CO frequencies at 1780 (phenolic acetyl groups), 1720 (keto group), and 1650 cm^{-1} (*N*-acetyl).

The mass spectrum of *(6)* is completely analogous to that of the catena-compound *(7)* prepared by *Schill* [4] by "planned" synthesis. Compound *(7)* is a homologue of *(6)*, having a heterocyclic ring smaller by 2×5 CH_2 groups; its mass spectrum was analysed by *Vetter* and *Schill* [5]. The mass spectrum of *(6)* shows the molecular ion at *m/e* = 1161; then follow, with increasing intensity, fragments at *m/e* = 1119, 1077, and 1035 (base peak) corresponding to stepwise removal of three molecules of ketene from the three *O*-acetyl groups; in the region *m/e* = 600 to 990 the mass spectrum is empty; below *m/e* = 600, the fragments of the separated rings appear, as is to be expected for a catenane of this structural type [5]. Thus the catena structure of *(6)* is proved too by the mass-spectrometric evidence.



This synthesis of *(6)* demonstrates unequivocally for the first time that, provided the steric stipulations are satisfactorily met, catenanes can be synthesized by a predominantly "statistical" method, which is simpler than the multi-step, strictly "planned" *Schill* principle[4] involving intermediate double linking of the two macrocycles. Further, our preliminary experiments indicate that the relative amounts of the stereomers *(2)* and *(3)* can be altered in favor of *(2)* by thermal equilibration of the conformers of *(1)* before the cyclization, so that the yield of *(6)* can also be increased.

Cyclization of (1) to (2) and (3):

Before the cyclization, the nitrile was heated in dioxane under nitrogen for 200 h at 100 °C. The dinitrile *(1)* (5.2 g) in anhydrous ether (250 ml) was added dropwise, with stirring, during 60 h to a boiling solution of Na-methylanilide in ether (0.66 M solution); after a further 5 h, water was added and the ethereal phase was separated. Ether, methylaniline, and ethylbenzene[2] were driven off in a vacuum and the residue was dissolved in propionic acid (20 ml) and treated with 50 % sulfuric acid (100 ml). The mixture was boiled under reflux in a nitrogen atmosphere for 9 h. Water was then added to the mixture and the whole was extracted with ether. After removal of the ether, the residue was dissolved in acetone (250 ml); dimethyl sulfate (10 ml) and potassium carbonate (20 g) were added, and the mixture was boiled, with stirring, under nitrogen for 5 h. The excess of dimethyl sulfate was hydrolysed, and the cyclization product was extracted into ether. The ethereal solution was washed with water and bicarbonate solution, dried with Na_2SO_4, and evaporated. The residue was chromatographed in benzene on a short column of neutral aluminum oxide. 3.2 g of eluate were obtained. The products *(2)* and *(3)* were separated by repeated chromatography on a SiO_2 column (55 cm long, 4 cm in diameter) with benzene.

Cleavage of (2) to (6), and (3) to (4) and (5):

Compound *(3)* (500 mg) was treated with HBr-saturated glacial acetic acid (50 ml), propionic acid (20 ml), and 48 % hydrobromic acid (10 ml) and boiled for 12 h under nitrogen. Water was added to the mixture and the whole extracted with ether. The ethereal solution was then washed with water and bicarbonate solution and finally evaporated. Further working up was analogous to that described by *Schill*[4]. The two separated rings *(4)* and *(5)* were obtained.

In the same way compound *(2)* (90 mg) afforded a product that was purified by chromatography on SiO_2 with ethyl acetate/benzene (7:3). The catenane *(6)* (60 mg) was obtained as a colorless oil.

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[*] Prof. Dr. A. Lüttringhaus and Dipl.-Chem. G. Isele
Chemisches Laboratorium der Universität
Albertstr. 21
78 Freiburg (Germany)

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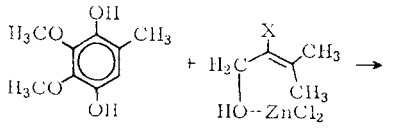
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Fluoro-coenzyme Q_1 (Fluoroubiquinone-5) [**]

By *H. Schumacher* and *H. Machleidt* [*]

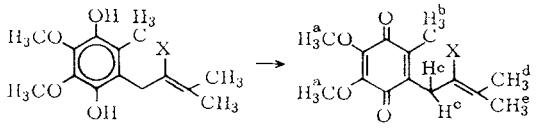
Ubiquinones (coenzyme Q)[1] are obtained on electrophilic substitution of *(1)* with isoprenols in the presence of Lewis acids and subsequent oxidation[2,3]. Homogeneous coenzyme Q_1 *(4a)* is obtained as a red oil, $\lambda_{max} = 274$ nm, $\log \varepsilon = 4.07$ (in CH_3OH), by treating *(1)* (0.51 g)[4] with 3-methyl-2-buten-1-ol *(2a)* (0.86 g) in anhydrous ether (75 ml) in the presence of anhydrous zinc chloride (12 g)[3] for 20 h with stirring under nitrogen, then distilling off the ether in a vacuum, partitioning the residue between petroleum ether/methanol/water (4:3:1), drying the petroleum ether layer, chromatographing it on Al_2O_3 (neutral, activity grade IV) with petroleum ether/ether (98 : 2), and treating the product with MnO_2[5]. 269 mg (39 %) of *(4a)* was obtained which was homogeneous on thin-layer chromatography on Kieselgel G with cyclohexane/ethyl acetate (8:2). A small amount (40 mg), of 2,3-dimethoxy-6-methyl-1,4-benzoquinone (coenzyme Q_0), arising from unreacted *(1)*, was also isolated from the products; it was characterized by $\lambda_{max} = 264$ nm, $\log \varepsilon = 4.14$ (in CH_3OH), and m.p. 54–57 °C.

Reaction of 2-fluoro-3-methyl-2-buten-1-ol *(2b)*[6] (2.40 g) with *(1)* (2.42 g) in anhydrous ether (90 ml) in the presence of $ZnCl_2$ (5.50 g), treatment of products as above, and preparative thin-layer chromatography on Kieselgel G with cyclohexane/ethyl acetate (8:2) gave coenzyme Q_1 *(4a)*



(1)

(2a), X = H
(2b), X = F
(2c), X = Cl



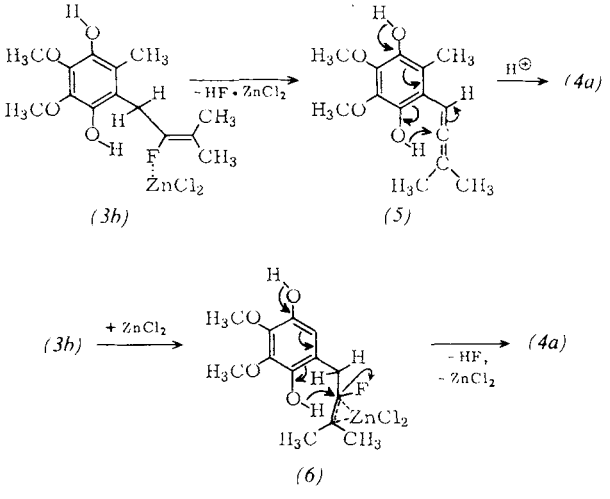
(3a), X = H
(3b), X = F
(3c), X = Cl

(4a), X = H
(4b), X = F
(4c), X = Cl

(95 mg) and fluoro-coenzyme Q_1 *(4b)* (53 mg). The latter is a red oil with λ_{max} = 272 nm, log ε = 4.08 (in CH_3OH); a better yield (20 %) of *(4b)* was obtained by condensing *(1)* (210 mg) with *(2b)* (500 mg) in anhydrous ether (15 ml) containing $AlCl_3$ (1.5 g) for 4 h. The ^1H–NMR spectrum of *(4b)* (60 MHz, in CCl_4) showed 6 H-a at 4.00 ppm, 3 H-b at 2.06 ppm (singlet), 2 H-c at 3.45 ppm (doublet, J = 22 Hz), 3 H-d at 1.78 ppm (doublet, J = 2.5 Hz), and 3 H-e at 1.62 ppm (doublet, J = 3.5 Hz).

Following a reaction under N_2 by thin-layer chromatography showed that formation of *(4a)* and *(3b)* begins about 5 min after the start and that the amount of *(4a)* increases during the reaction at the expense of *(3b)*. Oxidation of the sample gives compounds *(4a)* and *(4b)* and coenzyme Q_0. The coenzyme Q_1 *(4a)* that accompanies *(4b)* must arise by an intramolecular redox reaction *(3b)* → *(4a)* + HF. An intermolecular redox reaction *(1)* + *(3b)* → *(3a)* + Q_0 + HF or 2 *(3b)* → *(3a)* + *(4b)* + HF yields coenzyme Q_0 or *(4b)* directly and not only after oxidation of the sample.

The product *(4a)* can be formed from *(3b)* by an elimination-addition mechanism[7] by way of *(5)* or by an addition-elimination mechanism[8] by way of *(6)*.



(3b) (5) (6)

A solution of ethyl 2-chloro-3-methyl-2-butenoate (2.0 g) in anhydrous ether (5 ml) at −78 °C was added dropwise to a suspension of $LiAlH_4$ (500 mg) in anhydrous ether (45 ml). After 12 h at −50 °C the mixture was decomposed with saturated NH_4Cl solution and the products were subjected to the usual purification procedure to give 2-chloro-3-methyl-2-buten-1-ol *(2c)* (910 mg), b.p. 72 °C/11 mm. Condensing this product (400 mg) with *(1)* (350 mg) in anhydrous ether (20 ml) for 6 h in the presence of $AlCl_3$ (1.5 g), and working up as described for *(1)* → *(4a)*, gave coenzyme Q_0 (220 mg) and chloro-coenzyme Q_1 *(4c)* (31 mg). The latter product is a red oil with λ_{max} = 272 nm, log ε = 4.14 (in CH_3OH), whose ^1H–NMR spectrum shows signals due to 6 H-a at 4.00 ppm, 3 H-b at 1.83 ppm (singlet), 2 H-c at 3.58 ppm (singlet), 3 H-d at 2.08 ppm (singlet), 3 H-e at 1.98 (singlet). Chloro-coenzyme Q_1 *(4c)* is more stable than the fluoro compound *(4b)*. Compound *(4a)* could not be detected among the products from this reaction.

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[*] Dr. H. Schumacher
Organisch-chemisches Institut der Universität
Meckenheimer Allee 168
53 Bonn (Germany)
Priv.-Doz. Dr. H. Machleidt
Dr. Karl Thomae GmbH
795 Biberach an der Riss (Germany)

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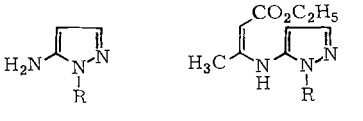
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Pyrazolo[3,4-*b*]pyridines [1]

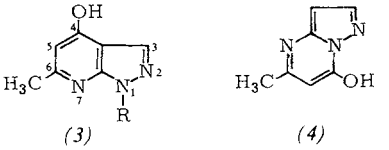
By *H. Dorn* and *A. Zubek* [*]

Pyrazolo[3,4-*b*]pyridines *(3)* are a new type of potential purine antagonists. The only members of this series known hitherto have an OH group on C-3[2] or a phenyl group on N-1 or N-2 [3] and are thus uninteresting as antimetabolites. These bicyclic compounds can be obtained in 80–90 % yield from 3-aminopyrazole *(1a)*, 5-amino-1-methylpyrazole *(1b)*, or 5-amino-1-benzylpyrazole *(1c)* (m.p. 70–72 °C) by reaction with a β-keto ester such as acetoacetic ester. Thus are obtained: 5-methylpyrazolo[1,5-*a*]pyrimidin-7-ol *(4)*[4] from *(1a)*; 1,6-dimethyl- *(3b)* (m.p. 270–272 °C) and 1-benzyl-6-methyl-pyrazolo[3,4-*b*]pyridin-4-ol *(3c)* (m.p. 227 to 288 °C) from *(1b)* and *(1c)*[5] respectively. We proved the positions of the substituents in *(3b)* and *(3c)* by a second synthesis, namely, cyclization of *(2b)* and *(2c)* in boiling ethylene glycol.



(1) (2)

(a), R = -H
(b), R = $-CH_3$
(c), R = $-CH_2C_6H_5$
(d), R = $-COCH_3$



(3) (4)

Hydrogenolytic debenzylation of *(3c)* in glacial acetic acid (Pd-charcoal) gave, surprisingly, 1-acetyl-6-methylpyrazolo-[3,4-*b*]pyridin-4-ol *(3d)* (m.p. 236–239 °C, needles from ethanol). The IR spectrum of *(3d)* in KBr showed, not only an intense, broad carbonyl band, ν(CO) = 1655 cm^{-1} (to be ascribed to the tautomeric 4-pyridone structure), but also a carbonyl absorption band for N–CO–CH_3 at 1749 cm^{-1}. The ^{1}H–NMR spectrum [in $(CD_3)_2SO$] contains a doublet for the 6-CH_3 group at τ = 7.69 and a singlet for N–CO–CH_3 at τ = 7.33; however, the NMR spectrum of *(3d)* in D_2O containing NaOD is exactly the same as that of *(3a)*, *i.e.* there is extremely rapid deuterium exchange at the *N*-acetyl group. Acidifying an alkaline solution of *(3d)* precipitates 6-methyl-1*H*-pyrazolo[3,4-*b*]pyridin-4-ol *(3a)* (m.p. 319 to 322 °C), which we were also able to obtain, in 95 % yield, directly from *(3c)*. This was achieved by treatment of *(3c)* with sodium in liquid ammonia. Compound *(3a)* is converted by $POCl_3$ into 4-chloro-6-methyl-1*H*-pyrazolo[3,4-*b*]pyridine (m.p. 154–156 °C). The IR spectrum (ν(CO) in KBr = 1650 cm^{-1}) shows that in the solid state *(3a)* exists mainly in the tautomeric 4-pyridone form.

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[*] Dr. H. Dorn and Dr. A. Zubek
Institut für Organische Chemie der Deutschen Akademie der Wissenschaften zu Berlin
An der Rudower Chaussee
DDR 1199 Berlin-Adlershof (Germany)

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Difluorothiophosphoryl Fluorosulfate [1]

By *Max Lustig* [*]

Phosphoryl fluorosulfate, $PO(OSO_2F)_3$, is the first compound reported with a fluorosulfate group attached to a phosphorus atom. This compound decomposes slowly to the lower fluorosulfates, $POF(OSO_2F)_2$ and POF_2OSO_2F [2] at temperatures above 100 °C. Difluorothiophosphoryl fluorosulfate, PSF_2OSO_2F, a colorless compound that is unstable at ambient temperature, has been synthesized in our laboratory.

The highest yield of this compound can be achieved by the slow addition of peroxydisulfuryl difluoride, $S_2O_6F_2$, (0.33 mmoles) to difluorothiophosphoryl bromide (0.57 mmole) in a 50 ml. Pyrex bulb at −45 °C. After the addition was completed the reaction mixture was allowed to stand for 1/2 h and then allowed to warm slowly to room temperature. Analysis revealed that the product mixture contained PSF_2OSO_2F (0.46 mmoles or 81 % yield), POF_3 (0.04 mmoles), SO_2 (0.09 mmoles) and PSF_3 (0.01 mmole) as well as unreacted PSF_2Br (0.03 mmole). A small quantity of a yellow solid remained in the reaction vessel. Purification is accomplished by passing the reaction mixture through cold traps maintained at −95 and −119 °C; the PSF_2OSO_2F is retained in the latter.

Immediately after purification of a sample of PSF_2OSO_2F, the molecular weight was determined (vapor density method) and found to be 197.1 (Calcd: 200.1). The ^{19}F-NMR spectrum showed resonances at φ = −47.5 [5], assigned to the fluorine bonded to the sulfur atom, and at φ = 27.6 and 57.7 (J_{P-F_2} = 1240 Hz) both of which are assigned to the fluorines attached to the phosphorus. The measurements are relative to CCl_3F as an internal standard. The area ratio of the two higher field resonances to that at low field was found to be 1.8:1.0. The low-field resonance is divided into a multiplet due to coupling with both the phosphorus and the fluorines attached to the phosphorus. However, both the high-field resonances are split into doublets (J_{F-F_2} = 4 Hz). The ^{31}P-NMR spectrum showed a triplet centered at −165 Hz (relative to H_3PO_4 used as an internal standard) where J_{P-F_2} = 1221 Hz. The NMR spectrum of POF_2OSO_2F is similar [2]. The mass spectrum shows major absorptions [reported as mass number (species) and relative abundance] as follows: 32(S^{++}) 24.4, 47(PO^+) 7.4, 48(SO^+) 4.6, 50(PF^+) 8.4, 64(SO_2^+) 28.4, 67(SOF^+) 31.2, 69(PF_2^+) 100, 80(SO_3^+) 8.5, 82(PSF^+) 3.1, 83(SOF_2^+) 78.5, 98($PSFO^+$) 9.5, 101(PSF_2^+) 37.9, 117(PSF_2O^+) 7.4, and 200($PSF_2OSO_2F^+$) 17.3. The infrared spectrum shows the following major absorptions (cm^{-1}): 1493(s), S=O asym. str., and 1250(s), S=O sym. str. [3]; at 985(vs) and 943(vs, broad) in the P–F and P–O str. region [2,4]; 862(s), S–F str. [3]; 788 (ms), S–O str., and at *ca.* 671 (m, broad), P=S str.

A pure sample of PSF_2OSO_2F was placed into an infrared gas cell at 10 mm pressure and periodically monitored. After 3 h nearly half the sample remained, after 7 h it was barely observable and after 24 h it had completely decomposed according to both infrared and mass spectral evidence. The gaseous decomposition products are SO_2 and POF_3, present in *ca.* 2:1 molar ratio, along with a small quantity of $S_2O_5F_2$. A yellow solid was also formed.

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[*] Dr. Max Lustig
Rohm and Haas Co.,
Redstone Research Laboratories
Huntsville, Alabama (U.S.A.)

[1] This work was carried out under the sponsorship of the U.S. Army Missile Command, Redstone Arsenal, Alabama, under Contract No. DAAH01-67-C-0655.

[2] *D. D. Des Marteau* and *G. H. Cady*, Inorg. Chem. *5*, 1829 (1966).

[3] *M. Lustig*, Inorg. Chem. *4*, 1828 (1965).

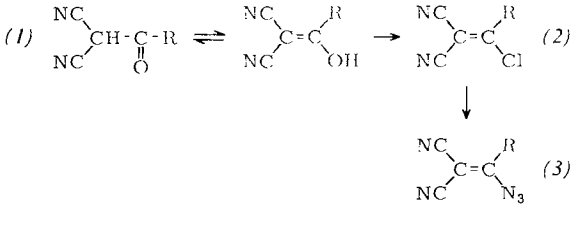
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Degradation of 2-Azidoethylene-1,1-dicarbonitriles [1]

By *K. Friedrich* [*]

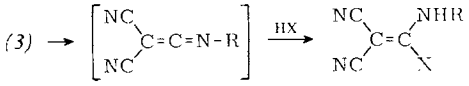
Acylmalononitriles *(1)*, R = H [2], CH_3 [3], or C_6H_5 [4], can be converted into the 2,2-dicyanovinyl chlorides *(2)* by phosphorus pentachloride, or, as their sodium salts, by phosphorus oxychloride. The reactivity of compounds *(2)* is comparable with that of carboxylic acid chlorides, in accord with the principle that structural elements =O and $=C(CN)_2$ are analogous in organic compounds [5]. For instance, 2-azidoethylene-1,1-dicarbonitriles *(3)* are obtained smoothly



	R	B.p. (°C/mm) M.p. (°C)	Yield (%)
(2)	H	83/18	70
	CH_3	92/15	62
	C_6H_5	126/0.1 74–75	55
(3)	H	79–80 (decomp.)	71
	CH_3	Oil	68
	C_6H_5	80 (decomp.)	79

from *(2)* by means of sodium azide in acetone-water (2 : 1 v/v) at 0–5 °C.

The azides *(3)* decompose slowly at 20 °C, and rapidly when warmed to 60–70 °C, with loss of one mol. equiv. of nitrogen. In inert solvents such as ether, benzene, or dimethoxyethane decomposition gives polymeric products. An indication of the course of the reaction is obtained by carrying out the decomposition in dimethoxyethane in the presence of compounds of the type HX such as ethanol, hydrogen chloride, or, if R = C_6H_5, also aniline[**]. Under such conditions, the 2-aminoethylene-1,1-dicarbonitriles *(5)* are obtained as decomposition products. When R = H, the intermediate *(4)* can be isolated as its tetramethyl-ammonium salt if the reaction is carried out in acetone-water; *(4)* is the tautomer of methanetricarbonitrile[6]. It may be concluded that, on evolution of the nitrogen, the group R migrates to the N atom that remains attached, with formation of the 2-imino-ethylene-1,1-dicarbonitriles *(4)*, which then react with HX to give *(5)*. The reaction thus corresponds to the Curtius degradation of carbonyl azides, the dicyanovinyl group here corresponding to the carbonyl group.



(4) *(5)*

(5)	X = Cl		X = OC_2H_5		X = NHC_6H_5	
	M.p. (°C)	Yield (%)	M.p. (°C)	Yield (%)	M.p. (°C)	Yield (%)
R = H	147 [a]	44	225 [b]	61	—	—
R = CH_3	164	35	98 [c]	58	—	—
R = C_6H_5	167	74	145	79	263 [d]	86

[a] Lit. [8], m.p. 147 °C. [b] Lit. [7], m.p. 225–226 °C.

[c] Lit. [7], m.p. 98–99 °C. [d] Lit. [9], m.p. 263–264.5 °C.

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[*] Dr. K. Friedrich
Chemisches Laboratorium der Universität
Albertstr. 21
78 Freiburg (Germany)

[1] This work was supported by the Deutsche Forschungsgemeinschaft.

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[**] Aniline can be used as trapping agent only when R = C_6H_5, as the other azides *(3)* exchange their azide group for the anilino group before evolution of nitrogen occurs.

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NH···S Hydrogen Bonds and the Structure of the Anions in Ammonium Diamidothiophosphate and in Diammonium Amidothiophosphate

By *D. Mootz, W. Look, G. Sassmannshausen*, and *J. Goldmann*[*]

The crystal structures of ammonium diamidothiophosphate *(1)*, $NH_4[POS(NH_2)_2]$, and of diammonium amidothiophosphate *(2)*, $(NH_4)_2[PO_2S(NH_2)]$, have been determined from three-dimensional photographic X-ray-reflection data[1]. The salt *(1)* crystallizes in the monoclinic system with the space group $P2_1$, and the salt *(2)* in the triclinic form belonging to space group $P\bar{1}$. Both contain two formula units in the unit cell.

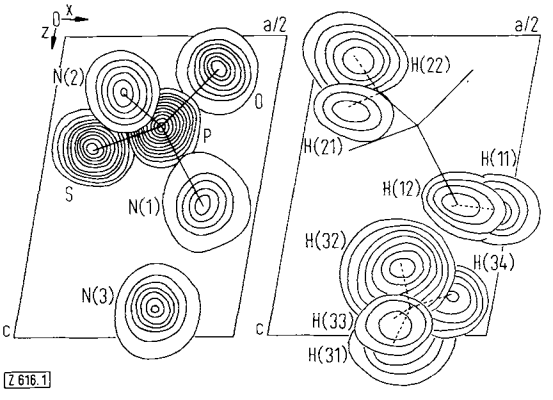


Fig. 1. Left: electron density distribution in $NH_4[POS(NH_2)_2]$ *(1)*. — Right: the maxima corresponding to hydrogen atoms in *(1)*.

The structures were determined from the Patterson functions and were refined by the method of least squares. The *R* factors attained were 0.063 for *(1)* (688 independently observed data) and 0.101 for *(2)* (1087 data). Refinement for *(2)* is not yet complete.

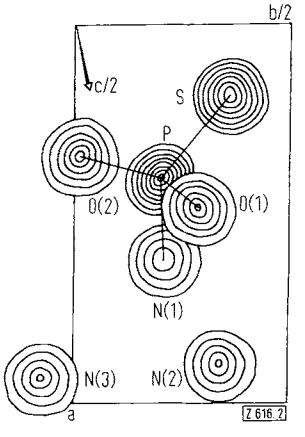


Fig. 2. Electron density distribution in $(NH_4)_2[POS(NH_2)]$ *(2)*.

The left-hand part of Fig. 1 shows the electron density function for *(1)* and on the right the maxima of a Fourier difference synthesis corresponding to the hydrogen atoms. The electron density function for *(2)* is shown in Fig. 2. The bond lengths and bond angles in the anions are listed in the Table; standard deviations amount to 0.004 to 0.008 Å and 0.3 to 0.5 °. The bond lengths for *(1)* are corrected for thermal vibrations.

As a result of additional d_π-p_π bond contributions[2], all the P–X bonds are shorter than pure single bonds. Analogous results have been obtained for other compounds of this type.

Analysis of the interatomic distances and angles showed that in both compounds the sulfur atom participates, by means

(1)		(2)	
P—O	1.533 Å	P—O(1)	1.532 Å
P—S	1.998	P—O(2)	1.510
P—N(1)	1.681	P—S	2.043
P—N(2)	1.693	P—N(1)	1.689
O—P—S	114.0°	O(1)—P—O(2)	114.3°
O—P—N(1)	110.4	O(1)—P—S	109.6
O—P—N(2)	105.5	O(1)—P—N(1)	105.3
S—P—N(1)	108.0	O(2)—P—S	111.3
S—P—N(2)	114.3	O(2)—P—N(1)	104.6
N(1)—P—N(2)	104.2	S—P—N(1)	111.6

of three hydrogen bridges NH···S, in the complex three-dimensional cross-linking of the ions. The corresponding distances between the nitrogen atom and the sulfur atom are 3.400, 3.452, and 3.484 Å for *(1)* and 3.312, 3.376, and 3.478 Å for *(2)*. These findings supplement the limited evidence, obtained by structure analysis, for hydrogen bridges in which a sulfur atom forms one end.

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[*] Doz. Dr. D. Mootz, Dr. W. Look, Dr. G. Sassmannshausen, and Dipl.-Chem. J. Goldmann
Institut für Anorganische Chemie der Technischen Hochschule Schleinitzstr.
33 Braunschweig (Germany)

[1] Preparations: *H. Falius*, Chem. Ber. *98*, 3270 (1965). We thank Dr. *Falius* for samples.

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Addition-Rearrangement Reactions of Transition Metal-Carbene Complexes with Selenophenol

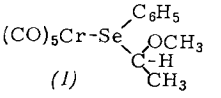
By *E. O. Fischer* and *V. Kiener* [*]

Pentacarbonyl[methoxy(methyl)carbene]chromium reacts with thiophenol with nucleophilic replacement of the OCH_3 on the carbene-carbon atom by the SC_6H_5 group, yielding the brown $(CO)_5CrC(SC_6H_5)CH_3$ [1]. However, on treating the pentacarbonyl[methoxy(methyl)carbene] complexes of chromium, molybdenum, and tungsten [2] with the stronger nucleophile selenophenol, in hexane with exclusion of air, we observed a new type of addition reaction, which yielded brownish - yellow $C_{14}H_{12}CrO_6Se$ (m.p. 74 °C), brown $C_{14}H_{12}MoO_6Se$, and greenish-yellow $C_{14}H_{12}WO_6Se$ (m.p. 85 °C). Table 1 gives the positions and the most plausible assignments of the NMR signals of the three diamagnetic $C_{14}H_{12}MO_6Se$ complexes [3]. The coupling constants J_{CH_3-CH} are 6 Hz in all cases.

Table 1. ^1H—NMR signals measured in $CDCl_3$ with tetramethylsilane as internal standard. Chemical shifts in τ. Relative intensities in parentheses. (D = doublet, S = singlet, Q = quartet, M = multiplet.)

	M = Cr	M = Mo	M = W
$-CH_3$	8.40 (3)D	8.42 (3)D	8.43 (3)D
$-OCH_3$	6.45 (3)S	6.47 (3)S	6.48 (3)S
—CH	4.80 (1)Q	4.85 (1)Q	4.88 (1)Q
$-C_6H_5$	2.37 (5)M	2.35 (5)M	2.60 (5)M

From the NMR data we conclude that the groups $-C_6H_5$ and $-CH(OCH_3)CH_3$ are present. In addition to the molecular peak at $m/e = 406$ and 408, the mass spectrum [4] of $C_{14}H_{12}CrO_6Se$ (Atlas CH4, 50 eV) contains fragments at $m/e =$ 266 and 268 $[CrSe(C_6H_5)-CH(OCH_3)CH_3]^+$, 207 and 209 $[CrSeC_6H_5]^+$ as well as 214 and 216 $[Se(C_6H_5)-CH(OCH_3)CH_3]^+$ which evidence a Cr-Se bond and thus also the structure *(1)*.



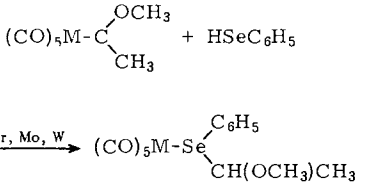
(1)

The complexes have a pseudooctahedral configuration and their IR spectra contain four ν_{CO} bands (Table 2), as is to be expected for lowering of the symmetry by the selenium ligands.

Table 2. Positions of the ν_{CO} vibrations of the compounds $C_{14}H_{12}MO_6Se$ in n-hexane (cm^{-1}).

M = Cr	M = Mo	M = W
2070	2078	2078
1990	1990	1980
1948	1951	1940
1934	1935	1932

The selenium ligand, which had become coordinated to the metal atom by nucleophilic replacement of the carbene-carbon atom and proton migration, is replaced by pyridine, with formation of yellow pentacarbonylpyridinechromium(0). Because of the similarity of their spectra, the structures of $C_{14}H_{12}MoO_6Se$ and $C_{14}H_{12}WO_6Se$ are assumed to be analogous to *(1)*. We thus formulate the reactions of the three metalcarbene complexes with selenophenol as:



If pentacarbonyl[methoxy(methyl)carbene]chromium is allowed to react with selenophenol in ethanol, a dark red oil is obtained from which ruby-red crystals are precipitated on treatment with concentrated aqueous KOH. Elemental analyses and IR and NMR spectra indicate a compound $[(CO)_5Cr-Se(C_6H_5)-Cr(CO)_5]^-K^+$.

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[*] Prof. E. O. Fischer and Dipl.-Chem. V. Kiener
Anorganisch-Chemisches Laboratorium
der Technischen Hochschule
Arcisstrasse 21
8 München (Germany)

[1] *U. Klabunde* and *E. O. Fischer*, J. Amer. chem. Soc., in press.

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[3] Experiments by Dr. *K. E. Schwarzhans*.

[4] Measurements by Dr. *J. Müller*.

Structure and Mode of Action of Aldolases

By *B. L. Horecker*[*]

Fructose diphosphate aldolase from rabbit muscle has a molecular weight of 160000 and appears to be built up according to the $\alpha_2\beta_2$ principle from four sub-units of equal molecular weight. The function of the various sub-units is not yet known. The active center of the enzyme contains an active lysine residue that forms a Schiff base with the substrate dihydroxyacetone phosphate. Reduction of this intermediate with sodium borohydride enables the active center to be labeled. A peptide containing this center could be isolated; it proved strongly hydrophobic in character. The fact that the corresponding peptide from rabbit-liver aldolase has a similar primary structure carrying numerous analogous amino-acid substituents provides evidence for the genetically independent origin of the two enzymes.

Investigations with reagents for the specific rearrangement of individual amino acids evidence further essential amino acids alongside the active lysine.

N-Ethylmaleimide reacts with sulfhydryl groups.The presence of the substrate inhibits this reaction and, consequently, the deactivation of the enzyme. The sulfhydryl groups may be oxidized to disulfides by *o*-phenanthroline. Since this reaction is also inhibited by the substrate, the sulfhydryl group must lie in the active center. Reaction with acetylimidazole provided evidence for the presence of essential tyrosine residues, and essential histidine residues were shown to be present by photooxidation. The properties of the aldolase that has been modified by acetylation or by photooxidation resemble those of transaldolase and, like the latter, such modified aldolases do not promote proton exchange between the substrate and water.

On the basis of the above and other observations, the following possible steps are discussed for the reaction of aldolases: 1. Formation of a Schiff base. 2. Reaction of the 6-phosphate group of the fructose diphosphate with a positively charged group in the active center, during which a negatively charged group is released. The latter abstracts a proton from the OH group on C-4 and thus initiates the aldol cleavage. 3. The resulting Schiff base carbanion reacts with a proton of the water *via* the histidine residue.

The aldol cleavage of fructose 6-phosphate with transaldolase is promoted by a histidine residue at the active center. This group retains the proton as long as the Schiff base structure remains intact.

Lecture at Göttingen (Germany) on May 29th, 1967 [VB 88 IE]
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[*] Prof. Dr. B. L. Horecker
Albert Einstein College of Medicine
1300 Morris Park Avenue
Bronx N.Y. 10461 (U.S.A.)

Demixing Phenomena in High Polymers and Their Technical Importance

By *H. Gerrens*[*]

Incompatibility between two polymers is the rule, compatibility the exception. In the chemical technology of high polymers, demixing phenomena are sometimes avoided and sometimes consciously utilized. Precipitation polymerization begins with a homogeneous starting mixture, from which the polymer is precipitated during the polymerization. The precipitation is either achieved by adding a precipitant to the monomer (example: copolymerization of styrene and acrylonitrile) or it arises by insolubility of the polymer in the monomer (example: bulk polymerization of vinyl chloride). In discontinuous copolymerization it is only with azeotropic mixtures[1] that the copolymer has the same composition as the starting mixture. In all other mixtures the composition of the copolymer changes during the course of the reaction and inhomogeneous copolymers are formed which tend to demix. Azeotropic mixtures very seldom contain more than two different monomers, although recently some have been found with three, four, or five different monomers.

Block copolymers occasionally demix to give ordered structures, some even showing Bragg reflections in visible light. Block and graft copolymers often cause a better compatibility of the corresponding homopolymers, which in principle results from intimate distribution of the two phases in each other: the copolymers act, as it were, as emulsifiers of a polymeric oil-in-oil emulsion. Almost all high-impact polystyrenes and ABS polymers are to be considered as such emulsions, consisting of a soft rubber and a hard polystyrene or poly(styrene/acrylonitrile) phase. The properties of such shock-resistant masses depend on which of the two components forms the coherent phase of the emulsion. When, *e.g.*, high-impact polystyrene is manufactured by polymerization of styrene in presence of polybutadiene dissolved in styrene, it is the polybutadiene that first forms the coherent phase; but as reaction continues, the volume of the polystyrene phase progressively increases and this leads to phase reversal so that the coherent phase then consists of polystyrene.

Lecture at Freiburg (Germany) on June 9th, 1967 [VB 92 IE]
German version: Angew. Chem. 79, 949 (1967)

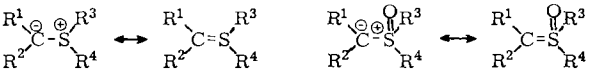
[*] Dr. H. Gerrens
Badische Anilin- & Soda-Fabrik AG.
Ammoniaklaboratorium
67 Ludwigshafen (Germany)

[1] A monomer mixture is termed azeotropic when the copolymer formed from it has the same composition as the monomer mixture over the whole range of conversion.

Chemistry of Sulfur Ylides

By *A. Hochrainer*[*]

Individual sulfur ylides have been known for a long time, but it is only in recent years that their chemistry has been intensively studied[1,2]. Sulfonium ylides *(1)* are formed from oxosulfonium ylides *(2)*:



(1a) *(1b)* *(2a)* *(2b)*

Sulfur ylides can be prepared in four general ways:

1. From the corresponding sulfonium salts and a base.

2. By direct condensation of CH-acidic compounds with sulfoxides (only with very strongly CH-acidic compounds; owing to electron delocalization in the carbanion of the ylide this yields particularly stable ylides).

3. By rearrangement of an ylide already present (particularly by replacement of one or both of the hydrogen atoms on the carbanion [R^1 and R^2 in *(1)* or *(2)*]).

4. By a few special processes, of which some appear capable of generalization, *e.g.*, reaction of diazo compounds with sulfides (yielding sulfonium ylides) or with sulfoxides (yielding oxosulfonium ylides)[3].

Many sulfur ylides have only limited stability: depending on the structure of the ylide various types of rearrangement or decomposition may occur:

a) Hofmann elimination (either normal *trans*-elimination or α',β-elimination).

b) Stevens rearrangement.

c) Sommelet rearrangement.

d) Decomposition to sulfide or sulfoxide and carbene; the carbene may dimerize, polymerize, or attack other molecules.

These complications can be avoided by attaching strong electron acceptors to the anionic carbon of the ylide (whereby, however, the reactivity is decreased) or by substituting the ylide-sulfur only by phenyl or methyl groups.

Reaction of sulfur ylides (i) with acylating agents leads to new ylides [if R^1 or R^2 in *(1)* or *(2)* is H], (ii) with nitroso compounds to nitrones[4], (iii) with Schiff bases to aziridines[5] and products of further reaction[6], and (iv) with α,β-unsaturated oxo compounds to oxiranes[1,2] in contrast to the phosphorylide Wittig reactions which afford olefins.

Lecture at Wuppertal (Germany) on July 5th, 1967 [VB 98 IE]
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[*] Dr. A. Hochrainer
Organisch-Chemisches Institut der Universität
Währingerstr. 38
A-1090 Wien (Austria)

[1] *A. Hochrainer*, Österr. Chem.-Ztg. *67*, 297 (1966).

[2] *A. Wm. Johnson*: Ylid Chemistry (Organic Chemistry, Vol. 7). Academic Press, New York, London 1966.

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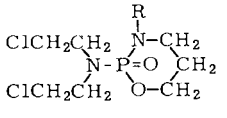
General Meeting of the Gesellschaft Deutscher Chemiker 1967

This year's General Meeting was held in Berlin (Germany) from 18th to 23rd September in conjunction with the centenary celebration of the Deutsche Chemische Gesellschaft. A selection of abstracts of the lectures and the discussions that took place on this occasion is given below. Only works that have not yet been published or presented for publication are included. The abstracts are listed in the alphabetical order of authors' names.

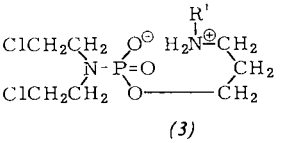
The Change in the Properties of Cyclic *N*-Lost Phosphoramidate on Substitution on the Ring Nitrogen

By *H. Arnold*[*]

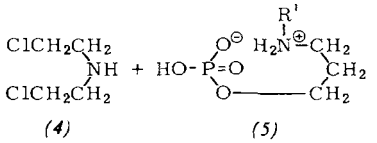
The introduction of substituents R′ on the ring nitrogen of the *N*-Lost-phosphoramidate *(1)* to give *(2)* affects the susceptibility of the molecule to hydrolysis in various ways, depending on the size and nature of the substituent.



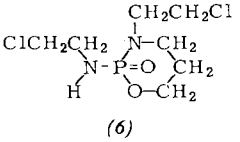
(1): R = H
(2): R = R′



(3)



(4) *(5)*



(6)

Solutions of the compounds *(2)* in ether are allowed to react with molar quantities of H_2O and HCl at 37.5 °C. If R′ = CH_3, the zwitterion *(3)* is formed. If R′ = C_2H_5, no hydrolysis takes place; when R′ = CH_2CH_2Cl, the molecule is cleaved at two points to form *(4)* and *(5)*. The compound *(6)*, which is isomeric with *(1)*, is also cleaved at two points to give the chloroethylamine salt of the acid *(5)*.

Compound *(1)* is a latent cytostatic[1], which is inactive *in vitro*, but is converted by metabolic enzymes *in vivo* into products having a strong cytostatic action. This activation involves ring cleavage of *(1)* with liberation of a hydroxyl function of the phosphoric acid (formation of an anion). In view of this structural change leading to alkylation, the rate of hydrolysis of *(3)* (R′ = CH_2CH_2Cl) and *(6)* was studied in comparison with that of *(1)* on the basis of the kinetics of chlorine ionization in neutral aqueous solution and with the aid of paper chromatography. The new *N*-chloroethyl derivatives *(3)* (R′ = CH_2CH_2Cl) and *(6)* exhibited interesting cytostatic properties in animal experiments. Since *(6)* contains no *N,N*-bis(chloroethyl)amine group, and so is not a nitrogen mustard, this compound embodies a new cytostatic principle with latent action.

[*] Prof. Dr. H. Arnold
Asta-Werke AG.
Bielefelder Str. 79–91
4812 Brackwede (Germany)

[1] Trade name: Endoxan®.

Radiochemical Investigation of the Fission of the Bismuth Nucleus with High-Energy Protons [1]

By *K. Bächmann*[*] and *J. B. Cumming*[**]

Thin bismuth targets were bombarded with 2.2 GeV protons (Cosmotron, Brookhaven) and the recoil products were caught in thin Mylar films; the differential range curves for ^{128}Ba, ^{131}Ba, ^{100}Pd, ^{101}Pd, ^{103}Pd, ^{109}Pd, ^{112}Pd, ^{82}Sr, ^{83}Sr, ^{89}Sr, ^{91}Sr, ^{61}Cu, ^{64}Cu, and ^{67}Cu could be determined by measurement of activity at angles of 15°, 19°, and 165° to the direction of the proton beam. The range curves were converted into energy curves by means of a range-energy relation. The angular distributions were also measured for these nuclides.

The energies of the neutron-deficient fragments are only about half as great as those of the neutron-excess fragments. The energy distribution curves of the neutron-poor nuclides are broader and asymmetric. This result leads to the conclusion that neutron-excess and neutron-deficient products are formed in different ways.

This conclusion is supported by the angular distributions. Neutron-deficient nuclides exhibit isotropic distribution in the moving system, whereas neutron-excess nuclides exhibit a maximum angle of 90° to the direction of the proton beam.

Analysis of these results by Monte Carlo calculations based on the two-step model[2] showed that this model (contrary to earlier belief) is also applicable to neutron-deficient

nuclides and that fragmentation cannot be proved. The neutron-deficient products are probably formed after the evaporation of many small particles from highly excited primary nuclei, whereas the neutron-excess products are formed from primary nuclei in a low state of excitation by a process comparable to low-energy fission.

[*] Dr. K. Bächmann
Lehrstuhl für Kernchemie, Technische Hochschule
Hochschulstr. 1
61 Darmstadt (Germany)

[**] Dr. J. B. Cumming
Chemistry Department, Brookhaven National Laboratories
Upton, N.Y. 11973 (U.S.A.)

[1] Research performed under the auspices of the U.S. Atomic Energy Commission.

[2] *R. Serber*, Physic. Rev. *72*, 1114 (1947).

Compound Formation in Ternary Metal(II)oxide, Phosphorus(V)Oxide, and Boron(III) Oxide Systems

By *H. Bauer*[*]

Though many mineral and synthetic borate silicates are known, borate phosphates were unknown until recently. We have systematically investigated compound formation in systems of the type $MO/P_2O_5/B_2O_3$[1].

The systems with M = Mg, Mn, Co, Ni, Zn, and Cd were found to contain $6MO \cdot P_2O_5 \cdot B_2O_3$, which are best prepared by thermal reaction of orthophosphate $3MO \cdot P_2O_5$ with orthoborate $3MO \cdot B_2O_3$ (molar ratio 1:1), slightly below the melting point of the compound formed. The compounds are isostructural and crystallize in the hexagonal system with lattice constants between $a_0 = 8.42$ and $c_0 = 12.40$ Å for the nickel compound and $a_0 = 8.82$ and $c_0 = 13.23$ Å for the cadmium compound.

Several compounds exist in the systems with M = Ca, Sr, and Ba:

1) Isostructural compounds $2\,MO \cdot P_2O_5 \cdot B_2O_3$, which crystallize in the hexagonal system[2].

2) Compounds of orthophosphate and orthoborate with a homogeneity range extending from a molar ratio of 1:1 toward the borate side; the powder diagrams are very similar to those of the above-mentioned compounds $6\,MO \cdot P_2O_5 \cdot B_2O$.

3) Phases with a larger homogeneity range and an apatite structure[3].

In the system $PbO/P_2O_5/B_2O_3$ we found $2\,PbO \cdot P_2O_5 \cdot B_2O_3$, which is isostructural with the compounds named under 1), and a phase having an apatite structure, as well as $2PbO \cdot P_2O_5 \cdot 1/3B_2O_3$ and $8PbO \cdot P_2O_5 \cdot B_2O_3$ ($6\,PbO \cdot P_2O_5 \cdot B_2O_3$ could not be obtained).

[*] Priv.-Doz. Dr. H. Bauer
Institut für Anorganische Chemie der Universität
Englerstr. 11
75 Karlsruhe (Germany)

[1] *H. Bauer*, Habilitation Thesis, Technische Hochschule Karlsruhe, 1963.

[2] *H. Bauer*, Z. anorg. allg. Chem. *337*, 183 (1965); *345*, 225 (1966).

[3] *H. Bauer*, Lecture at Colloque international sur les phosphates mineraux solides, Toulouse, May 16–20, 1967; Bull. Soc. chim. France, in press.

Some Aromatic Complexes of the Transuranium Elements

By *F. Bäumgartner, E. O. Fischer, B. Kanellakopulos*, and *P. Laubereau*[*]

The following aromatic complexes of the transuranium elements have so far been obtained: $Np(C_5H_5)_3Cl$; $Pu(C_5H_5)_3$ and $Am(C_5H_5)_3$.

These are all sublimable, benzene-soluble substances, which are sensitive to oxygen. The plutonium compound is pyrophoric. The complexes can be synthesized by double decomposition of the corresponding chlorides with $Be(C_5H_5)_2$ in the melt at 70 °C.

The magnetic susceptibilities were measured from 4.2 °K upward.

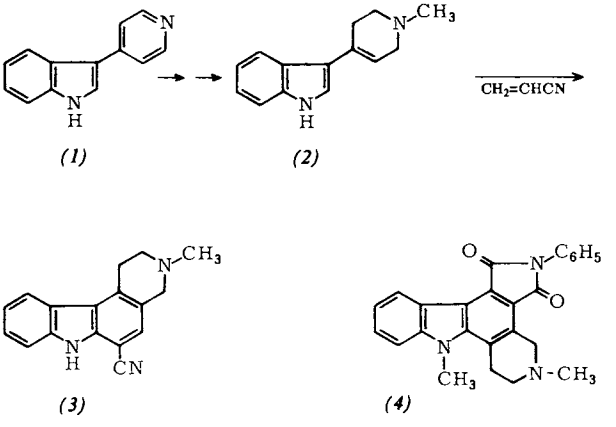
IR spectrometric studies indicate that, in contrast to the behavior of the corresponding lanthanide compounds, the ionic bond character increases with increasing atomic number.

[*] Prof. Dr. F. Baumgärtner, Dr. B. Kanellakopulos, and Dr. P. Laubereau
Kernforschungszentrum
75 Karlsruhe (Germany)
Prof. Dr. E. O. Fischer
Anorganisch-Chemisches Laboratorium
der Technischen Hochschule
Arcisstr. 21
8 München 2 (Germany)

Diels-Alder-Type Cycloadditions with Indoles

By *D. Beck* and *K. Schenker*[*]

3-(4-Pyridyl)indole *(1)* was quaternized and converted into the 1,2,3,6-tetrahydropyridine derivative *(2)* by reduction with $NaBH_4$. The carbazole derivative *(3)* could be isolated in the pure state from the mixture of reaction products obtained from this diene and acrylonitrile. Compound *(4)* was obtained from 1-methyl-2-(1-methyl-1,2,3,6-tetrahydro-4-pyridyl)indole with *N*-phenylmaleimide.



[*] Dr. D. Beck and Dr. K. Schenker
Chemische Forschungslaboratorien der Pharmazeutischen Abteilung
CIBA Aktiengesellschaft
CH-4000 Basel (Switzerland)

Electrophoretic Painting on the Rotating Disk Electrode

By *F. Beck*[*]

Electrophoretic painting is widely used nowadays. An anionic binder is very often deposited on an iron electrode from aqueous solution or dispersion. The binder particles are transported from the interior of the bath by convection, and in the diffusion layer in front of the electrode by transport and diffusion. During electrolysis, the binder anions $P^{n\ominus}$ coagulate and their charge disappears. It remains to determine whether the charge is transferred directly to the anode or whether it is indirectly neutralized by the cations such as H^+ or Fe^{2+} formed in secondary electrolytic processes.

The Lewitsch rotating disk electrode has proved a valuable aid to the investigation of the primary processes in electrophoretic painting. Films are deposited on Fe and Pt anodes under galvanostatic conditions ($j = 1-6$ mA/cm²) from an aqueous solution of an acrylate-based model binder with an acrylic acid content of 10%. The start of deposition can be recognized by a sharp increase in voltage.

When the rotation speed exceeds a certain limit n_{lim}, no further deposition is observed. The limiting speed increases with the square of the current density j. The value of n_{lim} decreases with increasing degree of neutralization; this can be quantitatively interpreted by the diffusion of free amine. The critical hydrogen ion concentration is calculated to be about 10^{-4} mole/l. The values of n_{lim} pass through a maximum as the content of organic solvents is increased. The increase in n_{lim} is due to a decrease in the dissociation constant of the polyacid, and the decrease to the increasing solubility of the polyacid in the solvent. If the acrylic acid content of the binder is increased, n_{lim} decreases because of the increasing solubility of the binder in water. n_{lim} increases rapidly at low and high binder concentrations. The addition of foreign electrolytes leads to a decrease in the limiting speed, since the more mobile foreign anion reduces the transport of the polymeric anion in the boundary layer.

The very long induction periods required close to the limiting speed are explained by nucleation processes and viscosity increases in the diffusion layer.

The experimental results are in agreement with the view[1] that the binder coagulates in an acidic boundary layer in front of the anode. Protons are injected at the phase boundary by electrolytic processes such as the decomposition of water.

[*] Dr. F. Beck
Hauptlaboratorium der Badischen Anilin- und Soda-Fabrik AG.
67 Ludwigshafen (Germany)

[1] *F. Beck*, Farbe u. Lack *72*, 218 (1966).

Isotope Concentration by Countercurrent Electrolysis at High Electrolyte Concentrations with the Aid of Separating Columns having Capillary Properties[1]

By *B. A. Bilal* and *K. Wagener*[*]

In separations by countercurrent electrolysis, the relationship between the total separation factor Q of a separating column, the elementary separation factor $1 + \varepsilon$ of the process, and the number of theoretical plates n in the column is given by

$$Q = (1 + \varepsilon)^n$$

A high separation factor in the separation of isotopes is therefore achieved by increasing the elementary effect ε (in this case the relative difference in the rate of migration of the ions $\Delta u/\bar{u}$) and by increasing the number of plates n.

The use of high electrolyte concentrations offers a possibility of significantly increasing the elementary effect. Complex-formation equilibria in the homogeneous phase can sometimes lead to large isotope effects between two chemical states of the element in question, which differ in charge, and can therefore be utilized for isotope separation by ion migration.

In a separating column with a given maximum cooling performance N_{max}, the field strength E to be applied must be reduced with increasing specific conductivity $\varkappa$ of the electrolyte in accordance with the equation

$$E_{max} = (N_{max}/\varkappa)^{1/2}$$

Consequently, a lower flow speed (v_L) along the column must be used in order to maintain the steady state condition

$$E \cdot \bar{u} + v_L = 0$$

required for the countercurrent electrolysis. ($\bar{u}$ = mean mobility of the two isotopes.)

For a column of length X, the relationship

$$n = X\, v_L/D_{eff}$$

(D_{eff} = effective diffusion coefficient of the ions in the solution in the longitudinal direction of the column).

is valid in the ultimate separation state. This relationship shows that the use of high electrolyte concentrations results in an unavoidable decrease in the number of theoretical plates. This disadvantage was overcome by development of columns with a high specific cooling power, in which the separation takes place in capillaries. In these columns the number of theoretical plates was increased, not only by the use of higher flow rates, but also by the fact that smaller values of D_{eff} were obtained in the capillary spaces.

We developed two types of column. In the first the separating space takes the form of a thread of liquid inside a capillary, while in the second (to increase the throughput) it is a capillary layer of liquid between two externally cooled parallel plates, arranged vertically and open at the top.

Using these two types of column we obtained a fast separation of ^7Li in 0.5 N CH_3COOLi solution. The ε value calculated from the slope of the concentration curve is an order of magnitude higher than that in a 0.05 N CH_3COOLi solution.

[*] Dr. B. A. Bilal and Priv.-Doz. Dr. K. Wagener
Hahn-Meitner-Institut für Kernforschung,
Sektor Kernchemie
Glienicker Str. 100
1 Berlin 39 (Germany)

[1] Cf. *K. Wagener* and *B. A. Bilal*, Z. Naturforsch. *21*, 1352 (1966).

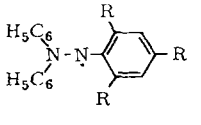
Stable Triarylhydrazyls Containing no Nitro Groups

By *D. Braun* and *G. Peschk*[*]

Triarylhydrazyls containing nitro groups, such as α,α-diphenyl-β-picrylhydrazyl *(1)*, are among the most stable nitrogen radicals known. On the other hand, apart from the unstable triphenylhydrazyl, which exists mainly as the dimer, triarylhydrazyls containing no nitro groups were unknown until now.

Stable triarylhydrazyls can also be obtained when ester groups are incorporated instead of the nitro groups in *(1)*. Trimethyl 2-(2,2-diphenylhydrazino)trimesate is prepared by reaction of an excess of α,α-diphenylhydrazine with trimethyl 2-fluorotrimesate in ether (lemon-yellow crystals, m.p. 155–156 °C). When a solution of this product in benzene is shaken for several hours with a tenfold excess of active lead dioxide in the absence of air, the hydrazyl *(2)* is obtained as a black crystalline substance (m.p. 152 °C) having a metallic luster. A solution of the radical in benzene gives an ESR spectrum with 7 lines.

Hydrazyls with no nitrogroups are of particular interest as free-radical interceptors and as inhibitors for radical-initiated polymerization reactions. Unlike *(1)*, they contain no retarding substituents, which make it impossible in inhibition experiments to distinguish between a reaction involving the radical function of the molecule and one involving the nitro groups. For example, the free-radical polymerization of styrene is completely inhibited in the induction period by *(2)* [but not by *(1)*] until all the hydrazyl radicals have been consumed. The subsequent polymerization is no longer



(1) R = NO_2
(2) R = $COOCH_3$

influenced by *(2)*, whereas *(1)* or some other polynitro compound strongly retards the polymerization after the induction period.

[*] Prof. Dr. D. Braun and Dipl.-Ing. G. Peschk
Deutsches Kunststoff-Institut
Schlossgartenstr. 6 R
61 Darmstadt (Germany)

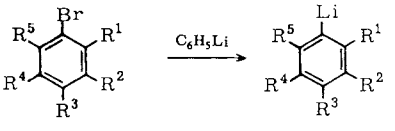
Stable Nitroaryllithium Compounds

By *P. Buck* and *G. Köbrich* [*]

Halogen-metal exchange on nitrobromoaromatic compounds proceeds satisfactorily only at low temperatures (about −100 °C) and in THF. Higher temperatures and less polar solvents favor the oxidation of the lithium compound by the nitro group. Owing to the purely inductive promotion of the halogen-metal exchange by the nitro group, the best yields of nitroaryllithium compounds are obtained with *o*-substituted nitrobromoaromatic compounds, *e.g.* 97% of *o*-nitrophenyllithium from *o*-nitrobromobenzene and phenyllithium, and 92% of 2-methyl-6-nitrophenyllithium from 2-bromo-3-nitrotoluene.

With a bromine *m* or *p* to the nitro group, halogen-metal exchange is suppressed considerably in favor of the redox reaction. No lithium compound can be detected (by carboxylation) in the reaction product obtained from *p*-nitrobromobenzene.

A further competitive reaction in the case of di- and trinitroaromatic compounds is addition to the aromatic ring, but up to 25% of 2,4-dinitrobenzoic acid can still be obtained (after carboxylation) from 2,4-dinitrobromobenzene and a maximum of 9% of 2,4,6-trinitrobenzoic acid from picryl bromide. If the nitro groups are prevented from becoming coplanar with one another and with the ring, halogen-metal exchange is promoted (see Table for yields of the carboxylic acids formed).



	R^1	R^3	R^3	R^4	R^5	Yield (%)
(1)	NO_2	H	NO_2	CH_3	H	63–77
(2)	NO_2	CH_3	NO_2	H	H	82–85
(3)	H	NO_2	CH_3	NO_2	H	41
(4)	NO_2	H	H	H	NO_2	61–67
(5)	NO_2	Br	H	Br	NO_2	63
(6)	NO_2	Br	NO_2	Br	NO_2	80–85

The reaction of *(6)* with an excess of phenyllithium yields 1,3,5-trinitro-2,4,6-trilithiumbenzene together with 2,4,6-trinitro-3,5-dilithiumbiphenyl.

Nitroaryllithium compounds are stable only at low temperatures. They dimerize on warming and can be converted in good yields into 2,2′-dinitrobiphenyl derivatives after oxidation with methyl chloroformate. The linkage point is the carbon atom that formerly carried the metal.

[*] Dipl.-Chem. P. Buck and Doz. Dr. G. Köbrich
Organisch-Chemisches Institut der Universität
Tiergartenstr.
69 Heidelberg (Germany)

Structural Analysis of Polymers in Solution

By *H.-J. Cantow* [*]

Various columns (one for use on the microscale) were developed to permit the continuous fractionation of polymers on the basis of differences in solubility. The change in the quality of the solvent with time is achieved by temperature programming, working with *one* critical solvent. The polymer concentration in the eluate is recorded refractometrically [1]. The columns may be combined with a continuously recording apparatus for the measurement of the scattered light so that the molecular weight distribution curve is recorded simultaneously with the separation process. In a pseudo-ideal solvent, the molecular weight can be measured directly by means of a special optical-electronic arrangement, even when intraparticle interference occurs [1].

In the case of copolymers, the mass concentration can be determined refractometrically and the chemical composition of the system UV-spectroscopically. Gel-permeation chromatographic studies [2] have been carried out on block copolymers of the type A–B–A and the corresponding homopolymers (styrene-butadiene system).

The significance of the turbidimetric titration in the determination of the molecular-weight distribution and the chemical heterogeneity of polymers is discussed. Dissolution titration [3] is superior to conventional precipitation titration, since time-dependent retardation effects are practically eliminated.

First attempts to obtain turbidity curves in a temperature gradient using a critical solvent showed that the process, which has a good separating efficiency, is suitable for use as a fast method [4]. The turbidity gradient that is rapidly established may be related to the molecular-weight distribution.

The sequence-length distribution in copolymers, particularly in the methyl methacrylate-methacrylic acid system, was investigated by high-resolution nuclear magnetic resonance spectroscopy. Combined studies on polymers obtained by copolymerization and by partial hydrolysis of polymethyl methacrylates facilitate the interpretation of the spectra, in which the resonances due to 'chemical' sequences and those due to 'configurative' sequences overlap [5].

Finally, the incompatibility of polymers was studied by measurement of the light scattering from ternary polymer-polymer-solvent systems and by determination of the turbidity point of such systems. If one polymer and the solvent are isorefractive components, the second virial coefficient of the osmotic pressure of the other polymer is a measure of the incompatibility of the two polymers. The dependence of the Θ point on the molecular weight of the polymer that is isorefractive with the solvent is discussed, as well as its temperature-dependence. The turbidity point determinations permit the prediction of the compatibility limits (of polystyrene and polymethyl methacrylate in the case in question), even in the solid state. [6]

[*] Prof. Dr. H.-J. Cantow
Institut für makromolekulare Chemie der Universität
Stefan-Meier-Str. 31
78 Freiburg i. Br. (Germany)

[1] *H.-J. Cantow*, *E. Siefert*, and *R. Kuhn*, Chem.-Ing.-Techn. *10*, 1032 (1966).

[2] *H.-J. Cantow* and *C. Stojanov*, unpublished.

[3] *H.-J. Cantow*, Angew. Chem. *76*, 350 (1964); *H. Giesekus* in *M. Cantow*: Polymer Fractionen. Academic Press, New York 1966.

[4] *H.-J. Cantow*, unpublished.

[5] *E. Klesper*, *W. Gronski*, and *H.-J. Cantow*, unpublished.

[6] *R. Kuhn*, *H.-J. Cantow*, and *W. Burchard*, Makromolekulare Chem., in press.

Measurement of Heats of Adsorption on the Surfaces of Single Crystals with the Field Electron Microscope

By *M. Drechsler* [*]

Heats of adsorption on the surfaces of single crystals can be experimentally determined with the aid of the Clausius-Clapeyron equation if the pressure, temperature, and emission current are measured with a special field electron microscope, as has been shown by a preliminary measurement [1].

The method has been improved to permit more accurate and systematic measurement. 1. The electrons emitted from the surface of a single crystal are now stopped down and measured directly, 2. the partial pressure in the adsorption equilibrium between 10^{-5} and 10^{-8} mm Hg is determined with a mass spectrometer, and 3. an improved ultrahigh vacuum technique is used, the partial pressure of the impurities being less than 2×10^{-11} mm Hg. For hydrogen on tungsten, the differential heat of adsorption on several faces of the single crystal has been determined as a function of the degree of coverage. The value *e.g.* for the (122) face is 15 kcal/mole for a coverage $\theta = 0.1$ and for the (001) face a value was obtained of 4 kcal/mole at a coverage of $\theta = 0.8$.

[*] Priv.-Doz. Dr. M. Drechsler
Fritz-Haber-Institut der Max-Planck-Gesellschaft
Faradayweg 4–6
1 Berlin 33 (Germany)

[1] *M. Drechsler* and *H. Liepack*, Colloques internat. Centre nat. Rech. sci. *152*, 49 (1965).

Spectrophotometric Studies on the Hydrolysis and Complex Formation of the Plutonyl and Neptunyl Ions

By *S. H. Eberle*, *J. B. Schäfer*, and *W. Robel*[*]

The absorption spectra of pentavalent neptunium and of hexavalent plutonium both show an extremely sharp and intense line such as is rarely found for other elements. The extinction of this line changes on complex formation or chelation and on hydrolysis, *i.e.* when the central atom forms coordinate bonds; in many cases new absorption maxima also appear. This phenomenon was used to follow quantitatively the reaction of the two transuranium ions with aliphatic α-hydroxycarboxylic acids and pyridinecarboxylic acids.

Extinction measurements with variation of the pH value of the solution demonstrate the formation of the compounds $Pu^{VI}O_2L^+$, $Pu^{VI}O_2L_2$ and $Np^{V}O_2L$ (L = anion of the acid). In the series of acids $C_nH_{2n}(OH)COOH$, the stability increases with increasing chain length; the chelates with pyridine-α-carboxylic acid are still more stable. The course of hydrolysis is also recognizable from the spectrum; it begins at pH = 7 for the neptunyl(v) ion and at pH = 4 for the plutonyl(vi) ion. The results were evaluated quantitatively by least-squares calculations on a computer. The principles of measurement and evaluation appear to be generally applicable to the study of the complex formation of both ions.

[*] Dr. S. H. Eberle, Dipl.-Chem. J. B. Schäfer, and Dipl.-Chem. W. Robel
Lehrstuhl für Radiochemie, Universität Karlsruhe
und Institut für Radiochemie, Kernforschungszentrum
75 Karlsruhe (Germany)

The Binding of Water in Crystalline Zeolites

By *G. Ebert*, *W. Matron*, and *F. H. Müller*[*]

In dielectric studies on Linde molecular sieves (LMS) 3A, 4A, and 13X[1] between 300 Hz and 400 kHz, −190 to +90 °C, and 0 to 215 mg of water/g of LMS, three Debye-type dispersion regions[2] were found. The behavior described by us as a β-relaxation process occurs between 300 Hz and 400 kHz in LMS 3A at −60 to +20 °C. The α process is observed at temperatures about 100 °C higher. The β mechanism appears in a very similar manner with LMS 4A and 13X. It is largely independent of the crystal structure and of the water content. The ε′- or ε″-ω curves[3] simply undergo a parallel displacement toward the frequency axis with increasing water content (at the same temperature). The Cole arcs are largely independent of temperature in the β process. For example, between −60 and −20 °C one obtains a single circular arc, the center of which (in contrast to the results for ice and liquid water) lies far below the abscissa, thus indicating a broad relaxation time distribution. The activation energy for 4A and 13X, unlike that of γ-Al_2O_3 or silica gel, increases rapidly with the water content.

We assume that the β process is due to transport of water molecules between the cages. This process is hindered as more water is added, since the additional H_2O molecules, owing to the small size of the cages (maximum 13 Å), couple the H_2O molecules present with the cage wall, with the result that their mobility is energetically and sterically hindered. The largest cages can accommodate 28 H_2O molecules. On the other hand, the clusters of liquid, unadsorbed water contain > 100 H_2O molecules. The transfer of H_2O molecules between the cages is greatly restricted by the very narrow pores (2.5, 4.2, and 8 to 9 Å for LMS 3A, 4A, and 13X, respectively).

In the case of LMS 3A, the activation energy is constant (15 kcal/mole) up to a water content of about 100 mg/g, and only then begins to increase. This is evidently due to the $K^{\oplus}$ present in LMS 3A.

In the α process, ε′ and ε″ increase rapidly with the water content. This relaxation region is probably connected with interchange of sites by ion pairs. The γ process seems to result from the re-orientation of mobile H_2O molecules in the interior of the cages.

As expected no dielectric hysteresis of the ε′- and ε″-temperature curves was observed, such as is found with γ-Al_2O_3 which has much larger cavities.

[*] Dr. G. Ebert, Dipl.-Phys. W. Matron, and
Prof. Dr. F. H. Müller
Institut für Polymere der Universität
Marbacher Weg 15
355 Marburg/Lahn (Germany)

[1] These molecular sieves are zeolites pretreated at 300 °C. Manufacturer: Union Carbide Corporation.

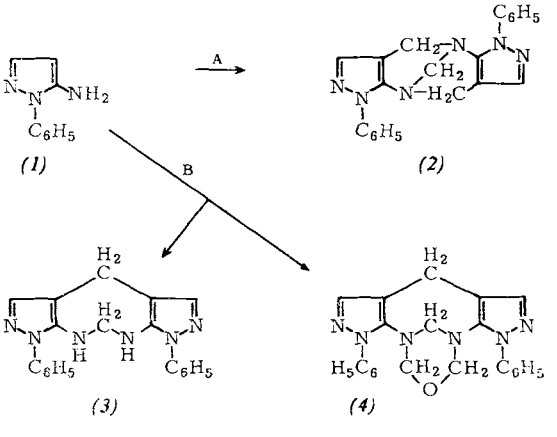
[2] We term these α-, β-, and γ-process, the α-process being the slowest and the γ-process the fastest.

[3] ε′, ε″, and ω are the real and the imaginary part of the complex dielectric constants and the circular frequency.

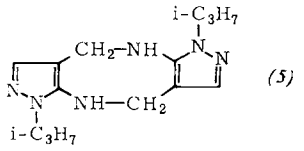
Reactions of Heterocyclic Amines with Formaldehyde

By *K. Eichenberger*, *F. A. Stuber*, and *P. Schmidt*[*]

The reaction of 1-phenyl-5-aminopyrazole *(1)* with paraformaldehyde in sulfuric acid yields a polycyclic ring system *(2)* of the Tröger base type (path A). If the reaction is carried out in formic acid and formalin, *(3)* and *(4)* are formed (path B).



If the phenyl group is replaced by an isopropyl group, the isopropyl derivative corresponding to *(3)* is formed in formic acid and formalin, whereas with paraformaldehyde in sulfuric acid, the bis-fused eight-membered ring *(5)* is obtained along with the isopropyl compound corresponding to *(2)* as by-product.



(5)

The structures of the compounds obtained were established mainly by NMR spectroscopy.

[*] Dr. K. Eichenberger, Dr. F. A. Stuber, and Dr. P. Schmidt
Chemische Forschungslaboratorien der
Pharmazeutischen Abteilung
CIBA Aktiengesellschaft
CH-4000 Basel (Switzerland)

The Gas-Chromatographic and Spectrophotometric Investigation of Essences

By *H. Farnow* and *E. Klein*[*]

The IR spectra of the juniper oils of *J. communis, phoenica,* and *macropoda* show characteristic differences in some band intensities, which permit the identification of the only one that is of interest in the production of essences, *i.e.* that of *J. communis*. The gas-chromatographic examination of the monoterpene fraction of these oils (58% for *J. communis*, 88% for *J. phoenica*, and 65% for *J. macropoda*) leads to the same result.

Oil of anise, which is obtained from the fruit of the evergreen tree *Illicum verum* Hooker f., consists of about 90% of *trans*-anethole, about 5% of limonene, about 1% of linalool, and about 20 other substances. The IR spectrum differs from that of anethole only in the presence of three weak bands.

For the gas-chromatographic examination of oil of anise, the components that boil before the anethole were distilled off. The distillate was then finely fractionated under vacuum in a packed column 120 cm high, with constant gas-chromatographic control. If individual components still could not be isolated, a preparative gas chromatograph was used. The maxima in the first gas chromatogram could be assigned after the isolated substances had been identified.

The gas chromatograms and IR spectra of Italian and Californian lemon oils are so similar that they are insufficient as a criterion of source. The UV spectrum is useful in this case. The extinction of a solution of 0.25 g of oil in 100 ml of 96% alcohol is measured between 400 and 270 nm. The CD value (distance between the maximum at 315 nm and the tangents to the branches of the curve at about 370 and 285 nm) is found from the curve; the values are about 0.60 extinction units for Italian lemon oils and 0.30 for Californian oils. The absorption at 315 nm is mainly due to citraptene, a coumarin derivative.

The components of essences belong to many classes of substances, and their number is usually large. Several methods are now available for taking into account the characteristic properties of the components in the evaluation of gas chromatograms: determination of area factors; construction of a calibration curve; and the use of an internal standard. The first two procedures presuppose that every component of the mixture is known, that it can be detected quantitatively, and that it is available in a sufficiently pure state. These conditions are generally not satisfied in multicomponent mixtures. The use of an internal standard fails because of the large number of components present.

The investigation of two test mixtures of terpene hydrocarbons and of terpene hydrocarbons with derivatives containing oxygen gave relative errors of 0 to ± 50%. The reproducibility was generally good.

[*] Dr. H. Farnow and Dr. E. Klein
Firma DRAGOCO
345 Holzminden (Germany)

Mass-Spectrometric Determination of the Structure of Peptide Alkaloids from Rhamnaceae

By *H.-W. Fehlhaber*[*]

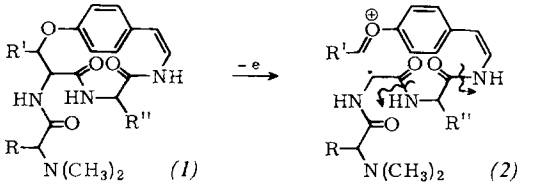
The fragmentation of peptide alkaloids of the type *(1)* on electron impact is substantially independent of the nature of the amino acid residues R, R′, and R″. The most important degradation reactions are a)–d).

a) Cleavage of the C–C bonds adjacent to the dimethylamino group leads to the ions $[M-R]^{\oplus}$ and $R-CH=\overset{\oplus}{N}(CH_3)_2$ (= *m/e* [57 + R]).

b) The cleavage of the 14-membered ring in accordance with *(2)* and subsequent cleavage at the amide groups with concomitant hydrogen shift lead to the fragment-ions

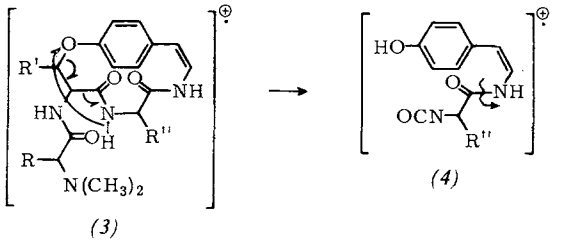
$R'-CH=\overset{\oplus}{O}-C_6H_4-CH=CH-NH-CO-CH(R'')-NH_2$ (= *m/e* [203 + R′ + R″]) and

$R'-CH=\overset{\oplus}{O}-C_6H_4-CH=CH-NH_2$ (= *m/e* [147 + R′]).



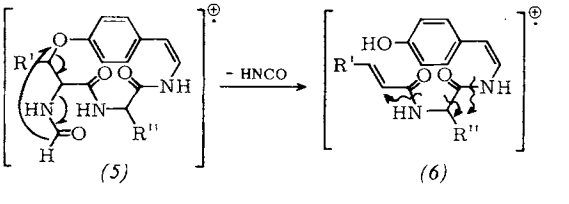
(1) (2)

c) The ring can also be cleaved, *e.g.* as formulated in *(3)*, by the typical decomposition accompanied by a hydrogen shift observed for phenol ethers, giving the fragment-ion *(4)* (*m/e* [217 + R″]). The fragment $[HO-C_6H_4-CH=CH-NH_2]^{\oplus}$ (= *m/e* 135) is also formed.



(3) (4)

d) Stepwise degradation of the side chain yields ions *(5)* (= *m/e* [287 + R′ + R″]) and *(6)* (= *m/e* [244 + R′ + R″]). *(6)* decomposes further into $R'-CH=CH-C\equiv O^{\oplus}$ (= *m/e* [54 + R′]), R′–CH=CH–CO–NH=CHR″ (= *m/e* [82 + R′ + R″]), and R′–CH=CH–CO–NH–CH(R″)–$C\equiv O^{\oplus}$ (= *m/e* [110 + R′ + R″]).



(5) (6)

The number of fragments is sufficiently large to permit a fast and definite assignment of the basic skeleton and the determination of the amino acid residues R, R′, and R″ for compounds of the type *(1)*. The method has so far been successfully used for six alkaloids.

[*] Dr. H.-W. Fehlhaber
Organisch-Chemisches Institut der Universität
Meckenheimer Allee 168
53 Bonn (Germany)

Anodic Behavior of Nickel in Aqueous Solution

By *E. Flechsig* [*]

Current density-potential curves were measured potentiostatically on nickel surfaces; the course of the curve depends much more strongly on the preparation of the surface than was formerly thought. This may explain the lack of agreement among published results. In particular, the occurrence of several current density maxima at potentials below the passivation potential and the puzzling acceleration of the dissolution of nickel by sulfate ions [1] must be attributed to oxide or Beilby layers formed on the surface during processing. Such layers dissolve only with great difficulty or not at all in acidic solution, as is shown by optical and electron-microscope studies.

For clean surfaces, the anodic dissolution of the metal, like the deposition of hydrogen, can be represented as a Tafel slope. It can be concluded that the rate-determining step in the dissolution of nickel is a charge transfer reaction. The highest current density that could be reached below the passivation potential was about 400 mA/cm³ at 25 °C and pH = 0.3, *i.e.* appreciably higher than the values reported so far. This corresponds to the values obtained for iron under comparable conditions. Passivation of the nickel took place over a narrow range of potentials and proceeded very rapidly. The potential of the steep decrease in current density and the current density maximum were pH-dependent, whereas the Tafel slope was not. At 25 °C, the passivation potential changes by 90 mV/pH unit; the value accepted until now was 58 mV/pH unit. It must be concluded from these results that earlier views concerning the passivation mechanism are not entirely correct. The following reaction is proposed as the decisive process in the formation of a passive layer:

$$Ni + 2\,H_2O \rightleftharpoons HNiO_2^- + 3\,H^+ + 2\,e$$

The $HNiO_2^-$ ions, as a monatomic adsorption layer, could strongly hinder the dissolution of the nickel.

[*] Dr. E. Flechsig
Institut für Metallkunde der Technischen Universität
Hardenbergstr. 34
1 Berlin 12 (Germany)

[1] *G. G. Lopovok, Ya. M. Kolotyrkin,* and *L. A. Medvedeva,* Zašč. Metallov *2,* 527 (1966).

Kinetics of the Extraction of Plutonium(IV) and of Uranium(VI) in the Purex Process

By *L. Finsterwalder* and *F. Baumgärtner* [*]

The most important reprocessing technique for irradiated nuclear fuel elements is liquid-liquid extraction with tributyl phosphate in the Purex process. Using the drop method, we tried to get a better understanding of the processes involved in the mass transfer of Pu(IV) and U(VI) across the boundary between the organic and the aqueous phases.

In the drop method, which was first used by *J. M. Coulsan* and *S. J. Skinner,* and was later improved by *W. Nitsch,* the rate of transfer of material from a stationary phase into the drops of the other phase is measured.

At 25 °C we obtained reaction orders of 1.28, 1.16, and 1.03 for the transfer of uranium from an aqueous solution which was 3 N in HNO_3 into an organic phase containing 20, 10, and 5 wt-%, respectively, of TBP. A reaction order of 1.0 was obtained for plutonium, The rate of transfer of Pu(IV) and U(VI) was found to vary linearly with the nitrate concentration.

The transfer rates into the organic phase decrease in the order U, Pu, HNO_3, while for back-extraction into the aqueous phase they increase in the order U, Pu, HNO_3. This explains the displacement effects of the three substances.

[*] Dipl.-Physiker L. Finsterwalder and Prof. Dr. F. Baumgärtner
Kernforschungszentrum
75 Karlsruhe (Germany)

New Peroxotungstates

By *J. Fuchs* and *J. Kurzidim* [*]

The peroxotungstates $b_2O{\cdot}WO_3{\cdot}4O_{act}{\cdot}aq$ *(1)* (b = monovalent cation, aq = water) and $b_2O{\cdot}2WO_3{\cdot}4O_{act}{\cdot}aq$ *(2)*, which can be obtained from aqueous solution, are already known. The question of whether salts of peroxidized polytungstic acids can also be prepared has until now been strongly disputed.

Other peroxotungstates have now been prepared by hydrolysis of tetramethyl tungstate(VI) in ethanol with 85% hydrogen peroxide in the presence of bases. They have the analytical composition $b_2O{\cdot}WO_3{\cdot}2O_{act}{\cdot}aq$ *(3)*, $3b_2O{\cdot}6WO_3{\cdot}10O_{act}{\cdot}aq$ *(4)*, $5b_2O{\cdot}12WO_3{\cdot}20O_{act}{\cdot}aq$ *(5)*, and $b_2O{\cdot}4WO_3{\cdot}4O_{act}{\cdot}aq$ *(6)*.

Potassium hydroxide, ammonia, piperidine, pyridine, quinoline, diethylamine, and triethylamine are examples of bases used. The type of compound formed in all cases depends on the concentration of the reaction components, the temperature, the p*K* value of the base, and possibly the steric structure of the base.

The IR spectra of compound types *(4)–(6)* are very similar in the region of the W–O vibrations; it may therefore be concluded that the structures of their polyanions are very similar. Results of ultracentrifugation indicate that aqueous solutions of the potassium salts of the types *(4)* and *(5)* contain hexameric anions. Proton magnetic resonance measurements show that the salts of these types contain both water of crystallization and OH (possibly O–OH) groups.

According to these findings, the following formulations are probably correct for *(4)–(6)*: $b_6[H_2W_6O_{32}]{\cdot}n\,H_2O$ *(4)*; $b_5[H_3W_6O_{32}]{\cdot}n\,H_2O$ *(5)*; and $b_3[H_5W_6O_{28}]{\cdot}n\,H_2O$ *(6)*.

Annealing of $K_5[H_3W_6O_{32}]{\cdot}9H_2O$ at temperatures up to 200 °C yields the peroxide-free potassium paratungstate B (intermediate of the potassium paratungstate A and Z), which was recently obtained for the first time by *K. F. Jahr, J. Fuchs,* and *E. P. Flindt* by hydrolysis of esters of tungstic acid in the presence of potassium acetate.

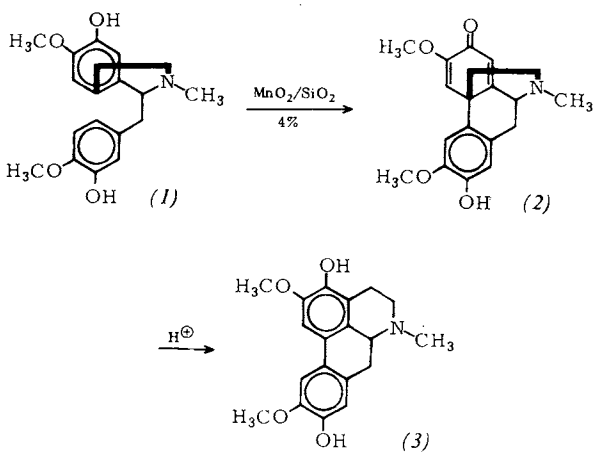
[*] Dr. J. Fuchs and J. Kurzidim
Institut für Anorganische Chemie der Freien Universität
Fabeckstr. 34/36
1 Berlin 33 (Germany)

Synthesis of Alkaloid Skeletons by Biogenetic-type Ring Closure

By *B. Franck, H. I. Lubs,* and *G. Dunkelmann* [*]

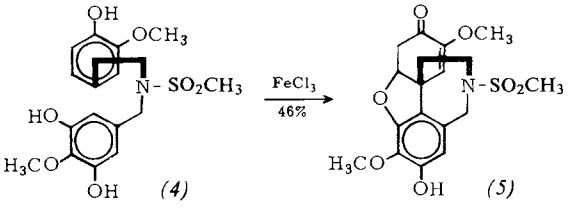
Morphine and galanthamine are the principal members of two important groups of alkaloids, whose skeletons are formed in the plant cell by oxidative condensation of phenolic precursors. The biosynthesis has now been successfully imitated on the preparative scale by prevention of polymerization and of side reactions on the nitrogen. Thus the oxidation of reticuline *(1)*, the biosynthetic precursor of the morphine alkaloids, with MnO_2/thin-layer silica gel 1:3 in $CHCl_3$ led for the first time to the isolation of a morphinan derivative *(2)* as the crystalline monoacetate (m.p. 203 °C). Like morphine, *(2)* can undergo proton-catalysed rearrangement into an apomorphine derivative *(3)*.

The additional adsorption surface presented in the form of the silica gel during the oxidation keeps the concentration of reticuline molecules on the MnO_2 particles low, thus substan-



tially preventing intermolecular condensation. This two-dimensional or heterogeneous variant of the Ziegler dilution principle also plays a part in enzymatic reactions.

The *N*-benzylphenylethylamine derivative *(4)*, in which the nitrogen is protected by a methylsulfonyl group, undergoes double ring closure on oxidation with aqueous $FeCl_3$ to give a 46% yield of the crystalline condensation product *(5)* (m.p. 239 °C) having the complete galanthamine ring skeleton.



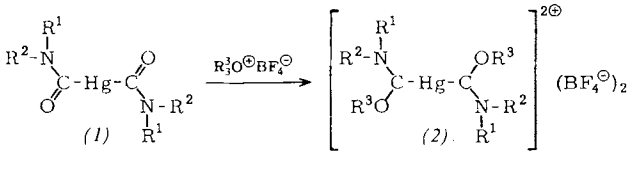
[*] Prof. Dr. B. Franck, Dipl.-Chem. H. I. Lubs, and Dipl.-Chem. G. Dunkelmann
Institut für Organische Chemie der Universität
Olshausenstr. 40–60, Haus 27
23 Kiel (Germany)

Synthesis and Reactions of Stable Mercury-Carbene Complexes

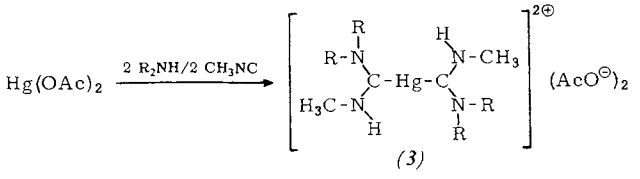
By *U. Schöllkopf* and *F. Gerhart* [*]

Stable carbene-metal complexes[1] have until now always been prepared from metal π-carbonyls. We have now examined the possibility of preparing carbene complexes from σ-carbonylmetal compounds.

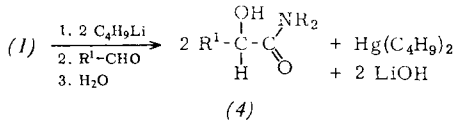
Bis(dialkylcarbamoyl)mercury compounds *(1)* [2], which can be prepared from mercury acetate, secondary amines, and CO, give stable adducts with strong protonic acids (100% H_2SO_4, 100% $HClO_4$) or with trialkyloxonium fluoroborates *(2)* [3].



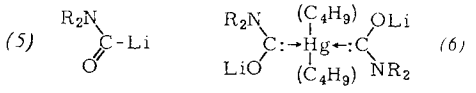
When $R^1 \neq R^2$, three stable, isolable isomers are obtained. Adducts *(3)* of diaminocarbenes are obtained directly from mercury acetate, secondary amines, and methyl isocyanide.



We attempted to prepare anionic carbene adducts from *(1)* and two moles of n-butyllithium. The reaction at −78 °C in tetrahydrofuran yields intensely yellow solutions, which readily give carbamoyl adducts such as *(4)* on treatment with acid chlorides, aldehydes, and ketones [4].



It is not yet possible to decide whether free carbamoyllithium *(5)* or a dialkylaminolithiumoxycarbene complex *(6)* functions as the reactive species.



(5) or *(6)* is the only known reagent suitable for the direct nucleophilic introduction of a carbonyl group into polar substrates [5].

[*] Prof. Dr. U. Schöllkopf and Dipl.-Chem. F. Gerhart
Organisch-chemisches Institut der Universität
Windausweg 2
34 Göttingen (Germany)

[1] *E. O. Fischer* and *A. Maasböl*, Angew. Chem. *76*, 645 (1964); Angew. Chem. internat. Edit. *3*, 580 (1964); *P. W. Jolly* and *R. Pettit*, J. Amer. chem. Soc. *88*, 5044 (1966).

[2] *U. Schöllkopf* and *F. Gerhart*, Angew. Chem. *78*, 675 (1966); Angew. Chem. internat. Edit. *5*, 664 (1966).

[3] *U. Schöllkopf* and *F. Gerhart*, Angew. Chem. *79*, 578 (1967); Angew. Chem. internat. Edit. *6*, 560 (1967).

[4] *U. Schöllkopf* and *F. Gerhart*, Angew. Chem. *79*, 819 (1967); Angew. Chem. internat. Edit. *6*, 805 (1967).

[5] This was formerly accomplished by devious routes, cf. *E. J. Corey* and *D. Seebach*, Angew. Chem. *77*, 1134 (1965); Angew. Chem. internat. Edit. *4*, 1075 (1965); *E. J. Corey*, *D. Seebach*, and *R. Freedman*, J. Amer. chem. Soc. *89*, 434 (1967); *D. Seebach*, Angew. Chem. *79*, 468 (1967); Angew. Chem. internat. Edit. *6*, 442 (1967).

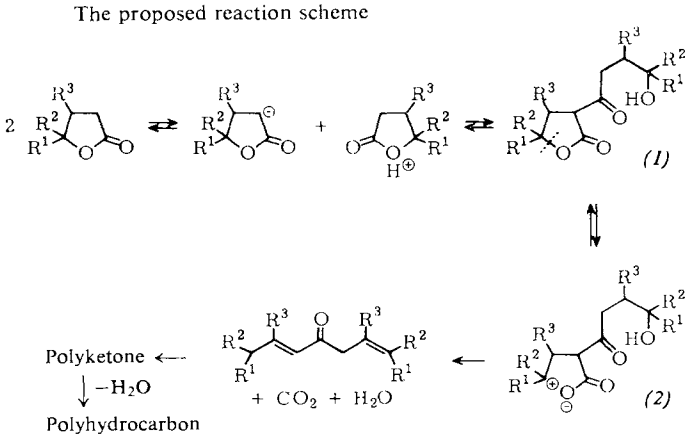
Behavior of Lactones Under Pressures of 20–24 kbar: A Model Reaction for the Formation of Petroleum

By *W. Glet* and *F. Korte* [*]

γ-Butyrolactone can be homopolymerized at 20–24 kbar [1] to give a polyester [2]. On the other hand, the polymerization of the more stable [3] alkyl-substituted γ- and δ-lactones at 20–24 kbar and 150–200 °C generally proceeds with elimination of water and carbon dioxide to form highly branched hydrocarbons. The ease with which the reaction takes place increases with the proximity of the alkyl group to the ring oxygen atom. Thus δ-caprolactone is simply decarboxylated, whereas the reaction of β-methyl-δ-valerolactone results mainly in polyester formation, together with slight decarboxylation. Both cases presumably involve competitive reactions. The decarboxylation may be favored because it is irreversible. However, the deciding factor is probably the nature of the lactone ring cleavage. Alkyl cleavage leads to decarboxylation, whereas acyl cleavage leads to polyester formation. The ring cleavage is influenced by the substituents, the strength of the influence depending on their position [4,5].

α,α-Dimethyl-δ-valerolactone gives polyester only, while α,α-dimethyl-γ-butyrolactone does not react at all. α-Methyl-γ-butyrolactone, on the other hand, is decarboxylated. It may be concluded from this behavior that decarboxylation cannot take place if the α position is blocked.

The proposed reaction scheme



is supported by the following observations:

1) The first step is supported by the fact that decarboxylation is favored by bases and inhibited by acids.

2) According to the scheme, an ω-hydroxy-α-acyllactone *(1)* is formed as an intermediate. α-Acyllactones give first poly-β-oxo acids, which are rapidly decarboxylated under normal pressure to form polyketones. Water is not formed from α-acyllactones when the OH group in *(1)* is not present. It is therefore possible that carbon dioxide is split off only at normal pressure, since water appears to play an important part in the removal of CO_2 at very high pressures.

α-Acyllactones exhibit a greater tendency toward alkyl cleavage than alkyllactones[4,5]. This facilitates the subsequent steps in the reaction and explains the relatively high reactivity of the α-acyllactones.

3) It is possible to prepare a polycondensation product from acetone that is very similar to those obtained from lactones. This is as might be expected from a comparison with the penultimate step of the scheme when $R^1 = R^2 = H$.

So far as we know, this is the first demonstration that carboxylic acids can be converted into hydrocarbons by pressures of 20–24 kbar at temperatures below 200 °C. Since petroleum does not appear to have reached temperatures higher than 200 °C during its formation[6], pressure could have played a part in its formation. The reaction of the lactones could be regarded as a model reaction for the formation of bituminous substances.

[*] Dr. W. Glet and Prof. Dr. F. Korte
Organisch-Chemisches Institut der Universität
Meckenheimer Allee 168
53 Bonn (Germany)

[1] *F. Korte, W. Glet,* and *H. Lechner,* Z. Naturforsch. *20b,* 703 (1965).

[2] *F. Korte* and *W. Glet,* Polymer Letters *4,* 685 (1966).

[3] *O. H. Weeler* and *E. E. Granell de Rodriguez,* J. org. Chemistry *29,* 1227 (1964).

[4] *C. K. Ingold*: Structure and Mechanism in Organic Chemistry. Cornell University Press, Ithaca 1953, p. 754.

[5] *E. S. Gould*: Mechanismus und Struktur in der organischen Chemie. Verlag Chemie GmbH., Weinheim 1964, p. 372ff.

[6] *A. F. Dobrianskii,* Trudy Vsesoyuz. Neft. Nauch.-Issledovatel. Geologorazvedoch. Inst. *123,* No. 5, p. 7 (1958); Chem. Abstr. *53,* 13910f (1959); *A. I. Bogomolov* and *V. K. Shamanskii, ibid. 105,* No. 4, p. 279 (1957); Chem. Abstr. *53,* 7736g (1959).

Investigations on the Biosynthesis of D-Apiose

By *H. Grisebach, H. Sandermann,* and *T. Tisue*[*]

Our investigations on the biosynthesis of D-apiose (3-*C*-hydroxymethyl-D-*erythro*-tetrose) in parsley with ^{14}C- and T-labeled precursors have shown that this sugar is formed from D-glucose by intramolecular rearrangement with expulsion of C-3; the C-6 of the glucose is lost[1]. An intermediate in this biosynthesis is D-glucuronic acid (possibly in the nucleotideactivated form), since this acid is specifically incorporated into the D-apiose of the glycoside apiin with loss of C-6[2].

In the transition D-glucose → D-apiose, an H atom migrates from the C-4 of glucose to the C-3′ of the apiose, as was shown with tritium-labeled glucose[1]. D-Apiose was detected in parsley in the UDP sugar fraction.

Incubation of ^{14}C–UDP-D-glucuronic acid with a protein fraction of acetone-dried powder from parsley, on addition of NaF or NaF + NAD, gave a new radioactive compound, from which radioactive D-apiose was obtained by hydrolysis.

[*] Prof. Dr. H. Grisebach, Dipl.-Chem. H. Sandermann, and Dr. T. Tisue
Isotopenabteilung des Chemischen Laboratoriums
der Universität
Albertstr. 21
78 Freiburg/Br. (Germany)

[1] *H. Grisebach* and *U. Döbereiner,* Biochem. biophysic. Res. Commun. *17,* 737 (1964); Z. Naturforsch. *21b,* 429 (1966).

[2] *H. Grisebach* and *H. Sandermann jr.,* Biochem. Z. *346,* 322 (1966).

Enzyme-Catalysed Changes in the Volatile Components of Peas

By *W. Grosch*[*]

Young freeze-dried green peas were extracted with water; after rough filtration, the extract was centrifuged at 17500 g and the supernatant liquid was freeze-dried. When the supernatant [dissolved in a phosphate buffer, pH = 6.5] was incubated aerobically at 15 °C with lipids isolated from peas[1], the typical aroma of peas in storage was evolved. The aroma that developed in the first hour gradually gave way to an unpleasant odor.

The following four fractions were vaporized under vacuum from the lipids emulsified in the buffer:

1. the compounds dissolved in the lipids; 2. the compounds formed during a 'blank incubation' (*i.e.* in the absence of supernatant); 3. the compounds adhering to the supernatant added to the emulsion; and 4. the compounds formed during incubation of the lipids for two hours with the supernatant. The third and fourth fractions were extracted with ether/pentane (2:1 v/v) and the extracts were analysed by gas chromatography and mass spectrometry. It was deduced from the results that hexanal, 2-heptenal, 2,4-heptadienal, pentanol, and 2-penten-1-ol (?) are formed in high concentrations and 2-pentenal, 2-hexenal, 3-pentanone, 3-octanone, 2-pentylfuran, and hexanol in low concentrations during the incubation at 15 °C.

Whitfield and *Shipton*[2] believe that the enzyme lipoxygenase (EC 1.13.1.13) is involved in the formation of carbonyl compounds during the storage of unblanched peas at −17.5 °C. Dialysis and precipitation with ammonium sulfate yielded a protein fraction[3] from freeze-dried peas in which the lipogenase and peroxidase activities (based on the dry weight) were 30 and 5 times as high, respectively, as in the peas themselves, and incubated the lipids aerobically for two hours at 15 °C with this preparation. The carbonyl compounds formed were isolated as the 2,4-dinitrophenylhydrazones and analysed. Result (in % of the total carbonyl compounds): n-alkanals C_2 (13), C_3(19), C_4(1), C_5(3), C_6(22), C_9(3); n-2-alkenals C_4(1.5), C_5(4.5), C_6(1.5), C_7(10), C_8(3), C_{9-11}(< 1); n-2,4-alkadienals C_7(3), C_9(< 1), C_{10}(2); acetone (6); unidentified (7).

According to *Bengtsson* and *Bosund*[1], 50% of the fatty acids of pea lipids consists of linoleic acid. Linoleic acid was therefore incubated with the enzyme preparation. Analysis of the volatile carbonyl compounds showed (%): n-alkanals

$C_5(5)$, $C_6(65)$, $C_9(11)$; n-2-alkenals $C_6(< 1)$, $C_7(9)$, $C_8(3.5)$; n-2,4-alkadienals $C_9(1)$, $C_{10}(4)$.

[*] Dr. W. Grosch
Institut für Lebensmittelchemie und
Lebensmitteltechnologie der Technischen Universität
Hardenbergstr. 34
1 Berlin 12 (Germany)

[1] *B. Bengtsson* and *I. Bosund*, J. Food Sci. *31*, 474 (1966).

[2] *F. B. Whitfield* and *J. Shipton*, J. Food Sci. *31*, 328 (1966).

[3] *F. A. Lee* and *A. C. Wagenknecht*, Food Res. *23*, 584 (1958).

Gas-Chromatographic Investigation of Lemon Oils

By *H. Günther*[*]

A total of 19 commercial lemon oils were studied gas-chromatographically (gas chromatograph Perkin-Elmer 116, Überlingen). The substances found are: α-pinene, β-pinene, limonene, γ-terpinene, citronellal, α(?)-terpineol, neral, and geranial (= citral), neryl acetate, geranyl acetate, and β-bisabolene. Myrcene, geraniol, bergamotene, and caryophyllene are also present (but in some cases were not separated from the above substances). The substances could be quantitatively estimated by manual measurement of the areas (though cutting out and weighing of a photocopy[1] should be more accurate[2]), by planimetry, or by means of an integrator. However, it is advisable to construct calibration curves for each substance, since the detector deflections are not the same for all substances, and since the curves obtained are often nonlinear or are linear only up to a certain concentration[3]. The nature of the substances should be verified by IR spectra, since the substances may undergo partial or complete decomposition on the metal of the gas chromatograph. The substances must be obtained on preparative columns in quantities of 0.5 to 1 g and then examined in the IR instrument either between two KBr disks or between two NaCl windows. The usual method of admixture with two different columns can be regarded only as a provisional identification.

[*] Dr. H. Günther
Bundesanstalt für Fleischforschung
865 Kulmbach (Germany)
Present address:
Staatliche chemische Untersuchungsanstalt
Annastr. 16
89 Augsburg (Germany)

[1] Paper: Agfa Cp 21×29.7 or 29.7×42 cm².

[2] *R. Kaiser*: Chromatographie in der Gasphase. Bibliographisches Institut, Mannheim 1964, Part IV, p. 97.

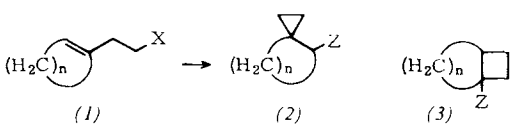
[3] *H. Farnow*: Gaschromatographie. Dragoco, Holzminden 1965, p. 77; *H. Farnow* and *F. Porsch*: Tips für die Praxis, 23 GC. Perkin-Elmer Bodenseewerk, Überlingen 1965; 1/23.

Rearrangements of Cyclic Homoallyl Compounds

By *M. Hanack*, *H. Schneider-Bernlöhr*, *H.-J. Schneider*, and *R. Hüttinger*[*]

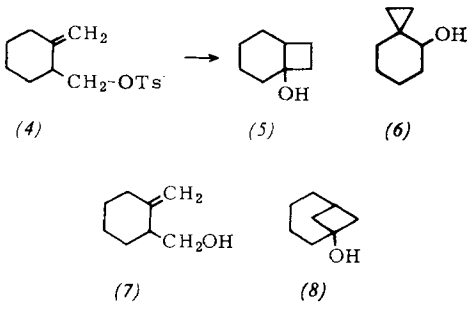
Cyclic homoallyl derivatives *(1)* (X = OTs, NH_2) rearrange during carbenium ion reactions to form cyclopropane spiro compounds *(2)*, Z = OH, OCOR, and condensed cyclobutane compounds *(3)*, Z = OH, OCOR.

This isomerization, which was first observed with the cyclohexenylethyl system *(1)*, $n = 4$, has now been applied to larger rings. Cycloheptenyl-, cyclooctenyl-, and cyclononenylethyl compounds also form cyclopropane spiro compounds *(2)*, $n = 5$–7, and condensed cyclobutane derivatives *(3)*, $n = 5$–7. The systems *(2)*–*(3)*, which are partly known only as hydrocarbons, are obtainable on the preparative scale in this way.



(1) *(2)* *(3)*

Systems having both the double bond and the C atom carrying the functional group outside the ring also tend toward substantial rearrangements in carbenium ion reactions. For example, the hydrolysis of 2-methylenecyclohexylmethyl *p*-toluenesulfonate *(4)* yields a mixture of the alcohols *(5)*, *(6)*, and *(7)*, and another component, which is assigned the structure *(8)*.



(4) *(5)* *(6)*

(7) *(8)*

[*] Priv.-Doz. Dr. M. Hanack, Dr. H. Schneider-Bernlöhr, Dr. H.-J. Schneider, and Dr. R. Hüttinger
Chemisches Institut der Universität
Wilhelmstr. 33
74 Tübingen (Germany)

Kinetics of the Oxidation of a Silver-Cadmium Alloy containing 51 Atom-% of Cd. A Contribution to the Hedvall Effect

By *K. Hardel*[*]

A Hedvall effect, *i.e.* the increased reactivity of a solid during a crystallographic transition is not to be expected if the reactants are separated by a layer of reaction product, and diffusion through this layer is the rate-determining process. A Hedvall effect is feasible, on the other hand, if in addition to this diffusion the counterdiffusion of another type of ion through the lattice of one of the reactants is rate-determining; the rate of the reaction then also depends on the structure of this reactant.

This situation can be realized in the internal oxidation of some alloys. The oxidation of the powdered silver-cadmium alloy containing 51 atom-% of Cd was therefore studied thermogravimetrically and with the aid of photomicrographs in oxygen at 1 atm and between 350 and 450 °C, *i.e.* above and below the transition point for the transition from the ζ-phase into the β-phase (430 °C).

Two reaction mechanisms were found to apply. In one range the linear law is valid and in a subsequent region the parabolic law is obeyed; in the latter the rate of oxidation is determined by the diffusion of oxygen through the inner oxidation zone and by the counterdiffusion of cadmium from the interior of the alloy. The rate constant of the parabolic time law changes steadily throughout the temperature range studied; the rate constant of the linear time law, on the other hand, decreases suddenly at the transition point. No abnormal increase in reactivity was observed at the transition point in either reaction and thus no Hedvall effect could be detected. The increase in the rate of oxidation of an alloy of the same composition in the vicinity of the transition point at 430 °C as reported by *Hedvall* and *Rosén*[1] is simply the result of the superposition of the reaction for which the linear time law is valid on the diffusion-controlled reaction.

[*] Dr. K. Hardel
Anorganisch-Chemisches Institut der Technischen Universität
Hardenbergstr. 34
1 Berlin 12 (Germany)

[1] *J. A. Hedvall* and *U. Rosén*, Z. anorg. allg. Chem. *229*, 413 (1936).

Curium Oxides[1]

By *H. O. Haug*[*]

In the thermal decomposition of curium dioxide (see Fig. 1), a phase $CmO_{1.71}$ was formed at 650 °C in oxygen. The strong lines of the X-ray powder photographs were characteristic of the fluorite lattice, while additional weak lines showed a strong similarity to the lines of the rhombohedral oxides $PrO_{1.71}$ and $TbO_{1.71}$. As the temperature was raised (in air), the $CmO_{1.7}$ lost oxygen ('$CmO_{1.7-x}$ phase') and the lattice constants increased. Above 800 °C, two phases appeared in the powder diagrams: $CmO_{1.7-x}$ and monoclinic Cm_2O_3 (B form). Only the stronger lines of the $CmO_{1.7-x}$ phase, *i.e.* those characteristic of the fluorite lattice, could be observed. The higher the temperature to which the samples were heated, the greater was the quantity of monoclinic Cm_2O_3 formed, until at 1100–1200 °C only very small quantities of $CmO_{1.7-x}$ remained. The lattice constants of the monoclinic Cm_2O_3 phase remained constant between 800 and 1200 °C.

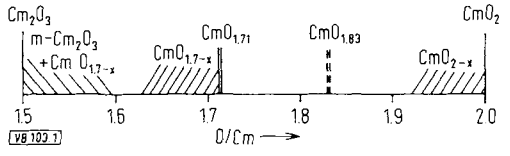


Fig. 1. Phases between Cm_2O_3 and CmO_2.

[*] Dr. H. O. Haug
Gesellschaft für Kernforschung
75 Karlsruhe (Germany)

[1] This work was carried out at the Argonne National Laboratory under the auspices of the United States Atomic Energy Commission.

Cycli-alkylation with 1,4-Dihalo Compounds as a Convenient Way of Preparing Polycyclic Hydroaromatic Compounds

By *D. Hausigk*[*]

Partially hydrogenated aromatic hydrocarbons such as tetralin, symmetrical octahydrophenanthrene, and symmetrical octahydroanthracene react with 1,4-dichlorobutane in the presence of catalytic amounts of $AlCl_3$, and the reaction leads to an enlarged molecule. Thus, dodecahydrotriphenylene is formed from tetralin *via* the intermediates of the octahydro derivatives of phenanthrene and anthracene. Other partially hydrogenated hydrocarbons that still contain one aromatic ring with replaceable hydrogen atoms (*e.g.* hydroindene, decahydropyrene, and hexahydrofluorene) similarly react with 1,4-dichlorobutane, and the reaction leads to the incorporation of further ring systems. With aromatic hydrocarbons themselves (except benzene), the reaction proceeds in widely differing ways.

Some alkyl-substituted benzenes (except methyl-substituted ones) similarly give dodecahydrotriphenylene with 1,4-dichlorobutane under the cleaving action of $AlCl_3$.

Using 1,2-bis(bromomethyl)cyclohexane as an alkylating agent, one obtains from the partially hydrogenated aromatic compounds enlarged hydroaromatic compounds always comprising two condensed rings. Thus octahydrophenanthrene gives hexadecahydrodibenzo[a,c]anthracene. The resulting rings are *trans* to each other.

All polycyclic hydroaromatic compounds obtained by cycli-alkylation can be readily dehydrogenated into the corresponding aromatic hydrocarbons; the latter can therefore be prepared by this method easily and in good yields.

[*] Dr. D. Hausigk
Bergbau-Forschung GmbH.
Frillendorfer Str. 351
43 Essen-Kray (Germany)

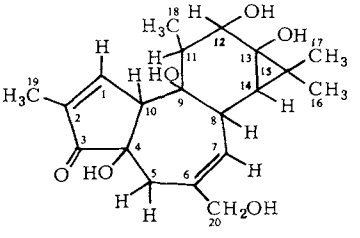
Etherification of Phorbol

By *G. Kreibich* and *E. Hecker*[*]

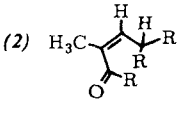
Phorbol is a tetracyclic polyfunctional diterpene[1]. Its diesters with one short-chain and one long-chain fatty acid exhibit strongly inflammatory properties. Phorbol is sensitive to heat, to acids, and to alkalis, and reduces Fehling's solution and Tollens' reagent[1–4].

The hydroxyl groups on C-20 and C-13 can be etherified in ether with diazomethane in the presence of aluminum isopropoxide[5]. With diazoethane, it is also possible to ethylate the secondary hydroxyl group on C-12. Rather surprisingly, the tertiary hydroxyl group on C-4 can be methylated with methyl iodide and silver oxide in dimethylformamide[6] if the hydroxyl groups on C-12, C-13, and C-20 are protected by acetate groups. When ethyl acetate is used as the solvent for this reaction, only the primary hydroxyl group is etherified if the cyclopropane hydroxyl group is protected. If the hydroxyl group on C-13 is free, the cyclopropane ring is oxidatively cleaved.

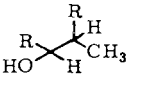
The partial structures *(2)* and *(3)*, which were verified by nuclear magnetic resonance spectrometry, were at first assumed to be joined to a secondary acyloin, since phorbol and its esters give positive Fehling and Tollens reactions[4,7]. However, it can be shown with ether derivatives of phorbol that the free hydroxyl group on the cyclopropane ring is alone responsible for the reducing properties. Independently of us[8], a similar reaction was recently observed with simple tertiary cyclopropanols. As is shown by the UV and circular dichroism data obtained for phorbol derivatives having the tertiary hydroxyl group on C-4 etherified or esterified this group is in the α position with respect to the carbonyl group. Phorbol therefore contains a tertiary acyloin grouping.



(1)



(2)



(3)

[*] Dipl.-Chem. G. Kreibich and Prof. Dr. E. Hecker
Deutsches Krebsforschungszentrum, Biochemisches Institut
Berliner Str. 23
69 Heidelberg (Germany)

[1] *E. Hecker et al.*, Tetrahedron Letters *1967*, 3165; Naturwissenschaften *54*, 282 (1967).

[2] *E. Hecker et al.*, Z. Naturforsch. *21b*, 1204 (1966).

[3] *B. Flaschenträger*, Zangger-Festschrift, Zürich 1934, p. 657.

[4] *T. Kauffmann* and *H. Neumann*, Chem. Ber. *92*, 1715 (1959).

[5] *A. Popelak* and *G. Lettenbauer*, Arch. Pharmaz. *295*, 427 (1962).

[6] *R. Kuhn*, *H. Trischmann*, and *I. Löw*, Angew. Chem. *67*, 32 (1955).

[7] *E. Hecker et al.*, Tetrahedron Letters *1965*, 1837.

[8] *S. Schaafsma*, *H. Steinberg*, and *Th. J. de Boer*, Recueil Trav. chim. Pays-Bas *85*, 73 (1966).

The Separation Efficiency in Gel Chromatography

By *W. Heitz*[*]

The efficiency of gel chromatography depends on the spread of the gaussian concentration profile of a substance during elution. This spread determines what substances can be

separated if their difference in elution volume is given and what details are still recognizable in the molecular-weight distribution.

A measure of the separation efficiency is the number of theoretical plates n or the height of the theoretical plate H:

$$n = \left(\frac{v_E}{\sigma}\right)^2 \text{ and } H = l/n$$

v_E = elution volume, σ = mean deviation (distance from the point of inflection to the perpendicular at the maximum), l = length of column.

Polyvinyl acetate gels and polystyrene gels with crosslinking-agent contents of 1 to 30 mole-% and particle sizes of 0.015 to 1 mm were used; the diffusion coefficient of the test substances was between 5×10^{-6} and 3×10^{-5} cm²/sec; the elution velocity was 2 cm/h to 2 m/h.

The separation efficiency of gel chromatography can be expressed in a general form with the aid of reduced quantities (*van Deemter, Giddings*)

$$h = a + b/\nu + c\nu$$

$$h = H/d_p,\ \nu = v \cdot d_p/D$$

d_p = particle diameter of the gel; v = elution velocity; D = diffusion coefficient; a,b,c = constants.

The constant a describes the regularity of packing, and is approximately 2 for good packing.

b is accounted for by diffusion broadening. The influence of the second term decreases with increasing flow rate; the reduced separation efficiency at high flow rates can thus be approximately represented by a linear relation. A minimum occurs at low reduced rates, *i.e.* there is an optimum elution velocity in gel chromatography. This optimum elution velocity depends on the substance: the diffusion coefficient is the normalizing factor.

c results from the lack of equilibration.

For gels with low crosslinking densities, the reduced separation efficiency can be represented by a single series of curves, which is independent of the above experimental parameters and the chemical nature of the gel. Diffusion in the gel is increasingly hindered with increasing crosslinking density. The curves obtained depend on the substance, but are independent of the particle size of the gel. It is estimated from the experimental data that values of the number of theoretical plates as high as 10^5 may be realized.

[*] Dr. W. Heitz
Organisch-Chemisches Institut der Universität
Johann-Joachim-Becher-Weg 18–20
65 Mainz (Germany)

Circular Dichroism in Phorbol Derivatives

By *H. Bartsch* and *E. Hecker*[*]

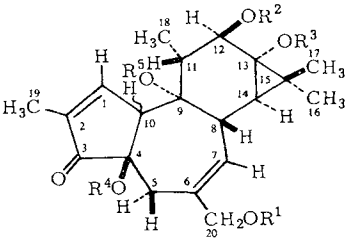
Oxidation of the secondary hydroxyl group on C-12 of phorbol 13,20-diacetate *(1)* with CrO_3/pyridine yields a diketone (phorbolone). The carbonyl group on C-3 can be selectively reduced with $NaBH_4$ in THF/isopropanol. This gives a monoketone that is isomeric with phorbol, and which is called neophorbol 13,20-diacetate[1]. If phorbol 13,20-diacetate has the formula first suggested[2], the diketone should contain α-carbonyl groups. However, the CD curve of phorbolone in the range 280–380 nm is made up additively from the curves of the monoketones. If the compound were an α- or β-diketone, *i.e.* if the carbonyl groups in this case were both situated in the same ring, electronic interaction of the chromophores would make an additive curve impossible[4]. The carbonyl group in position 3 and the hydroxyl group on C-12 are therefore clearly seen to be situated in different rings. By comparison of the dichroisms of various phorbol acetates and ethers with the values for unesterified and unetherified derivatives, it was possible to detect a tertiary acyloin grouping of the sequence C-3,4[3] [as in *(4)*][1]. The vicinal effects of an axial α-acetoxy group occur only in *(2)*. *(2)* and *(3)* also show a sign reversal of the R-band of the enone, which consists of a positive and a negative component in the case of *(3)*.

The magnitude of the dichroic absorption of neophorbol 13,20-diacetate permits the application of the rule for α,β-cyclopropyl ketones[4]. This gives an α three-membered ring for the absolute configuration of neophorbol, and hence also for phorbol (the conformation of the six-membered ring is the same in both compounds)[1]. X-ray analysis, on the other hand, gives the mirror image with a β three-membered ring[5].

The first restriction of the general validity of the α,β-cyclopropyl ketone rule is therefore shown by neophorbol 13,20-diacetate, an α,β-cyclopropyl ketone with a tertiary acetoxyl group on the three-membered ring.

Another unusual feature is the occurrence of a third CD band at 272 nm in phorbol derivatives. This anomaly is rigidly associated with the *trans*-fusion of the 5-membered ring and with the presence of the tertiary OH group on C-4.

It is not yet possible to explain this behavior.



(1) $R^2 = R^4 = R^5 = H$; $R^1 = R^3 = Ac$
(2) R^1-$R^5 = Ac$
(3) $R^5 = H$; R^1-$R^3 = Ac$; $R^4 = CH_3$
(4) R^1-$R^5 = H$

[*] Dipl.-Chem. H. Bartsch and Prof. Dr. E. Hecker
Deutsches Krebsforschungszentrum, Biochemisches Institut
Berliner Str. 23
69 Heidelberg (Germany)

[1] *E. Hecker, H. Bartsch, H. Bresch, M. Gschwendt, E. Härle, G. Kreibich, H. Kubinyi, H. U. Schairer, Ch. v. Szczepanski,* and *H. W. Thielmann,* Tetrahedron Letters *1967*, 3165.

[2] *E. Hecker, H. Kubinyi, Ch. v. Szczepanski, E. Härle,* and *H. Bresch,* Tetrahedron Letters *1965*, 1837.

[3] Cf. *G. Kreibich* and *E. Hecker,* Angew. Chem. *79*, 993 (1967); Angew. Chem. internat. Edit. *6*, 973 (1967).

[4] *P. Crabbé:* Optical Rotatory Dispersion and Circular Dichroism in Organic Chemistry. Holden-Day, San Francisco 1965.

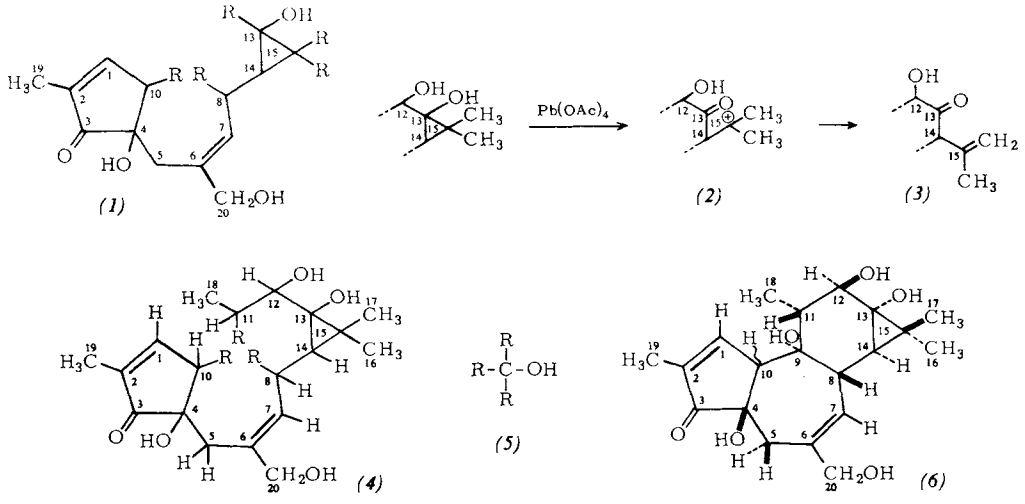
[5] *W. Hoppe, F. Brandl, J. Strell, M. Röhrl, I. Gassmann, E. Hecker, H. Bartsch, C. Kreibich* and *Ch. v. Szczepanski.* Angew. Chem. *79*, 824 (1967); Angew. Chem. internat Edit. *6*, 809 (1967)

Determination of Partial Structures of Phorbol by Cleavage with Periodate and with Lead Tetraacetate

By *M. Gschwendt* and *E. Hecker*[*]

Several observations indicate that phorbol contains a tertiary acyloin group on C-3/C-4[1]. This grouping can be detected by reduction to the secondary-tertiary glycol with $NaBH_4$ and cleavage of the glycol with sodium periodate to give a keto aldehyde. Reduction of the keto aldehyde with $NaBH_4$ gives a primary-secondary alcohol, in which the sequence C-10, C-4, C-5 [cf. *(1)*] is given by NMR measurements with spin decoupling (for further partial formulae deduced earlier, see[2]).

Oxidation with lead tetraacetate or sodium periodate results in cleavage of the cyclopropane ring. Bisdehydrophorbol *(3)*,



tiglophorbol[**], phorbolactone hemiacetal, and hydroxyphorbolactone hemiacetal[4] are formed from the resulting carbenium ion *(2)*.

(3) is found to be a key substance for the detection of the linkage of C-12 with C-13. The carbonyl group in bisdehydrophorbol *(3)* was reduced with $LiAlH_4$ to a secondary hydroxyl group, and the coupling of the new H-13 with H-12 was detected by nuclear magnetic double resonance measurements. The partial structure *(4)* deduced from this, together with the partial structure *(5)*, gives the structure of phorbol *(6)*.

The relative configurations of all the centers of asymmetry in phorbol except C-10 can be determined from the structures of its oxidation products and their NMR data. A half-chair conformation can be deduced for the bicyclo[4.1.0]heptane partial structure of phorbol (X-ray structure analysis, see reference[5].)

[*] Dr. M. Gschwendt and Prof. Dr. E. Hecker
Deutsches Krebsforschungszentrum, Biochemisches Institut
Berliner Str. 23
69 Heidelberg (Germany)

[**] Tiglophorbol was isolated earlier by *Kauffmann* in the oxidation of phorbol with lead tetraacetate [3].

[1] Cf. *G. Kreibich* and *E. Hecker*, Angew. Chem. *79*, 993 (1967); Angew. Chem. internat. Edit. *6*, 973 (1967); *H. Bartsch* and *E. Hecker*, Angew. Chem. *79*, 994 (1967); Angew. Chem. internat. Edit. *6*, 974 (1967).

[2] *E. Hecker, Ch. v. Szczepanski, H. Kubinyi, H. Bresch, E. Härle, H. U. Schairer*, and *H. Bartsch*, Z. Naturforsch. *21b*, 1204 (1966).

[3] *Th. Kauffmann, A. Eisinger, W. Jasching*, and *K. Lenhardt*, Chem. Ber. *92*, 1727 (1959).

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[5] *W. Hoppe, F. Brandl, I. Strell, M. Röhrl*, and *J. Gassmann* and *E. Hecker, H. Bartsch, G. Kreibich*, and *Ch.v.Szczepanski*, Angew. Chem. *79*, 824 (1967); Angew. Chem. internat. Edit. *6*, 809 (1967).

Petroporphyrins from Bitiminous Shales

By *W. Heller*[*]

Porphyrins and porphyrin-metal complexes have been obtained by very careful extraction from Swabian and North German Posidonia shale (Lias epsilon) and from the bituminous shales of the limiting bitumen horizon (Anis/Ladin) of Monte San Giorgio (Ticino, Switzerland). The material must be very finely ground and then extracted in stages in a Soxhlet apparatus so that it is finally free from porphyrins. We extracted successively with ether, hexane, chloroform, dioxane, benzene, pyridine, and DMSO. The porphyrins are almost quantitatively extracted in the ether. After further prepurification on aluminum oxide and Dowex, free porphyrins as well as porphyrin-metal complexes were found in the extracts.

Porphyrins both of acidic and of basic degradation occur in the shales. However, each shale zone contains only one type of degradation products.

Only an extremely small percentage of the metal complexes are of a physiological nature; the nonphysiological (V and Cu) complexes predominate. Chlorophyll degradation products that still contain Mg are not found either in the shales of Monte San Giorgio or in the Posidonia shales. This is probably because Mg is very readily replaced by V or Cu, even in chlorophyll. Thus the only physiological porphyrin-metal complexes found are the Fe complexes which may be derived from the hemin series. (The formation of the V and Cu complexes is a secondary process involving the degradation products.)

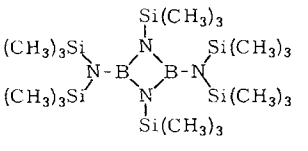
Moreover, nearly all the synthetic precursors of hemin and of chlorophyll, *e.g.* δ-aminolevulinic acid, uroporphyrin, coproporphyrin, and protoporphyrin, could be quantitatively detected in the bituminous shales. Porphobilinogen was also present in traces.

[*] Dr. W. Heller
Medizinische Universitäts-Poliklinik
Liebermeisterstr. 14
74 Tübingen (Germany)
Present address:
Chirurgische Klinik der Universität
Calwer Str. 7
74 Tübingen (Germany)

Crystal and Molecular Structures of Hexakis-(trimethylsilyl)-2,4-diamino-1,3,2,4-diazadiboretidine

By *H. Hess*[*]

Hexakis(trimethylsilyl)-2,4-diamino-1,3,2,4-diazadiboretidine *(1)*[1] was investigated by X-ray methods.



(1)

The compound crystallizes in the monoclinic system, space group $P2_1/a$, with $a = 22.11$, $b = 14.96$, $c = 10.93$ Å, $\beta = 108.6°$, and 4 molecules in the unit cell. The structural determination is based on 3500 reflection values, which were obtained with the aid of an automatic diffractometer and partly also by photometrization of integrated Weissenberg photographs. Three-dimensional Patterson and Fourier syn-

theses were used for the structural determination. The structure was refined by the method of least squares, first with isotropic, and later also with anisotropic temperature factors. The weighted R value is at present 10.6 %; the hydrogen atoms are not taken into account.

The proposed structure[1] could be confirmed. The four-membered ring is planar, within the limits of accuracy of the determinations, and the substituents on the N atoms are also arranged in a plane. The Si atoms attached to the exocyclic N atoms lie, not in the plane of the four-membered ring, but perpendicular to it. This can be attributed to steric factors. The following average bond lengths were found: B–N (endocyclic) 1.47, B–N (exocyclic) 1.43, N–Si 1.75, Si–C 1.88 Å. The shortness of the exocyclic B–N bond is surprising since the substituents on the B and N atoms are arranged perpendicularly to one another.

[*] Dr. H. Hess
Laboratorium für anorganische Chemie der Universität
Schellingstr. 26
7 Stuttgart (Germany)

[1] *P. Geymayer, E. G. Rochow*, and *U. Wannagat*, Angew. Chem. *76*, 499 (1964); Angew. Chem. internat. Edit. *3*, 633 (1964); *C. R. Russ*, and *A. G. MacDiarmid*, Angew. Chem. *76*, 500 (1964); Angew. Chem. internat. Edit. *3*, 509 (1964).

Acidolysis of Organolead Compounds

By *F. Huber, H. Horn* and *V. Bade*[*]

The action of acidic compounds HX on tetraorganoplumbanes PbR_4 proceeds in two steps.

$$PbR_4 + HX \rightarrow R_3PbX + RH \quad (1)$$

$$R_3PbX + HX \rightarrow R_2PbX_2 + RH \quad (2)$$

In all the cases studied (by acid titration, conductivity and / or gas volume measurements), both reactions are second order and proceed as competing consecutive reactions. In the reaction of aryl compounds ($R = C_6H_5$, $CH_3OC_6H_4$, *etc.*), the rates of both *(1)* and *(2)* are higher than in the reaction of alkyl compounds. For example, in reaction *(1)* (X = Cl, solvent CH_3OH) the reactivity increases with R in the order $n\text{-}C_4H_9 \approx n\text{-}C_3H_7 < C_2H_5 < CH_3 \ll C_6H_5 < CH_3OC_6H_4$.

The important question of the isolability of R_3PbX and/or R_2PbX_2 depends appreciably on the ratio of the rate constants k_1/k_2, and hence naturally on the reaction time and temperature. In establishing general rules for the preparation of R_3PbX and R_2PbX_2 by acidolysis of PbR_4 ($RPbX_3$ cannot be obtained by acidolysis), special attention must be paid to the group-specific properties and the acidity of HX, the influence of R, the polarity of the solvent, and the coordination-chemical effects. An S_E2 mechanism is suggested for *(1)*; for *(2)*, however, an S_N2 initiated multi-center reaction is proposed.

[*] Priv.-Doz. Dr. F. Huber, Dr. H. Horn, and
Dipl.-Chem. V. Bade
Institut für Anorganische Chemie und Elektrochemie
der Technischen Hochschule
Templergraben 55
51 Aachen (Germany)

Preparative Isolation of ^{242}Cm in the 100 Ci Range

By *G. Höhlein* and *H.-J. Born*[*]

A process for the isolation of ^{242}Cm in the 100 Ci range was developed and tested. The separation apparatus for the mechanical and chemical processing of a 200 mg sample of ^{241}Am irradiated in a high-flux reactor is remote-controlled and is continuously monitored by means of a gamma spectroscope.

The curium is separated from americium, plutonium, and the fission products on cation exchangers. The trivalent actinides and lanthanides are first absorbed on an exchanger column, and ^{103}Ru and ^{95}Zr, ^{95}Nb, and tetravalent $^{238,242}Pu$ are eluted as sulfato and oxalato complexes. ^{91}Y, ^{140}Ce, trivalent $^{238,242}Pu$, ^{241}Am, and ^{242}Cm are then separated on a larger column by an automatic pH-gradient elution technique with α-hydroxyisobutyric acid as the eluent. 91.6% of the ^{242}Cm is isolated with a purity of 98.5%. Pu is eluted after the Ce, indicating that Pu(III) has a weaker tendency toward complex formation with α-hydroxyisobutyric acid.

The influence of the weight ratios and the pH gradient on the effective number of plates and on the separation factor was studied by means of the elution curve. The effective number of plates in a column can be appreciably increased with respect to tracer and carrier quantities by the introduction of a gradient.

The elution of Am and Cm in a weight ratio of 8:1 showed that, despite its high specific α activity (10 mg of ^{242}Cm = 33.16 Ci), ^{242}Cm can be eluted on the mg scale on sulfonated polystyrene resins (AG 50 X 8, 200–400 mesh) without appreciable disturbance of the separation by the α-radiolytic decomposition of the cation exchanger. On absorption of pure ^{242}Cm on the mg scale, on the other hand, the resin is spontaneously decomposed because of the high energy density (16 Wh/ml of resin volume).

[*] Dr. G. Höhlein and Prof. Dr. H.-J. Born
Institut für Radiochemie der
Technischen Hochschule München
8046 Garching bei München (Germany)

Separation of Uranium and Plutonium by the Fractional Sublimation of the Chlorides

By *B. Kanellakopulos* and *H. Parthey*[*]

The separation of plutonium from uranium and fission products by the fractional sublimation of the chlorides was investigated. The preparation of uranium chloride characterized by the highest possible uniformity is essential for a good separation starting with the oxides. By heating the gaseous reaction products and annealing the condensates, we obtained predominantly UCl_4 in addition to $PuCl_3$. The reaction temperature, the temperature gradient, and the total pressure are important in the separation. Chlorination was carried out with a Cl_2–CCl_4–Ar mixture. There are two ways of volatilizing plutonium: (a) plutonium is eleminated as gaseous $PuCl_3$ in accordance with the vapor pressure of the solid at the temperature used and (b) plutonium is removed as $PuCl_4$, which is a gaseous component of the equilibrium

$$PuCl_3\,(s) + Cl_2\,(g) \rightleftarrows PuCl_4\,(g)$$

at elevated chlorine pressures and temperatures. At low chlorine pressures and temperatures, it decomposes without kinetic inhibition.

At a suitable temperature, uranium tetrachloride can be selectively sublimed off during chlorination, while $PuCl_3$ is left behind or is hardly formed. It is possible, moreover, to carry out a rapid selective chlorination at higher temperatures and to decompose the mixture of chlorides by fractional sublimation under reduced pressure. Separation factors of 300–600 can be reached in a single sublimation step.

[*] Dr. B. Kanellakopulos and Dr. H. Parthey
Kernforschungszentrum
75 Karlsruhe (Germany)

The Solid-State Chemistry of Neptunium Oxide

By *C. Keller*[*]

Many ternary oxides and oxide phases of tetravalent, pentavalent, and hexavalent neptunium can be prepared by reaction in the solid state or by hydrothermal synthesis. The compounds of tetravalent neptunium are very similar to the analogous oxometalates of the other tetravalent actinides. Typical examples are $BaNpO_3$ (cubic perovskite type), NpP_2O_7 (cubic α-ThP_2O_7 type), $NpTi_2O_6$ (monoclinic brannerite type), α-$NpSiO_4$ (tetragonal zircon structure), $NpO_{0.25}NbO_3$ (tetragonal defect perovskite type), and $NpNb_3O_{10}$ (hexagonal $UTa_3O_{10.67}$ structure). Whereas NpO_2 cannot be further oxidized in oxygen at high temperatures, pentavalent and hexavalent neptunium compounds such as Li_3NpO_4 and Na_3NpO_4 with Np(v) and $Na_2Np_2O_7$, $\alpha+\beta$-Na_2NpO_4, $\alpha+\beta$-Na_4NpO_5, $CaNpO_4$, or $BaNpO_6$ with Np(vi) are obtained in the presence of alkali metal and alkaline earth metal oxides. These are very similar to the uranium compounds having the same formula, but are less stable thermally.

Under inert and under oxidizing conditions, NpO_2 forms extended oxide phases with rare earth (RE) oxides. These phases contain two definite ternary oxides: $(Np^{V}_{0.5}, RE^{III}_{0.5})O_2$ with a fluorite structure and statistical distribution of the metal ions, and $NpO_3{\cdot}6REO_{0.5}$ with a hexagonal $UO_3{\cdot}6REO_{0.5}$ structure. In contrast to the uranium compound, the 1:6-Np(vi)–RE compound exists only as a stoichiometric compound. Whereas the solubility of $REO_{1.5}$(Lu,Tm,Ho) in NpO_{2+x} can be up to 60 mole-% between 1100 and 1700 °C, a maximum of 2–3 mole-% of NpO_{2x} dissolves in $REO_{1.5}$.

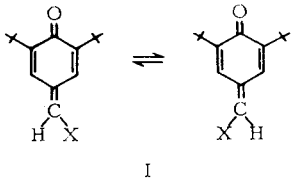
[*] Priv.-Doz. Dr. C. Keller
Lehrstuhl und Institut für Radiochemie,
Universität Karlsruhe und Kernforschungszentrum
75 Karlsruhe (Germany)

Detection of Intramolecular Mobility in Quinoid Systems by NMR Spectroscopy

By *H. Kessler*[*]

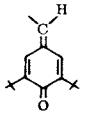
The isomerization at CC and CN double bonds in quinoid systems of the type *(1)–(3)* was studied by NMR spectroscopy.

The nuclear resonance spectra of the quinonemethides *(1a)–(1e)* exhibit no temperature-dependence up to 180 °C. The free energy of activation of the *cis-trans* isomerization is thus > 26 kcal/mole. In the case of the *o,p*-diphenoquinone *(2)*, the coalescence of the signals for the quinoid protons H_A and H_B at 155 °C ($\Delta\nu_{AB}$ = 44 Hz) gives a free energy of activation (for A ⇌ B) of 21 kcal/mole. A biradical transition state C is assumed.

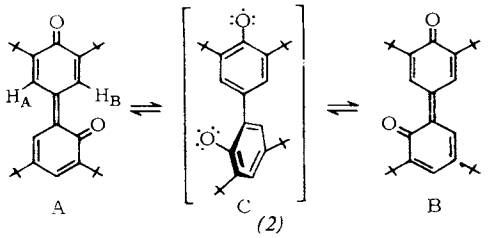


I

(1a) X = C_6H_5
(1b) X = OCH_3
(1c) X = $PO(Oi\text{-}C_3H_7)_2$
(1d) X =

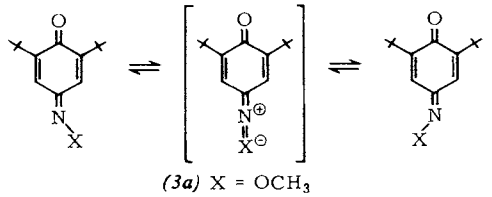


(1e) X = CN



A C B

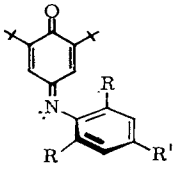
(2)



(3a) X = OCH_3
(3b) X = $SO_2C_6H_5$

The isomerization about the CN double bond requires more than 23 kcal/mole for *(3a)*; $\Delta G^{\ddagger}$ = 17.1 kcal/mole for *(3b)*, at 44 °C, and 18–23 kcal/mole for *(3c)*, depending on substitution.

When the substituents R and R′ in *(3c)* are varied, $\Delta G^{\ddagger}$ at 100 °C decreases with increasing size of R.



(3c), X = 2,6-R-4-R′-C_6H_2

R = R′	H	CH_3	C_2H_5	i-C_3H_7	t-C_4H_9
$\Delta G^{\ddagger}$ 100 °C [kcal/mol]	21.7	20.1	20.0	19.8	18.6

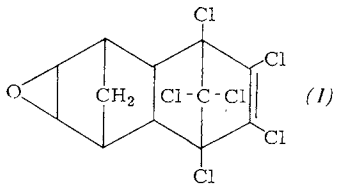
On the basis of the electronic effects of the substituents, the values would be expected to vary in the opposite direction. This was shown by systematic variation of R′ in compounds of the type *(3c)* (R = H). The rates of isomerization as found by NMR spectroscopy can be correlated with the Hammett σ_p values ($\rho = +1.5 \pm 0.3$ at 100 °C). The isomerization is therefore hindered by electron-repelling substituents. The increasing ease of reaction with increasing size of R in *(3c)* is therefore due to steric factors. It can be deduced from this that the isomerization in quinoneanilines proceeds, not by rotation about the CN bond, but by inversion (folding in the bond plane on the nitrogen.)

[*] Dr. H. Kessler
Chemisches Institut der Universität
Wilhelmstr. 33
74 Tübingen (Germany)

Metabolic Fate of Endrin, Dihydroheptachlor, and Heptachlor

By *W. Klein, F. Korte, N. Poonavalla, I. Weisgerber, R. Kaul, W. Müller,* and *A. Djirsarai*[*]

Endrin *(1)*: Experiments in which this insecticide labeled with ^{14}C was administered orally or intravenously to male and female rats in doses of 16–200 µg/kg of body-weight showed that the biological half-live of endrin is 3–6 days. When the labeled compound was given to rats in a daily dose of 8 µg, a steady state of storage was reached in about six days. It was found to be stored mainly in the fatty tissues.



(I)

When [14C]-endrin is administered orally, *ca.* 25 % is eliminated unchanged in the first day through the alimentary canal. After this, and after intravenous injection, two hydrophilic metabolites are excreted, mainly with the feces. The chief metabolite is chromatographically identical with the keto rearrangement product of endrin.

Experiments on mosquito larvae (*Aedes aegypti*) have shown that up to 80 % of the administered [14C]-endrin is eleminated in the form of hydrophilic metabolites. In the first hour after the exposure of the larvae, up to 20 % of the substance is converted. An increase in the concentration of the insecticide in the nutrient solution by a factor of 10 accelerates the metabolism by about 10 %.

Four weeks after treating varieties of cabbage with 14C-endrin, we recovered 5–25 % of the radioactivity, according to the conditions of life of the plants. About 40 % of the original amount evaporates from the plant surfaces, and 35–55 % is eliminated by transpiration. Almost only endrin was found on the surface of the leaves, while the leaves themselves contained 7 % of their radioactivity in the form of metabolites, the corresponding values being 26, 40, and 51 % for the stem, the root, and the soil, respectively. As regards the total radioactivity measured in the various parts, there is a decrease in the concentration from the leaves to the roots. Blank tests have shown that the conversion products are metabolites of the living plant.

Experiments with *Aspergillus flavus* have shown that a dose of 55 µg of endrin is metabolized to an extent of 22 % by 170 g of fungus mycelium within 3 weeks.

β-Dihydroheptachlor: This insecticide is metabolized to an extent of about 5 % in 15 days by fungi (*A. flavus*, *Penicillium urticae*, and soil microorganisms).

Heptachlor: After the intravenous injection of 14C-heptachlor into rabbits and rats, the compound is converted quantitatively into two metabolites, namely into the *exo*-epoxide and into a substance that is chromatographically identical with the 5-*exo*-hydroxy-3,4-*exo*-epoxy derivative of heptachlor.

[*] Dr. W. Klein, Prof. Dr. F. Korte, Dr. N. Poonavalla, Dr. I. Weisgerber, Pharm.-Chem. R. Kaul, Dipl.-Chem. W. Müller, and A. Djirsarai
Organisch-Chemisches Institut der Universität
Meckenheimer Allee 168
53 Bonn (Germany)

Photochemical Formation of Titanium Peroxide

By *H. Knoll* and *U. Kühnhold*[*]

Very pure TiO_2·aq prepared by hydrolysis of $Ti(C_2H_5O)_4$ irreversibly turns yellow on exposure to UV light of wavelength 365 nm after recrystallization to anatase (by heating below 450 °C). Samples prepared between 110 and 150 °C in a bomb tube and anatase-brookite mixtures (about 60 % of brookite) recrystallized at 40 °C are particularly sensitive to light. Anatase that contains anions such as $Cl^{\ominus}$, $F^{\ominus}$, $SO_4^{2\ominus}$, or $PO_4^{3\ominus}$ as well as pure, well crystallized anatase and rutile are insensitive. Discolored preparations absorb in the long-wave part of the absorption edge of TiO_2·aq. Measurement of the diffuse reflection against unexposed TiO_2·aq as standard gives a band having a maximum at 395–405 nm, similar to that of acido-titanium peroxide complexes in solution.

The absorption of oxygen during the photoreaction can be detected in the tensio-eudiometer. From the positive result of the Riesenfeld-Liebhafsky test, it is concluded that a peroxide bond is present. The formation of the colored compound is associated with the presence of mobile surface water. Preparations that have been substantially freed from adsorbed water by pumping (25 °C) discolor only slightly on illumination. When the sample is re-wetted, the absorption band re-appears in its original intensity on illumination.

The sensitivity to light is independent of the partial pressure of the oxygen between $p_{O_2} = 100$ and $p_{O_2} = 30$ mm Hg (peroxide formation range). After the adsorbed water has been released between 30 and 10 mm Hg, strong photosorption of oxygen is observed. Photolysis suddenly begins at 4 mm Hg, with an increase in pressure and blue coloration of the TiO_2. The dependence of the photoreaction on the wavelength of the incident light is determined by monochromatic illumination between 280 and 500 nm. Maximum discoloration takes place at $\lambda = 360$–370 nm. The intensity gradually decreases toward shorter wavelengths. Between 370 and 420 nm (the long-wave limit of the effect), the decrease follows the course of the absorption of unexposed TiO_2·aq. Graphic differentiation (in 5 nm steps) over the active range gives a point of inflection at 380 nm only.

From the result of the experiment, it is concluded that a surface compound similar to $H_4[TiO_3 \cdot O_2 \cdot aq]$ is formed. The time-dependence of the reaction can be described by the differential equation for second-order reactions, with $k = 2.3 \times 10^{-4}$ (25 °C). It is not yet possible to give any data on the individual reaction steps. There is no evidence that the active electrons are excited out of defects. The absorption edge can therefore be interpreted at present only as a valence band/conduction band transition of the electrons in anatase. The photochemical activity is then determined only by the surface state of the titanium dioxide. The blocking of peroxide formation by anions suggests the possible participation of surface OH in the photochemical reaction.

[*] Dr. H. Knoll and U. Kühnhold
Institut für Anorganische Chemie der Freien Universität
Fabeckstr. 34/36
1 Berlin 33 (Germany)

Investigation of the Preparative Uses, Kinetics, and Energetics of Photosensitized Processes at Low Temperatures

By *E. Koch*[*]

Photosensitized processes are possible even at −150 °C in suitable solvents. Thus O_2-transfers onto numerous dienes and olefins in dilute solution are diffusion-controlled; between +30 and −130 °C and with an adequate oxygen supply, they follow a simple kinetic scheme in which two competing processes and a preliminary diffusion step have to be taken into account. The evaluation of the O_2-absorption curves from numerous experiments with several acceptors, sensitizers (rose bengal, tetrachlorofluorescein, eosin, tetrachloroeosin, methylene blue, hematoporphyrin, binaphthylenethiophene), and solvents at various temperatures permits the absolute calculation of rate constants and activation energies. Since these values show a strong dependence on the sensitizer, the acceptor must react, not with excited oxygen, but with its adduct with the sensitizer. This adduct has a maximum life of 10^{-6} to 10^{-8} sec in methanol, depending on the sensitizer.

The course of the photosensitized O_2-transfers could also be followed thermochemically in a specially developed 'photocalorimeter'. During irradiation, the quantity of heat produced was accurately compensated by a Peltier element at +20 °C. The extent of Peltier cooling required showed that the formation of the peroxides from furan, 2-methylfuran, α-terpinene, cyclohexadiene, and trimethylethylene is exothermic (30 to 70 kcal/mole).

In many cases the peroxides formed are unstable and can be isolated only transiently by working-up at low temperatures;

this was so for furan and many substituted furans, dimethylfulvene, and cyclopentadiene. Malealdehyde acid pseudoesters are formed from furan itself above −40 °C, while substituted furans in alcoholic solvents are partly converted into 2-alkoxy-5-hydroperoxydihydrofurans. Transformations of this type can be followed particularly easily by differential thermal analysis. In the case of photochemical reactions that have not yet been studied in detail, this method can provide valuable preliminary information on the stability of the primary products obtained at low temperatures. In conjunction with a photocalorimetric study, therefore, the heats of formation of the primary products can be determined in two ways:

1) From the heats of formation of the starting materials and the energy liberated on irradiation and 2) from the heat of formation of the end products and the energy liberated on decomposition of the primary products.

Both methods give a heat of formation of about −80 kcal/mole for the ozonide-like epidioxyfuran, which is stable below −80 °C.

[*] Dr. E. Koch
Max-Planck-Institut für Kohlenforschung
Abteilung Strahlenchemie
Stiftstr. 34–36
433 Mülheim/Ruhr (Germany)

Liquid-Liquid Extraction of Tetravalent and Hexavalent Actinide Nitrates by a Long-chain Trialkylmethylammonium Nitrate [1]

By *G. Koch* [*]

During a search for new extractants for the aqueous reprocessing of spent nuclear fuels, tricaprylmethylammonium nitrate (TCMAN) (Aliquat-336®, nitrate form; 'capryl' = mainly n-octyl and n-decyl) was studied. Tetravalent actinides are extremely efficiently extracted from nitric acid solution. The order of extraction is Pu(IV) > Np(IV) > U(IV) > Th(IV). The partition coefficients exhibit a maximum between 2 and 4 M aqueous HNO_3; the values for a 0.5 M TCMAN solution in Solvesso-100® are between 1.7×10^4 (Pu(IV)) and 4.2×10^2 (Th(IV)). Hexavalent actinides are efficiently extracted; the partition coefficients exhibit a maximum at 6–7 M aqueous HNO_3, and under the same conditions as above have the maximum values 28 for Pu(VI) and 11 for U(VI).

Back-extraction from the organic phase with dilute HNO_3 is possible in the case of the hexavalent actinides and of thorium, whereas for Pu(IV) and Np(IV), the use of foreign acids (*e.g.* CH_3COOH, H_2SO_4) or conversion into an unextractable valence state (Pu(III), Np(V)) is necessary.

Spectroscopic studies show that the tetravalent actinides are extracted as hexanitrato complexes $[M(NO_3)_6]^{2\ominus}$ and the hexavalent actinides as trinitrato complexes $[MO_2(NO_3)_3]^{\ominus}$. The nitrate ions act as bidentate ligands, so that the coordination numbers of hexavalent and of tetravalent actinides are 8 and 12 respectively. Deviations from 'ideal' behavior in the plot of the partition coefficient against the extractant concentration can be used to calculate the activity coefficients of the organic extractant.

Advantages over the Purex process (extraction of U + Pu with tributyl phosphate) are that TCMAN extracts the more valuable metal (Pu(IV)) better than the less valuable (U(VI)) and that the U/Pu separation is possible without the use of a reducing agent (selective back-extraction of the uranium with dilute HNO_3). Disadvantages are the poorer hydrodynamic behavior of TCMAN solutions, which leads to longer residence times in the extraction apparatus, the stronger tendency toward emulsification and three-phase formation, the unavoidable use of (expensive) aromatic diluents, and the increased extraction of fission product ruthenium. The prospects for the replacement of the Purex process by extraction with quaternary ammonium nitrates appear poor at present. Better prospects exist in the isolation of neptunium from uranium product solutions or from highly radioactive waste solutions.

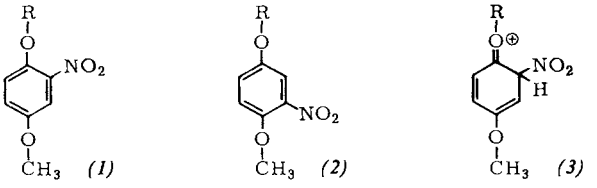
[*] Dr. G. Koch
Gesellschaft für Kernforschung m.b.H.
75 Karlsruhe (Germany)

[1] This work was carried out as part of the joint program of EURATOM and the Gesellschaft für Kernforschung m.b.H., Karlsruhe, in the field of fast reactors.

Some Chain-Length Effects of Paraffins

By *F. Korte, H. Schumacher, M. Haag,* and *R. Adatia* [*]

To determine the influence of the chain length of paraffins on electrophilic aromatic substitution, the nitration of unsymmetric alkyl methyl hydroquinone diethers was studied. The nitration leads to the isomers *(1)* and *(2)*, whose concentration ratio was determined as a function of the chain length



(1) *(2)* *(3)*

(R = C_1–C_{16}), the branching and substitution of the chain, the solvent and nitrating agent, and the temperature. The isomer ratio *(1)*/*(2)* increases with increasing chain length (*(1)*/*(2)* = 1.54 for R = C_2H_5, and 1.81 for R = n-$C_{16}H_{33}$).

The hydrogen-bridge-bonded solvents used at first were replaced by nonpolar solvents (sulfolane, n-hexane), and the nitrating agent was varied (HNO_3, NO_2BF_4, CH_3CONO_3). The isomer ratio still depends on the chain length.

If one considers the limiting resonance structures and the transition states in the electrophilic nitration of alkyl methyl hydroquinone diethers, the resonance-stabilized state *(3)* should decide the course of the reaction. We attempted to explain the increase in resonance stabilization of the oxonium structure *(3)* with increasing chain length. The change in the isomer ratio per C atom is greatest on going from the dimethyl to the methyl ethyl hydroquinone ether. Steric control of the reaction is unlikely, since the alkyl group approaches the *ortho* position on rotation, and does not influence the *meta* positions.

Steric hindrance should increase with the introduction of isopropyl or t-butyl groups instead of n-alkyl groups, but the extent of *ortho* substitution is found to increase with increasing dipole moment.

The IR spectra show that inhibition of rotation occurs only in derivatives with very long chains (C_{16}). The reaction is evidently directed primarily by the polarizability of the alkyl chain. The electronic control of the reaction is particularly obvious in the nitration of hydroquinone diethers containing electronegatively substituted alkyl groups [chain substituents = Cl, Br, F]. The expected inversion of the isomer ratio is found even with as few as six saturated C atoms between the substituent and the oxonium oxygen. The same results are obtained on bromination as on nitration.

The experiments described show that straight and branched paraffin chains can give rise to a charge density on an electron acceptor that increases with increasing length or with increasing branching; this influences the aromatic system, and is thus responsible for the course of certain reactions. In addition to this, Mössbauer measurements of some iron complexes of fatty acids show that the charge density on the

iron atom increases with increasing chain length. The results can be interpreted by means of a rod model [1], according to which primary carbanions are more stable than secondary and tertiary carbanions.

[*] Prof. Dr. F. Korte, Dr. H. Schumacher, Dr. M. Haag, and Dipl.-Chem. R. Adatia
Organisch-Chemisches Institut der Universität
Meckenheimer Allee 168
53 Bonn (Germany)

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Fragmentation of Bicyclic Keto-*p*-toluenesulfonates

By *W. Kraus* and *W. Rothenwöhrer* [*]

Solvolysis of 8-ketobicyclo[3.2.1]oct-2-yl and 9-ketobicyclo-[3.3.1]non-2-yl *endo-p*-toluenesulfonates in anhydrous glacial acetic acid yields only the acetates. On the other hand, solvolysis of the 8-ketobicyclooctyl *p*-toluenesulfonate in 80% aqueous formic acid and hydrolysis in water/acetone (1:4) leads to fragmentation and formation of 4-cycloheptenyl-1-carboxylic acid only. The 9-ketobicyclononyl *p*-toluenesulfonate does not fragment under these conditions. This decreasing tendency toward fragmentation with increasing ring size is attributed to the decrease in ring strain. A synchronous mechanism in which the carbonyl group is nucleophilically attacked by water is proposed. Simultaneous ring cleavage and release of the *p*-toluenesulfonate group lead to the fragmentation product.

Reduction of the two keto-*p*-toluenesulfonates with $LiAlH_4$ in ether is also accompanied by fragmentation. The overwhelmingly predominant product obtained from 8-ketobicyclo[3.2.1]oct-2-yl *p*-toluenesulfonate is 4-cycloheptenylmethanol, which is formed together with small quantities of *syn*- and *anti*-bicyclo[3.2.1]octan-8-ol; 9-ketobicyclo[3.3.1]-non-2-yl *p*-toluenesulfonate gives 35% of 4-cyclooctenylmethanol and 65% of bicyclo[3.3.1]nonan-9-ol. The tendency toward fragmentation again decreases with increasing ring size. The extremely high rate of this new reaction, which is described as 'reductive fragmentation', indicates a synchronous mechanism [1].

When the *p*-toluenesulfonates of the corresponding ethyleneketals are reduced with $LiAlH_4$, the bicyclo[3.2.1]octane derivative undergoes fragmentation to form 4-cycloheptenyl aldehyde acetal. Similar behavior is observed with the ethyleneketal of 2-keto-1-methylbicyclo[2.2.2]oct-4-yl *p*-toluenesulfonate. In the ketal of 9-ketobicyclo[3.3.1]non-2-yl *p*-toluenesulfonate, on the other hand, only the *p*-toluenesulfonate group is reductively removed. Since the carbonyl group cannot take part in the reactions of these compounds, an ionic multi-step mechanism must be assumed.

[*] Priv.-Doz. Dr. W. Kraus and Dr. W. Rothenwöhrer
Chemisches Institut der Universität
Wilhelmstr. 33
74 Tübingen (Germany)

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Syntheses and Reactions of Cyclic Amine Oxides with Activated Methylene Groups [**]

By *R. Kreher* [*]

Amine oxides [1] are most easily obtained by oxidation of tertiary amines with H_2O_2. The thermolysis of *N*-(β-phenylethyl)dialkylamine *N*-oxides containing a β-methylene group activated by the phenyl residue generally proceeds in accordance with the scheme of the Cope elimination with loss of styrene, and is a convenient method for the preparation of *N*,*N*-dialkylhydroxylamines. Dehydrogenation of these products with mercury(II) oxide yields nitrones [2]. This route has been used for the preparation of *e.g.* 4,7-(3′-cyclobuteno)-4,7,8,9-tetrahydro-1*H*-isoindolenine *N*-oxide [3] and 5*H*-dibenzo[*ce*]azepine *N*-oxide [4] as 5-membered and 7-membered cyclic nitrones.

N-Alkyl-Δ^3-pyrroline *N*-oxides, in which the cyclic α-methylene groups are activated by a CC double bond, undergo Cope-type elimination to only a small extent on thermolysis, with elimination of alkene and formation of the *N*-hydroxy-Δ^3-pyrroline. The main reaction is elimination of water to form *N*-alkylpyrroles, which are practically the only products formed on acetolysis (reaction of the amine oxides with acetic anhydride at 0 °C) [1,5]. The acetolysis of *N*-alkylisoindoline *N*-oxides, which follows a similar course, provides a convenient route to the *N*-alkylisoindoles [6]. Reaction with dialkyl acetylenedicarboxylates at room temperature gives 1:2 adducts, which are also formed from the *N*-alkylisoindoline *N*-oxides and a very large excess of acetylenedicarboxylate *via* *N*-alkylisoindole intermediates [7].

[*] Dr. R. Kreher
Institut für Organische Chemie der Technischen Hochschule
Schlossgartenstr. 2
61 Darmstadt (Germany)

[**] We are grateful to the Deutsche Forschungsgemeinschaft for support of this work.

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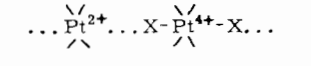
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Pt^{3+} Compounds

By *K. Krogmann* [*]

The Pt^{3+} compounds discussed here can be described as adducts of halogen-amine complexes of Pt^{2+} and Pt^{4+}. Structures of this type consist of chains in which halogen atoms (X) form bridges between Pt^{2+} and Pt^{4+}.



The substances studied were compounds of the type $enPtX_3 = [enPtX_2]\cdot[enPtX_4]$ (X = Cl, Br, I) and mixed-halogen variants thereof. All these compounds crystallize in the orthorhombic system, space group Ccmc (D_{2h}^{17}).

	a	*b*	*c*
$enPtCl_3$	5.52 Å	13.52 Å	9.77 Å
$enPtBr_3$	5.66 Å	13.97 Å	10.28 Å
$enPtI_3$	5.95 Å	14.54 Å	11.12 Å

The compounds are very sparingly soluble in water and are dark colored (red to black). The Pt–X....Pt chains are parallel to one another; Pt atoms in different oxidation states cannot be distinguished crystallographically.

Compounds having the composition $enPtX_2Z$ can form isomeric chains if the distribution of the halogen atoms is regular:

a) Z as the bridge atoms, X as side atoms;

b) X as the bridge atom and as the side atom on Pt(1), Z as side atoms on Pt(2);

c) X as the bridge atom, X and Z as side atoms on Pt(1) as well as on Pt(2).

Isomers of the types a) and b) can be distinguished IR spectroscopically by the fact that the Pt–X and Pt–Z stretching vibrations have different frequencies according to whether X (or Z) is a bridge atom or a side atom. For example, the isomer a) $enPtCl_2(Br)$ gives $\nu(Pt-Cl) = 325$, $\nu(Pt-Br) = 227$ cm^{-1}; the isomer b) $enPtBr_2Cl$ gives $\nu(Pt-Cl) = 341$ and 321, $\nu(Pt-Br) = 230$ cm^{-1}.

Isomers of type a), with different bridge atoms and similar side atoms, *e.g.* $enPtBr_2(Cl)$, $enPtBr_2(Br)$, and $enPtBr_2(I)$, have practically identical values for *b* and *c*, while the distance *a* between chains varies. However, the last is not constant for a given bridge atom, but depends on the side atoms: for $enPtCl_2(Cl)$ and $enPtBr_2(Cl)$, $a = 5.52$ and 5.64 Å respectively; for $enPtCl_2(Br)$ and $enPtBr_2(Br)$, $a = 5.58$ and 5.66 Å respectively.

The isomeric compounds of types a) and b) were obtained as follows: a) $enPtX_2$ dissolved in DMF is treated with a highly diluted aqueous solution of K_2PtZ_6.

$$2enPtX_2 + PtZ_6^{2\ominus} \longrightarrow [enPtX_2] \cdot [enPtX_2Z_2] + PtZ_4^{2\ominus}$$

(with Z in *trans* positions as bridge atoms).

b) $enPtX_2 + enPtZ_4 \longrightarrow [enPtX_2] \cdot [enPtZ_4]$

[*] Priv.-Doz. Dr. K. Krogmann
Laboratorium für Anorganische Chemie der Universität
Schellingstr. 26
7 Stuttgart 1 (Germany)

Determination of Some Excitation Functions for Deuteron Reactions with ^{141}Pr

By *J. Lange* and *H. Münzel*[*]

The excitation functions of the (d,3n), (d,2n), and (d,p) reactions for the target nuclide ^{141}Pr were measured at energies up to 50 MeV. The samples were irradiated with the internal beam of the Karlsruhe isochronous cyclotron. The deuteron flux was determined by means of an aluminum monitor. Contrary to the usual practice, a homogeneous mixture of the target substance and the monitor (chemical compound) was used. The excitation functions studied were discussed.

In these investigations the half-lives of the nuclides ^{140}Nd, ^{141}Nd, and ^{142}Pr were re-determined. The values obtained were 3.37 ± 0.02 d, 2.60 ± 0.12 h, and 19.09 ± 0.07 h, respectively. Furthermore, an isomeric state of ^{139}Nd with a half-life of 29.7 min was discovered.

[*] Dr. J. Lange and Dr. H. Münzel
Institut für Radiochemie, Kernforschungszentrum
75 Karlsruhe (Germany)

Isolation and Properties of a Crystalline β-Glucosidase from *Aspergillus wentii*

By *G. Legler*[*]

One of the six β-glucosidases shown to be present in *Aspergillus wentii* was isolated in an electrophoretically uniform, crystalline state by ammonium sulfate precipitation and column chromatography on CM- and DEAE-cellulose. The molecular weight as determined by gel filtration was 165000 to 170000. The enzyme is very slightly soluble in water at pH = 4.0 (about 0.2 mg/ml), but readily soluble at pH > 4.5 and in the presence of neutral salts. The thermal stability in the weakly acidic range is relatively high; the half-life of the inactivation in glycine/HCl (pH = 3.5) at 66.5 °C is 90 min.

The enzyme is specific for β-D-glucopyranosides, aliphatic glucosides being rather more weakly bound by the enzyme and also somewhat more slowly hydrolysed than the aromatic compounds. One exception is cellobiose, which is cleaved very rapidly. The rate of cleavage of phenyl-β-D-6-deoxyglucopyranoside was 1/10 and that of *p*-nitrophenyl-β-D-xylopyranoside 1/200 of the value for the corresponding glucosides.

The pH-dependence of the hydrolysis follows a sigmoid course, which can be explained by participation of a group that dissociates as an acid with $pK_A = 5.4$, and is active in the protonated form. Strong substrate inhibition is observed with *p*-nitrophenyl- and to a smaller extent with phenyl-β-D-glucopyranoside. *p*-Nitrophenyl-β-D-thioglucoside and D-gluconic acid 6-lactone act as competitive inhibitors with $K_i = 3 \times 10^{-4}$ M and 1.3×10^{-5} M respectively. The enzyme is rapidly and irreversibly inactivated by 10^{-4} M Condurit B epoxide[1] ($t_{1/2} = 22$ min at 25 °C and pH = 3.5), the rate of inactivation being strongly reduced by competitive inhibitors. The enzyme activity is not affected by heavy metal salts and *N*-ethylmaleimide.

[*] Dr. G. Legler
Organisch-Chemisches Institut der Universität
Meckenheimer Allee 168
53 Bonn (Germany)

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Nuclear Quadrupole Interaction and Molecular Structure

By *J. M. Lehn*[*]

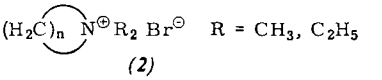
The ^1H- and ^{14}N–NMR spectra of substances containing nitrogen depend on the field gradient and on the molecular movements. The stronger the quadrupole interaction ($e^2qQ/\hbar$) and the longer the correlation time τ_K of the molecular movements, the smaller is the quadrupole relaxation time T_q of the ^{14}N nucleus. If the ^1H and ^{14}N nuclei are coupled by spin-spin interaction, the form of the ^1H line will depend on T_q. A triplet is observed when T_q is long (^{14}N has a spin $I = 1$), and a singlet when T_q is short; broadened lines are obtained in intermediate cases. T_q can be calculated from the form of the ^1H line and from the widths of the ^{14}N resonance lines.

Small molecules, locally symmetrical (in the vicinity of the ^{14}N nucleus) have long quadrupole relaxation times T_q. This value is affected by the electronic structure, symmetry, and correlation time of a molecule.

When *n* in the substances *(1)*[1] and *(2)*[2] is large, the electric symmetry on the ^{14}N is high, and T_q is long (^1H triplet; narrow ^{14}N line); when *n* is small, the field gradient becomes greater and T_q becomes shorter (^1H singlet; broad ^{14}N resonance).

$$(C_2H_5)_3\overset{\oplus}{N}-(CH_2)_n-\overset{\oplus}{N}(C_2H_5)_3 \; 2\,Br^{\ominus}$$

(1)



(2)

These predictions are confirmed by the ^1H and ^{14}N spectra

The broad lines observed for the proton on C-2 or C-3 in nitrogen containing heterocycles (pyridine, thiazole, isothiazole, oxazole, isoxazole, *etc.*) can be attributed to the incomplete elimination of a $^{14}N-^1H$ coupling.

[*] Dr. J. M. Lehn
Institut de Chimie, Université de Strasbourg
1 rue Blaise Pascal
Strasbourg (France)

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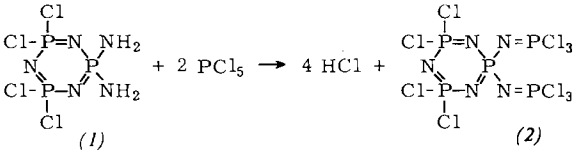
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Substitution in Trimeric Phosphorus Nitride Chloride: The Formation of a Spirane Compound

By *W. Lehr*[*]

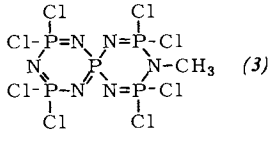
Double substitution of the chlorine atoms on the planar ring of trimeric phosphorus nitride chloride by a suitable bifunctional substituent leads to the formation of a new ring. It is still uncertain whether an ansa compound or a spirane compound is formed.

A more reliable route to a spirane compound starts with a geminally substituted compound. The diamide *(1)* was converted into the compound *(2)*, which has two geminal side chains.



(1) *(2)*

Ring closure with heptamethyldisilazane instead of with methylamine, which is too reactive, leads to the spirane compound *(3)* (2,2,4,4,8,8,10,10-octachloro-9-methyl-2,4,6,8,10-pentaphospha-1,3,5,7,9,11-hexazaspiro[5.5]undeca 1,3,5,7,10-pentaene) (m.p. 226 °C, decomp.), in which both rings contain only phosphorus and nitrogen atoms.



(3)

[*] Dr. W. Lehr
Anorganisch-Chemisches Institut der Universität
Tiergartenstr.
69 Heidelberg (Germany)

Quasibinary Phase Diagrams of the Systems Rare Earth Metal (Ho, Tm, Lu) Oxide / Actinide (Th, U, Np, Pu) Dioxide

By *L. Leitner, H. Engerer, U. Sriyotha,* and *C. Keller*[*]

Samples of definite composition obtained by mixed hydroxide precipitation were calcined under oxidizing, inert, and reducing conditions. The resulting oxide phases and their lattice constants were then determined. The actinide dioxides, which crystallize in a fluorite lattice, take up different quantities (up to 72 mole-%) of the rare earth metal oxides, which crystallize in a C-type lattice (Mn_2O_3 structure). The fluorite phases always have a fully occupied cation lattice, whereas the anion lattice (at least in the systems with ThO_2) exhibits vacancies. In the systems $UO_2/REO_{1.5}$, $NpO_2/REO_{1.5}$, and $PuO_2/REO_{1.5}$, these anion vacancies are partly filled under oxidizing conditions, with simultaneous oxidation of the actinide metal to valence states higher than +4. The solubility of the actinide dioxide in the rare earth metal oxide is significantly lower (maximum 30 mole-%). The solubility and its temperature-dependence are definite functions of the radii of the cations. As the difference between the radii increases, the oxide phase becomes narrower; *e.g.* 35 mole-% of $HoO_{1.5}$, 15.5 mole-% of $TmO_{1.5}$, or 11 mole-% of $LuO_{1.5}$ dissolve in ThO_2 at 1550 °C.

The phase diagrams of the systems $ThO_2/REO_{1.5}$ and $UO_2/REO_{1.5}$ (in a current of hydrogen) have a two-phase region between the fluorite phase and the C-type phase. Whereas pure NpO_2 is not oxidized by oxygen at high temperatures, oxidation of tetravalent neptunium is observed in the system $NpO_2/REO_{1.5}$. The $NpO_2/REO_{1.5}$ systems are therefore similar to the $UO_2/REO_{1.5}$ systems (1 atm of O_2); a rhombohedral compound having the limiting composition $MO_3 \cdot 6REO_{1.5}$ (M = Np, U) also occurs in both systems together with the fluorite and C-type phases. In the $UO_2/REO_{1.5}$ system, this compound forms a rhombohedral phase between 72 and 85.7 mole-% of $REO_{1.5}$ in the mixed oxide. The analogous system with neptunium oxide exhibits no phase width of the compound $NpO_3 \cdot 6REO_{1.5}$. Moreover, the solubility of MO_{2+x} in the rare earth metal oxide is about 1 to 2 mole-% in both systems, *i.e.* significantly lower than that of MO_2 in $REO_{1.5}$.

[*] Dr. L. Leitner, Dr. H. Engerer, Dipl.-Chem. U. Sriyotha, and Priv.-Doz. Dr. C. Keller
Lehrstuhl für Radiochemie, Universität Karlsruhe und
Institut für Radiochemie, Gesellschaft für Kernforschung
Kernforschungszentrum
75 Karlsruhe (Germany)

Determination of ^{239}Pu in Unirradiated Nuclear Fuel Samples by γ-Spectroscopy

By *L. Lindner* and *A. von Baeckmann*[*]

Though only about 10^{-3}% of all disintegrations of ^{239}Pu result in the emission of a 380 keV γ quantum, such quanta can be used for the determination of ^{239}Pu in the gram and milligram range. No interference is to be expected from the other long-lived plutonium isotopes. The measurements were carried out with an NaI(Tl) scintillation counter fitted with a lead screen, in conjunction with a multi-channel analyser. The determination of ^{239}Pu in this apparatus is subject to interference from ^{237}U (333 keV), which is formed by decay of ^{241}Pu. However, this interference is negligible when the plutonium has a constant isotope composition and contains less than 1% of ^{241}Pu. Under these conditions the detection limit in pure plutonium solution is about 0.5 mg of ^{239}Pu. The interference due to secondary products of uranium is slight (< 0.2% of the intensity of ^{239}Pu for equal weights of uranium and ^{239}Pu). The same is true of the other secondary products of the long-lived plutonium isotopes.

The plutonium content of PuO_2–UO_2 pellets of definite geometry was determined both by wet chemical methods and by γ spectroscopy. The standard deviation between the two processes was 0.6% for about 80 pellets containing about 3 g of ^{239}Pu. This non-destructive and time-saving γ-spectroscopic method thus seems suitable for process control of the plutonium content in the production of nuclear fuels.

[*] Dr. L. Lindner [**] and Dr. A. von Baeckmann
Institut für Radiochemie, Kernforschungszentrum
75 Karlsruhe (Germany)

[**] Present address:
AEG-Kernenergieanlagen
Seligenstädter Str.
8752 Grosswelzheim (Germany)

The Structure of Hexacyanobenzene

By *W. Littke*[*]

On crystallization from anhydrous acetonitrile or on fast sublimation in a high vacuum, hexacyanobenzene is obtained in the form of colorless octahedra. The crystals are isotropic to polarized light. Powder and single-crystal photographs with CuK_α radiation showed a primitive cubic unit cell ($a = 10.820 \pm 0.005$ Å) with four formula units per cell. The Weissenberg diagrams indicate the space group Pa3. It should be noted that only about ten organic compounds with such high symmetry are known.

Fine-structure analysis shows that the centers of gravity of the molecules are situated at the corners and in the face centers of the cubic cell. The hexacyanobenzene molecules at

the corners lie in the octahedral faces. Each molecule is so arranged that one cyano group from each of three adjacent molecules above the molecule in question and three below points exactly toward the center of the molecule, the groups from molecules above alternating with those from molecules below. These six groups tend to draw the π electrons back, so that the planarity of the benzene ring is substantially retained. This structural determination may be accepted as reliable since, R has now been reduced to 0.10.

[*] Dr. W. Littke
Chemisches Laboratorium der Universität
Albertstr. 21
78 Freiburg (Germany)

Investigations on the Age and Place of Origin of Paintings by Neutron Activation Analysis

By *F. Lux*, *L. Braunstein*, and *R. Strauss*[*]

Neutron activation analysis can be used to examine the relationships between the contents of trace elements in the white lead of paintings and the age and place of origin of the paintings. The investigations are being carried out jointly with the Dörner-Institut at Munich.

The contents of Mn, Cu, Ba, Cr, Ag, and Sb in Dutch and Venetian pictures were determined. The white leads from these two sources were found to differ significantly in their Mn, Ag, and Sb contents[1]. A distribution of the trace element contents in the white lead that depended on the place of origin of the paintings was found in two Tiepolo paintings executed in Italy and in Würzburg. Differences between modern and old white leads can be used for the detection of forgeries. The differences found agree, as regards the Cu content, with the results obtained by *Houtman* and *Turkstra*[2].

In further work, Sn, Au, and Hg were also determined. Each sample for analysis is divided into a short-time irradiation sample (irradiation time 4 h; ^{56}Mn, ^{64}Cu, ^{139}Ba, ^{198}Au) and a long-time irradiation sample (irradiation time 400–500 h; ^{51}Cr, ^{110m}Ag, ^{113}Sn, ^{122}Sb, ^{203}Hg). The trace components are determined by combination of radiochemical separation and γ spectrometry.

The separation operations were carried out without determination of the yield. Model analyses gave standard deviations of $\pm$ 2.1 to $\pm$ 3.4 % for the determination of the trace components. On analysis of three white lead samples from different parts of the same picture, the largest difference between two values for the same trace component was 20%.

To check variations in the binder content of white lead, the lead content in the solution of the irradiated sample before the addition of the carrier was determined on 1/10 of the solution by inverse polarography (in a Teflon vessel). The standard deviation of the lead determination is $\pm$3.4% for 5×10^{-7} g of Pb and $\pm$2.4% for 5×10^{-6} g of Pb.

A selection of the works of painters who worked mainly in Southern Germany during the 17th and 18th centuries is now being studied. In addition to Dutch and Venetian white leads, other types were also found:

	Type of white lead	Sb content (ppm)	Ag content (ppm)
1		< 8	15–75
2a	(identical with Venetian white lead [1])	10–70	< 7
2b		10–70	10–30
2c	(identical with white lead from 2 *Rubens* paintings [1])	10–70	> 30
3a	(identical with *Tiepolo*'s Würzburg white lead [1])	> 70	< 5
3b	(identical with Dutch white lead [1])	> 70	8–50
3c	(identical with Dutch white lead [1])	> 70	> 50

Types 1 and 2c were used in southern Germany up to about 1640, 2a after 1615, 3c after 1640, and 2b after 1670. This time scale was also established for pictures by one painter: *Johann Heinrich Schönfeld* used white lead 2a in 1633 and 3c in 1681.

Pictures by *Peter Candid* and by *Johann Georg Fischer* have become distinguishable for the first time by the application of chemical methods. The paintings that have been shown by recent historical findings to be by *Fischer* were formerly attributed to *Candid*. Paintings by *Candid* contain white lead 2a, while the *Fischer* paintings formerly attributed to *Candid* contain white lead 1,2b, 2c, and 3b.

[*] Doz. Dr. F. Lux, Dr. L. Braunstein, and
Dipl.-Chem. R. Strauss
Institut für Radiochemie
der Technischen Hochschule München
8046 Garching bei München (Germany)

[1] *F. Lux* and *L. Braunstein*, Angew. Chem. *78*, 720 (1966); Angew. Chem. internat. Edit. *5*, 679 (1966); Z. analyt. Chem. *221*, 235 (1966).

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Measurement of Self-Diffusion Coefficients of Na by Heterogeneous Solid/Melt and Solid/Solid Isotope Exchange on Sodalite, Obsidian, and NaCl

By *W. Lutze* and *H. W. Levi*[*]

Studies on the exchange kinetics of silicate ion exchangers have so far generally been carried out with powdered material. The results could therefore be used for the calculation of diffusion coefficients only for small penetration depths (low conversions). We used samples having a definite shape and size, so that the complete exchange process could be measured and used for the calculation of diffusion coefficients. Moreover, the rate-determining step of the exchange (film or volume diffusion) could be determined on the same sample by an interruption test.

Spheres (diameter $\geqslant$ 0.4 mm; deviation from spherical shape $\leqslant$ 3%) of the materials in question were prepared with the aid of a slightly modified ball mill. The Na present in the substances was isotopically labeled by adsorption of ^{22}Na on the surface followed by heating for a sufficiently long time to ensure homogeneous distribution in the solid phase.

Na self-diffusion coefficients were first determined for natural sodalite and two natural volcanic glasses by isotope exchange with $NaNO_3$, NaBr, and NaCl melts and with ^{22}Na as a tracer. The sample spheres were repeatedly immersed in a salt melt, and the progress of exchange was followed by measurement of the residual radioactivity of the solid. The following functions $D_{Na}(T)$ were obtained from the experimental results:

Sodalite (Canada) $D = 1.2\times10^{-2} \exp(-1.18\ \mathrm{eV}/kT)\ \mathrm{cm^2\ sec^{-1}}$ (500–850 °C)

Obsidian I (Italy) $D = 2.9\times10^{-3} \exp(-0.80\ \mathrm{eV}/kT)\ \mathrm{cm^2\ sec^{-1}}$ (360–600 °C)

Obsidian II (Italy) $D = 9.2\times10^{-3} \exp(-0.78\ \mathrm{eV}/kT)\ \mathrm{cm^2\ sec^{-1}}$ (400–540 °C)

Exchange between two solid phases was investigated with radioactively labeled sodalite spheres in polycrystalline NaCl tablets. A sphere was embedded in NaCl powder and a tablet was made from this in a laboratory press at 15 t/cm^2. The tablets were heated at between 570 and 700 °C. The exchange process could again be followed by measurement of the residual activity in the sphere after separation of the phases by dissolution of the NaCl. The rate-determining step in this

case is diffusion in the NaCl. To evaluate the results, the second Fick law was solved under the appropriate boundary conditions. The self-diffusion coefficient of Na in polycrystalline NaCl was found to be:

$$D = 2.7 \exp(-1.75\ \mathrm{eV}/kT)\ \mathrm{cm^2\ sec^{-1}}\ (570\text{–}700\ ^\circ\mathrm{C})$$

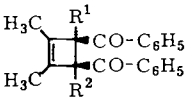
Ion exchange processes could also be carried out in tablets of powdered sodalite and salts of cations other than Na. Thus Li-sodalite was formed within a few minutes with LiCl at 400 °C.

[*] Dipl.-Chem. W. Lutze and Dr. H.W. Levi
Hahn-Meitner-Institut für Kernforschung
Glienicker Str. 100
1 Berlin 39 (Germany)

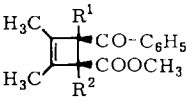
Reactions of Benzoylcyclobutenes

By *G. Maier* and *M. Wiessler*[*]

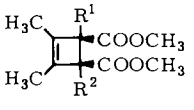
The cyclobutene derivatives *(1)*, *(2)*, and *(3)*, which are possible starting materials for the synthesis of derivatives of 3,4-diazabicyclo[4.2.0]octa-2,4,7-triene, exhibit unusual reactions under the action of bases, and when heated.



(1)



(2)



(3)

(a): $R^1 = R^2 = H$ *(b)*: $R^1 = H$, $R^2 = CH_3$ *(c)*: $R^1 = R^2 = CH_3$

With CH_3OH/CH_3ONa, *(1a)*, *(2a)*, and *(3a)* first rearrange to form *trans*-derivatives. In a stereoselective secondary reaction, *(1a)* adds a molecule of methanol across the 'unactivated' double bond of the four-membered ring. In *(1c)*, the addition takes place preferentially on the C=O double bond.

The compounds *(1)*, *(2)*, and *(3)* are converted by heating, and in some cases even at room temperature, conrotatorily into butadiene derivatives. The dibenzoylbutadienes formed from *(1)* give derivatives of furo[3,2-*b*]furan on heating. The esters *(2)* give esters of benzoylbutadienecarboxylic acid, which form pyrans by a Cope-type rearrangement involving the carbonyl double bond. The rate and direction of this secondary reactions can be influenced by the addition of SiO_2.

[*] Priv.-Doz. Dr. G. Maier and Dipl.-Chem. M. Wiessler
Institut für Organische Chemie der Universität
Richard-Willstätter-Allee
75 Karlsruhe (Germany)

α-Aminoalkylation of White Phosphorus

By *L. Maier*[*]

The reaction of white phosphorus with *N*-hydroxymethyldialkylamines *(1)* leads mainly to three products: tris(dialkylaminomethyl)phosphine oxides *(4)*, bis(dialkylaminomethyl)phosphinic acids *(3)*, and dialkylaminomethylphosphonic acids *(2)*.

$$2\ P_4 + 20\ R_2NCH_2OH \rightarrow \underset{(1)}{} \quad \underset{(2)}{R_2NCH_2P(O)(OH)_2} +$$

$$2\ (R_2NCH_2)_2P(O)OH + 5\ (R_2NCH_2)_3P{=}O + 8\ H_2O$$
$$\underset{(3)}{} \qquad \underset{(4)}{}$$

The ratio *(2)*:*(3)*:*(4)* depends mainly on the ratio of the reactants, the pH, and the solvent. The highest yield of *(4)* is obtained at a ratio of $P_{white}:CH_2O:HNR_2 = 1:2.5:2.5$ in weakly basic to neutral media (water/alcohol). Tertiary phosphine oxides with $R_2N = (CH_3)_2N$, $(C_2H_5)_2N$, $(C_4H_9)_2N$, (cyclo-$C_6H_{11})_2N$, pyrrolidino, piperidino, and morpholino were prepared[1].

This new α-aminoalkylation appears to be confined to white phosphorus. Red phosphorus, arsenic, silicon, and tin do not react with *N*-hydroxymethyldialkylamines under these conditions.

[*] Dr. L. Maier
Monsanto Research S.A.
Binzstr. 39
CH-8045 Zürich (Switzerland)

[1] *L. Maier*, Angew. Chem. *77*, 549 (1965); Angew. Chem. internat. Edit. *4*, 527 (1965).

Electrochemical Reactions at Electrodes of Solid Hydrocarbons

By *W. Mehl*[*]

We used single crystalline aromatic hydrocarbons as electrodes in the investigation of oxidations and reductions. The oxidizing and reducing agents were 'simple' ions, in which rearrangements take place only in the outer solvation sphere during electron transfer. The charge transfer reaction was discussed on the basis of the Marcus theory of adiabatic electron transfers. According to this theory, electrons can pass from an ion to the electrode only if the solvation sheath of the ion is so arranged by thermal excitation that the difference between the energies of interaction of the oxidized and of the reduced forms of the ion with the solvation sheath corresponds to a permitted energy level for electrons in the surface of the electrode.

For quantitative estimates of the rate constants of fast reactions at electrodes of solid hydrocarbons, the reorientatio of the lattice polarization cannot be neglected in relation to the energy of rearrangement of the solvation sheath of the ions taking part in the charge transfer. The ratio of the exchange current for redox reactions measured at a metal electrode and the value measured at an anthracene electrode agreed satisfactorily with the predicted result.

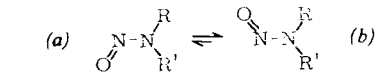
The procedure is particularly suitable for use in the study of the electrochemical behavior of the excited states of aromatic compounds, whose reaction rates can be determined in the form of a limiting photo-current through the crystal. From the energy of the first excited singlet state and the electron affinity and ionization energy of the crystal, it is possible to predict a redox potential for 'simple' redox reactions at which a maximum of the photo-current is observed.

[*] Dr. W. Mehl
Cyanamid European Research Institute
91, Route de la Capite
Cologny, Genève (Switzerland)

Separation and Equilibration of Conformeric Nitrosamines and Formamides

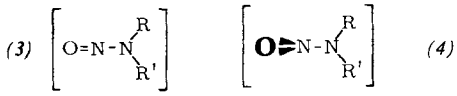
By *A. Mannschreck* and *H. Münsch*[*]

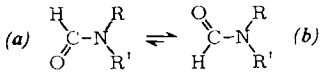
The conformers *(a)* and *(b)* of the nitrosamines have until now been detected only in equilibrium. In a few cases we have been able to separate *(a)* and *(b)* completely, or to a large extent, by fractional crystallization and preparative thin-layer chromatography at low temperatures. Some examples are *(1a)*, m.p. 62–63.5 °C, *(1b)*, m.p. 86.5–88 °C[1], *(2a)*



(1) R = CH_2-C_6H_5, R' = 2,6-$(CH_3)_2C_6H_3$
(2) R = CH_2-C_6H_5, R' = CH_2-$C(CH_3)_3$

and *(2b)*, m.p. 40–42 °C; *(2a)* melted at 15–21 °C and still contained 19% of *(2b)*. When one isomer is dissolved, the equilibrium *(a)* ⇋ *(b)* is established at a measurable rate at room temperature[2]. Equilibrations of this type at 36 ° C in CCl_4 gave half-lives of 5 to 100 min and free energies of activation of 22.3 to 24.2 kcal/mole, depending on R and R'. Feasible transition states for this reorientation of the nitroso group are the structures *(3)* and *(4)*, which correspond to a linear and an angular O–N–N system respectively.





(5) R = CH_2–C_6H_5, R' = 2,6-$(CH_3)_2C_6H_3$
(6) R = CH_2–C_6H_4 [*o*-$N(CH_3)_2$], R' = 2,4,6-$(CH_3)_3C_6H_2$

The only formamides that have so far been obtained in the pure state are *(5b)*, m.p. 76–79 °C, and *(6b)*, m.p. 66–69 °C. *(5a)* could not be separated; the sample of *(6a)*, m.p. 72 to 76 °C, that was isolated still contained 8% of *(6b)*. *Siddall*[3] concentrated one rotational isomer of each of two other formamides. The equilibrations in $CDCl_3$ at 35 °C gave half-lives of 17 min for *(5)* and 30 min for *(6)*, and free energies of activation of 22.6 to 23.7 kcal/mole[2]. This reorientation of the formyl group cannot proceed *via* a transition state analogous to *(3)*, with a linear O–C–N system. The transition state of the internal rotations in the formamides corresponds instead to the structure *(4)*.

[*] Dr. A. Mannschreck and Dipl.-Chem. H. Münsch
Organisch-Chemisches Institut der Universität
Tiergartenstr.
69 Heidelberg (Germany)

[1] *A. Mannschreck, H. Münsch,* and *A. Mattheus,* Angew. Chem. *78*, 751 (1966); Angew. Chem. internat. Edit. *5*, 728 (1966).

[2] For details of the method, see *A. Mannschreck, A. Mattheus,* and *G. Rissmann,* J. molecular Spectroscopy *23*, 15 (1967).

[3] *T. H. Siddall III,* Inorg. nuclear Chem. Letters *1*, 155 (1965) and personal communication.

The True Nature of the Transuranium Elements Reported by *O. Hahn, L. Meitner,* and *F. Strassmann*

By *H. Menke* and *G. Herrmann*[*]

Between 1934 and 1938, *O. Hahn, L. Meitner,* and *F. Strassmann* obtained a number of radionuclides by irradiation of uranium with slow neutrons. On the basis of the then current views on nuclear reactions and the position of the heaviest elements in the periodic system, these nuclides were thought from their chemical behavior to be transuranium elements[1].

After the discovery of nuclear fission, it was realized that these were fission products. The 66 h 'eka-iridium' was found to be a mixture of 67 h ^{99}Mo and 78 h ^{132}Te, from which 2.3 h ^{132}I, or 'eka-platinum', was formed[2].

To identify further components, ammonium diuranate samples that had been irradiated in the Mainz reactor were dissolved in 2 N hydrochloric acid, $PtCl_4$ was added, and platinum sulfide, with which the 'transuranium elements' had been isolated as a group, was precipitated from the solution. The fission products belonging to the hydrogen sulfide group were then isolated from this precipitate and their isotopes were identified by γ-spectroscopy; their contribution to the β activity of the sulfide precipitate was also measured.

Each of the 'transuranium' nuclides is simulated by a mixture: 16 min 'eka-rhenium' mainly by ^{101}Mo, ^{101}Tc, ^{104}Tc, ^{131}Sb, and ^{131g}Te; 59 min 'eka-osmium' by ^{133m}Te, ^{134}Te, ^{134}I, and ^{130g}Sb; and 5.7 h 'eka-osmium' by ^{129}Sb and ^{105}Ru. The iodine isotopes are secondary products from tellurium precursors. Complications are raised by the fact that several main components belong to mother-daughter pairs having similar half-lives, *i.e.* to the pairs molybdenum-technetium-101, antimony-tellurium-131, and tellurium-iodine-134.

	$_{93}$Eka-Rhenium	$_{94}$Eka-Osmium	$_{95}$Eka-Iridium	$_{96}$Eka-Platinum
$t_{1/2}$	2.2 min	59 min	66 h	2.5 h
$t_{1/2}$	16 min	5.7 h	60 d	

[*] Dr. H. Menke and Prof. Dr. G. Herrmann
Institut für Anorganische Chemie und Kernchemie
der Universität
Johann-Joachim-Becher-Weg 24
65 Mainz (Germany)

[1] *O. Hahn, L. Meitner,* and *F. Strassmann,* Ber. dtsch. chem. Ges. *70*, 1374 (1937); Naturwissenschaften *26*, 475 (1938).

[2] *O. Hahn* and *F. Strassmann,* Naturwissenschaften *27*, 451 (1939).

Structural Investigations on Polyolefins by means of Pyrolysis and Gas Chromatography

By *L. Michailov, P. Zugenmeier,* and *H. J. Cantow*[*]

Polyethylene samples obtained by various methods, and also ethylene-propylene copolymers, were pyrolysed in the carrier gas stream of a gas chromatograph. Simultaneous hydrogenation, achieved by using hydrogen as the carrier gas and introducing a hydrogenation catalyst, simplified the pyrograms. The experimental conditions were chosen to favor the formation and identification of fragments of as great a length as possible. This was achieved by a low pyrolysis temperature (680 °C), a low dead volume between the pyrolysis unit and the column inlet, and a linear temperature programming of the column. This enabled fragments with molecular weights > 700 to be separated.

Highly branched high-pressure polyethylene of low density and relatively linear Ziegler polyethylene of high density could be readily distinguished on the basis of the iso-compounds derived from the chain branching, and by the mass distribution of the straight chain fragments. The pyrograms of Ziegler and Phillips polyethylene samples also showed significant differences.

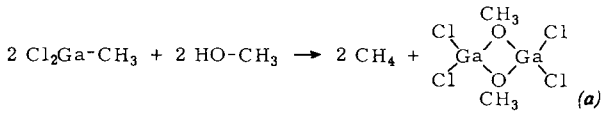
In the case of the ethylene-propylene copolymers, three pairs of products were discussed, having approximately the same overall composition but differing in the detailed structure of the polymer chains. In the sequence length distribution of the copolymers, even slight deviations showed up in the fragment distribution. A measure of the content of ethylene sequences capable of crystallization was obtained. The data from the pyrograms are supported by X-ray diffraction data. In addition, pyrograms can provide information on the sequence distribution in amorphous ethylene-propylene rubbers that cannot be obtained by other analytical methods.

[*] Dipl.-Ing. L. Michailov, Dipl.-Chem. P. Zugenmeier, and Prof. Dr. H.-J. Cantow
Institut für makromolekulare Chemie der Universität
Stefan-Meier-Str. 31
78 Freiburg/Br. (Germany)

The Reaction of Alkylgallium Halides with Lower Aliphatic Alcohols

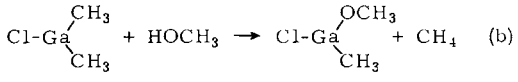
By *L. Mögele* [*]

Alkylgallium dihalides, $R-GaX_2$ ($R = CH_3$, C_2H_5; $X = Cl$, Br), react with lower aliphatic alcohols to give the hydrocarbon and the dimeric alkoxygallium dihalide [1] (eq. (a)).



(a)

However, dialkylgallium halides, R_2GaX, undergo solvolysis, even with an excess of alcohol and under severe reaction conditions, with substitution of only one alkyl group to give alkylalkoxygallium halides (eq. (b)). Unlike the alkoxygallium dihalides, which are crystallized at room temperature and are highly sensitive to moisture, the alkylalkoxygallium halides are highly viscous to waxy substances with no definite melting point, and are surprisingly stable towards hydrolysis. Studies by differential thermal analysis, osmometry, mass spectrometry, and nuclear magnetic resonance spectroscopy show that in the solid phase highly condensed systems are present in an isomeric equilibrium having a high rate of exchange; the tetrameric ring systems that are present in solution, split up into dimeric units in the vapor phase.



(b)

[*] Dr. L. Mögele
Siemens AG.
8520 Erlangen 2 (Germany)

[1] *L. Mögele*, Proceedings IX ICCC, St. Moritz-Bad 1966, p. 28.

Dependence of the Kinetic Energy of some ^{239}Pu Fission Fragments on the Excitation Energy of the Fissioning Nucleus

By *G. Rohde* and *H. Münzel* [*]

The mean ranges of some fission products formed in the reactions $^{239}Pu(n_{th},f)$, $^{239}Pu(d_{20},f)$ and $^{239}Pu(d_{50},f)$ were determined by the 'thick target – thick catcher' method [1]. From the range and the irradation conditions, the kinetic energy of the primary fission fragments and the average excitation energy and nucleon number of the fissioning nucleus were calculated. The following conclusions were drawn from the results. The values of the total kinetic energy at a mass ratio of about 0.8 and 1.3 (asymmetric fission) are independent of the excitation energy of the fissioning nucleus. The value for the total kinetic energy in the symmetric fission range increases by 8 MeV as the excitation energy of the fissioning nucleus increases from 5 to 20 MeV, and then remains practically constant. This result may be interpreted on the basis of the hypothesis of two independent types of fission. The often used assumption about the distribution of the excitation energy of the fissioning nucleus among the primary fission fragments according to their nucleon numbers does not seem to apply. This could be estimated from the number of evaporated neutrons in the range of symmetric fission.

[*] Dr. G. Rohde and Dr. H. Münzel
Institut für Radiochemie, Kernforschungszentrum
75 Karlsruhe (Germany)

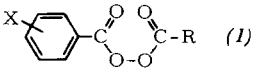
[1] *M. Hollstein* and *H. Münzel*, Radiochim. Acta *6*, 9 (1966).

Induced Decomposition of Unsymmetrical Acyl Peroxides

By *W. P. Neumann, K. Rübsamen, Ra. Sommer*, and *U. Frommer* [*]

The decomposition of diacyl peroxides in dilute solutions is accelerated by several orders of magnitude if stannyl radicals $R_3Sn\cdot$ are present. These are produced in the reaction mixture from organotin hydrides. ^{18}O-labeling of the carbonyl groups permitted a synchronous mechanism (S_R2) to be demonstrated, in which the attack of the stannyl radical occurs at one of the peroxide oxygens, simultaneously with the breaking of the peroxide bridge [1].

In contrast to other radicals, the stannyl radical is nucleophilic. Its attack on the peroxide bridge is rendered easier (or, indeed, made possible in the first place) if electron-withdrawing groups create an electron deficiency at this point. This can be confirmed with unsymmetrical acyl peroxides



(1)

where $X = CN$, NO_2, Cl, H, OCH_3, OC_2H_5, *etc.* The more positive of the two bridge oxygens will be attacked preferentially by the stannyl radical.

The reaction rates were measured in dilute benzene solution and all the reaction products were determined qualitatively and quantitatively.

Experiments with trialkyltin deuterides enabled side reactions to be clarified, *e.g.* the cleavage of C–Sn bonds by acyloxy radicals and the cleavage of C–H bonds.

The unsymmetrical peroxides were prepared in good yield from the perbenzoates and an aliphatic carboxylic acid chloride ($R = CH_3$, C_2H_5, *etc.*).

[*] Prof. Dr. W. P. Neumann, Dipl.-Chem. K. Rübsamen, Ra. Sommer, and U. Frommer
Institut für Organische Chemie der Universität
Ludwigstr. 21
63 Giessen (Germany)

[1] *W. P. Neumann* and *K. Rübsamen*, Chem. Ber. *100*, 1621 (1967) and further literature cited there.

Chemical Affinity and Structural Relationships Between Protein and Inorganic Components in Biogenous Mineralization

By *H. Newesely* [*]

The reactions involved in the calcification of hard biological substances have been largely clarified for the inorganic phase and for the protein component of the hard tissue by micromorphological, analytical, and structural investigations by several research groups.

Relationships were recognized between the crystal morphology (in the electron-microscopic range) and the structural type of the sparingly soluble calcium phosphates and the influence of accessory ions (F, Mg) on the reaction mechanisms. (Example: transformation of octacalcium phosphate/apatite; whitlockite.)

The attachment of the crystal component to the protein can be interpreted by metric similarities in the elementary dimensions (geometric factor, orientation properties) and by affinity relationships of the components (energy factor, H bonds >CO–NH.....O(F)).

We prepared substitution series in the calcium phosphate system (for example, $Ca_5(PO_4)_3OH$, $Ca_4H(PO_4)_3\cdot 2\,H_2O$, $CaHPO_4\cdot 2\,H_2O$ as well as model experiments with natural material) and studied the substances by X-ray and electron diffraction and by spectroscopy [1]. In dental enamel (keratin-

like organic matter, apatite crystals), there exist analogies of the lattice parameters that almost amounted to epitaxy relationships.

[*] Priv.-Doz. Dr. H. Newesely
Forschungsgruppe für Mikromorphologie im
Fritz-Haber-Institut
Faradayweg 16
1 Berlin 33 (Germany)

[1] *H. Newesely*, Forsch. u. Fortschr., in press.

Epitaxy of Gallium Arsenide with Gallium Arsenide from Organogallium Compounds [1]

By *J. Nickl*[*]

An attempt was made for the first time to use halogen containing organogallium compounds as sources of Ga in the epitaxy of GaAs/GaAs. There was a danger that the organic ligands might be cracked to carbon (soot) at the overgrowth temperature and inhibit the monocrystalline growth. However, it was found that highly perfect monocrystalline GaAs layers can be produced with $GaCH_3Cl_2$ if the vaporized compound is heated with H_2 and arsenic at $\approx$ 1000 °C before layering.

With a flow rate of 1.5 cm/sec (700 °C) and a gas composition of $\approx$ 35–65 vol-% of H_2, $\approx$ 15–30 vol-% of arsenic, and 20–35 vol-% of $GaCH_3Cl_2$, the overgrowth rate on (111) is about 0.3–1 μm/min.

Only polycrystalline layers have so far been obtained with $Ga(CH_3)_2Cl$. At 350–700 °C and at low $GaCH_3Cl_2$ concentrations, GaAs whiskers are preferentially formed with falling temperature. Between 550 and 650 °C, the whiskers sometimes grow in two steps. In the first step a (111)-oriented whisker $\leqslant$ 1 μm thick is formed, and this thickens radially to 3–50 μm in the second step, giving rise to a six-pointed cross-section. The electrical properties, particularly the resistance as a function of temperature, were studied on highly perfect GaAs whiskers grown in one step.

[*] Dr. J. Nickl
Institut für Anorganische Chemie der Universität
Forschungslaboratorium für Festkörperchemie
Anzinger Str. 1
8 München 8 (Germany)

[1] Messrs. *Bertinger*, *Schweitzer*, and *Duck* took part in the experiments.

Preparation and Properties of Titanium Silicides

By *J. Nickl*[*]

Attempts were made to grow single crystals of titanium silicides by transport reactions [1], by deposition from the gas phase, and in copper-rich melts. Titanium and silicon were also fused together without a crucible and zone-melted. The results are shown in the table, and may be summarized as follows:

1. $TiSi_2$, TiSi, and Ti_5Si_3 could each be prepared from the gas phase as polycrystalline layers; single crystals with a stoichiometric composition were obtained only in the case of $TiSi_2$.

2. TiSi was prepared for the first time in the monocrystalline form by a transport reaction with $TiSi_2 + Br_2$.

3. The Lebeau process [2] did not give $TiSi_2$ as described in the literature, but yielded, for the first time, a ternary (TiCuSi) [3] and quaternary E phase ($Ti_{0.5}Zr_{0.5}CuSi$) [4].

4. The graphite-like complex carbide Ti_3SiC_2 was prepared for the first time from the gas phase [5].

5. A crucible-free "drop-melt process" [6], in which the starting materials in the form of grains on a suspended drop of the melt are melted by high frequency methods, was developed for the preparation of titanium silicides from Ti + Si.

Compound	Form and properties sc = single crystal pc = polycrystalline	Preparation TR = transport reaction M = melt
$TiSi_2$	sc, $\approx$ 10 mm³ octahedron or needle-shaped, cryst., soluble in HF	$TiSi_2 + Br_2$ $Ti + Si + Br_2$ } TR; 1000→800 °C
	sc, $\approx$ 4 mm³ octahedron, dendritic cryst. and pc layers $\approx$ 0.01–3 mm	$TiCl_4 + SiCl_4 + H_2$ on heated graphite rods at 1000–1400 °C. sc at > 90 vol-% of H_2
	pc rods, always two-phase with $\leqslant$ 0.5% of the second phase; rods: diameter 5–8 mm	Ti + Si by 'drop-melt process'[6] followed by zone melting in high vacuum
TiSi	sc, platelets $\leqslant$ 3 mm² soluble in HF	TiCuSi + Br_2, TR 1000→750 °C
	pc layers, 0.01–1 mm	$TiCl_4 + SiCl_4 + H_2$ } gas phase deposition on graphite rods at $\leqslant$ 1000 °C
Ti_5Si_3	pc layers, 0.01–1 mm	$TiCl_4 + SiCl_4 + H_2$
TiCuSi E-phase	sc, column-shaped, dia. $\leqslant$ 1 mm, length $\leqslant$ 10 mm. Soluble only in HF + HNO_3. Dec. above 1000 °C into Ti_5Si_3 + Cu silicides. $\sigma = 1 \times 10^3\ \Omega^{-1}\ cm^{-1}$ paramagnetic $\chi = 2 \times 10^{-6}$	$TiSi_2 + CuO$ Ti + Si + Cu } fusion
$Ti_{0.5}Zr_{0.5}CuSi$ E-phase	sc, form and behavior toward acids as for TiCuSi	($TiSi_2 + ZrSi_2$ + Cu) melts.
Ti_3SiC_2	pc lamellae or slate-like crusts, graphite-like material[5], soluble only in HF + HF + HNO_3. Is slowly oxidized to anatase and amorphous silica in O_2 (1 atm at 300 °C)	$TiCl_4 + SiCl_4 + CCl_4 + H_2$ on heated graphite or titanium rods at 1000–1400 °C

[*] Dr. J. Nickl
Institut für Anorganische Chemie der Universität
Forschungslaboratorium für Festkörperchemie
Anzinger Str. 1
8 München 8 (Germany)

[1] *J. Nickl*, *M. Duck*, and *J. Pieritz*, Angew. Chem. *78*, 822 (1966); Angew. Chem. internat. Edit. *5*, 839 (1966).

[2] *P. Lebeau* and *J. Figueras*, C. R. hebd. Séances Acad. sci. *136*, 1329 (1903).

[3] *J. Nickl* and *H. Sprenger*, Naturwissenschaften *54*, 18 (1967).

[4] *J. Nickl* and *H. Sprenger*, Naturwissenschaften *54*, 490 (1967).

[5] The structure was recently determined by *W. Jeitschko* and *H. Nowotny* (Mh. Chem. *98*, 329 (1967).

[6] *J. Nickl*, unpublished.

Investigation of High Polymers by Pyrolysis

By *D. Noffz*[*]

A *Simon* pyrolysis apparatus combined with a gas chromatograph and a mass spectrograph was used for the investigation of the fragmentation products of homopolymers and copolymers. Examples of the results [1]:

1. The fragmentation products of polyvinyl chloride are mainly aromatic hydrocarbons (benzene, toluene, ethylbenzene, the xylenes, styrene, C_3-alkyl- and alkylenebenzenes,

azulene, indan and indene with their methyl derivatives, naphthalene and its methyl derivatives, biphenyl, fluorene, and higher hydrocarbons).

2. Polyvinylidene chloride gives mainly chlorohydrocarbons, together with chloroolefins: mono-, di-, and trichloro derivatives of C_4 and C_5 mono- and diolefins, mono-, di-, and trichlorobenzene, di- and trichloro derivatives of toluene, styrene, and indene, and polychlorophenylacetylenes.

3. The copolymer of vinyl chloride and vinylidene chloride yields the main components formed by the homopolymers, together with chloro compounds having degrees of chlorination intermediate between those of the fragments from the two homopolymers: chlorotoluene, mono- and dichloronaphthalene, chlorobiphenyl.

4. In addition to the homologues of benzene, polystyrene yields diphenylethane and diphenylpropane, as well as about 20 compounds having the composition $C_{16}H_{16}$ = dimeric styrene. However, the main products are not the 'true' dimers, *i.e.* the 1,3-diphenylbutenes, but 1-benzyl-2-methyl-3,4-benzocyclobutene, which is probably formed by cyclization from the 'true' dimers.

5. Polypropylene occupies a special place in this investigation, because of the influence of steric effects. Thus polypropylenes of different tacticities can be readily distinguished by pyrolysis. This is possible by separation of the diastereoisomeric olefins formed by pyrolysis.

[*] Dr. D. Noffz
Badische Anilin- & Soda-Fabrik AG.
Untersuchungslaboratorium
67 Ludwigshafen (Germany)

[1] For further examples, see *D. Noffz* and *W. Pfab*, Z. analyt. Chem. *228*, 188 (1967).

Polymerization Reactions on Adsorption Layers of Solids

By *K. Nollen* and *K. Hamann*[*]

The adhesion of polymers to powdered solids, *e.g.* pigments or fillers, is of great importance for a number of technological properties of filled or pigmented plastics and paints. The adhesion of the macromolecules could be considerably increased if the solid, or reactive groups on its surface, could be incorporated into the macromolecule as a comonomer or as an initiator, since the bond between the surface of the solid and the macromolecule is chemical and is therefore very strong. Fillers and inorganic pigments do not generally possess such properties. However, if they are provided with firmly-adhering reactive adsorption layers, they will participate in many polymerization reactions.

Adsorption layers of this type are formed *e.g.* on inorganic oxide pigments by the adsorption of low molecular-weight polar compounds such as organic acids or amines. Though the molecules adsorbed directly on the surface are generally not bound chemically to the solid, they still adhere relatively strongly. If these adsorption layers have a suitable structure they can be used for initiation or as a 'comonomer', the polymer formed being firmly bonded to the pigment surface.

For example: sodium hydrogen oxalate adsorbed on several titanium dioxide pigments can initiate the polyaddition of epoxides; silicates on a wide range of powders act as initiators for the anionic copolymerization of phthalic anhydride and glycol carbonate to form polyesters. If the adsorption layer consists of polymerizable acids such as acrylic or methacrylic acid, vinyl compounds can be polymerized with these adsorption layers by a free-radical mechanism.

Organic powders, such as organic pigments, cannot generally be provided with firmly-adhering adsorption layers. However, initiating or polymerizable groups can be incorporated into the pigment, so that polymerizations become possible directly on the surface of the substances. For example, the copolymerization of phthalic anhydride and glycol carbonate can be initiated by the carboxylate and sulfonate groups of salt-like azo pigments. Since the initiator is incorporated into the resulting macromolecule in these reactions, the polymer adheres very firmly to the pigment surface.

[*] Dr. K. Nollen and Prof. Dr. K. Hamann
Forschungsinstitut für Pigmente und Lacke e.V.
Wiederholdstr. 10/1
7 Stuttgart N (Germany)

Extraction of Macro-Quantities of Plutonium with Tributyl Phosphate in the Presence of Uranium[1]

By *W. Ochsenfeld*[*]

In the reprocessing of irradiated fuel elements of high plutonium content, such as those of fast breeder reactors, the behavior of macro-concentrations of plutonium in the presence of uranium is of interest in the extraction and separation. The data found for the partition of plutonium and of uranium between 20% tributyl phosphate in n-dodecane and aqueous nitric acid solutions show that each of the two elements influences the extraction of the other.

Of the essential steps in a possible flow scheme for the processing of a fuel containing 10% of PuO_2 + 90% of UO_2 only the separation of the plutonium from uranium is mentioned.

The reduction of Pu(IV) to Pu(III) by U(IV) and the instability of Pu(III) and U(IV) at the high plutonium concentrations present make the separation difficult. It is well known that Pu(III) is oxidized to Pu(IV) by nitric acid and its reaction products, as well as by air. Under countercurrent operation, the plutonium losses in the uranium product could be reduced to $< 0.2\%$ by an 8- to 10- fold stoichiometric excess of U(IV), aqueous solution stabilized with 0.2 M hydrazinium nitrate at acid concentrations lower than 2.5 N, and suitable flow conditions. The plutonium product need not be absolutely free from uranium, since it is made into a PuO_2/UO_2 mixed oxide in any case.

[*] Dr. W. Ochsenfeld
Gesellschaft für Kernforschung mbH.
75 Karlsruhe (Germany)

[1] This work was undertaken as part of the joint research program of EURATOM and the Gesellschaft für Kernforschung mbH., Karlsruhe, in the field of fast reactors.

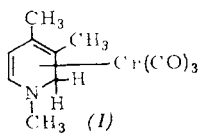
Carbonylmetal π-Complexes of Dihydropyridine Derivatives

By *K. Öfele*[*]

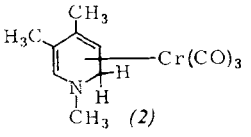
N-Methyldihydropyridines react with $Cr(CO)_6$ or $(CH_3CN)_3Cr(CO)_3$ to form red, sublimable *N*-methyldihydropyridinecarbonylchromiums(0). In these complexes, which, unlike the free dihydropyridines, are remarkably stable, the heterocyclic ring is evidently bonded to the metal *via* two C=C double bonds and the free electron pair on the nitrogen. These are therefore the first known complexes with a vinylamine group as a chelating ligand.

Tricarbonylchromium complexes have so far been obtained only from 1,2-dihydropyridine derivatives; *N*-methyl-1,2-dihydropyridine complexes are also obtained by rearrangement from *N*-methyl-1,4-dihydropyridines and $Cr(CO)_6$ or $(CH_3CN)_3Cr(CO)_3$. No tricarbonylchromium compound has so far been obtained from 1,4,4-trimethyl-1,4-dihydropyridine, the rearrangement of which to the 1,2-dihydropyridine is strongly hindered[1].

The reaction of 1,3,4-trimethyl-1,2-dihydropyridine with $(CH_3CN)_3Cr(CO)_3$ always yields 1,4,5-trimethyl-1,2-dihydropyridine-$Cr(CO)_3$ *(2)* as well as the complex *(1)* of the starting compound.



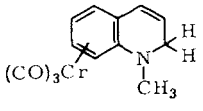
(1)



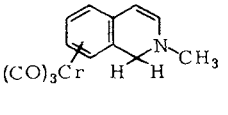
(2)

When heated to *ca.* 100 °C, *(1)* and *(2)* are reconverted to a mixture of isomers.

N-Methyldihydroquinoline and *N*-methyldihydroisoquinoline react with $(CH_3CN)_3Cr(CO)_3$ to form yellow *N*-methyldihydroquinoline-$Cr(CO)_3$ *(3)* and *N*-methyldihydroisoquinoline-$Cr(CO)_3$ *(4)*, respectively, the metal in these complexes being bonded to the benzenoid ring. Owing to the free enamine group, they are more reactive than the dihydropyridine complexes; in contrast to the latter, *e.g. (4)* reacts with trityl tetrafluoroborate with loss of hydride to form yellow [*N*-methylisoquinolinium-$Cr(CO)_3$]BF_4. NMR spectroscopy has proved very useful in the determination of the structure of these complexes.



(3)



(4)

Surprisingly, $Fe(CO)_5$ and $Ni(CO)_4$ are reduced directly to carbonylmetalates by dihydropyridine derivatives. Thus the reactions of *N*-methyl-1,2- and -1,4-dihydropyridines with $Fe(CO)_5$ and $Ni(CO)_4$ yield the *N*-methylpyridinium salts of $[Fe_4(CO)_{13}]^{2\ominus}$ and $[Ni_4(CO)_9]^{2\ominus}$.

[*] Dr. K. Öfele
Anorganisch-Chemisches Laboratorium
der Technischen Hochschule
Arcisstr. 21
8 München 2 (Germany)

[1] *E. M. Kosower* and *T. S. Sorensen*, J. org. Chemistry *27*, 3764 (1962).

Liquid Scintillation Counting of Benzene and Ethanol for ^{14}C Measurements in the Low-Level Range

By *R. L'Orange, K. Wagener*, and *K. E. Zimen*[*]

In the determination of ^{14}C, the test material is converted into pure benzene in the complete absence of air by three main steps: 1. Combustion to CO_2; 2. reduction to Li_2C_2 and preparation of acetylene; and 3. cyclization on a contact catalyst. The CO_2 is reduced with liquid Li in a vacuum-tight steel chamber. Continuous heating between 680 and 850 °C gives up to 98% of C_2H_2, the trimerization of which yields up to 95% of benzene, so that the total yield is over 90%. The trimerization is complete within an hour. During the reaction, the catalyst grains are spread out over a contact area of about 100 cm^2, which is cooled or heated as required.

The ^{14}C in the benzene is monitored at room temperature in a specially constructed apparatus with double coincidence and summation circuitry by means of a fully transistorized single-channel spectrometer. With a scintillator volume of 12 ml, a background of 6.5 counts per minute (above the tritium end point) is achieved by means of special shielding with boron/paraffin and low-radiation Pb and Hg. Range for dating with 10 ml of benzene: 48000 years. With 40 ml of benzene in a scintillator volume of 44 ml (measurement in quartz cells with windows plane-parallel to the photocathodes and a TiO_2 reflector), the background is 14 counts per minute and the maximum range of the age determination is 57000 years (2 sigma criterion, counting time 48 h, $T_{1/2} = 5570$ years).

The increase in ^{14}C from nuclear explosions, which began about 1954, can be used to date wines. A histogram of the ^{14}C content of German wines from 1952 to 1966 permits the determination of the age of the wine. The purified wine alcohol and toluene + scintillator (4:6 v/v) are counted directly in a volume of 44 ml. It is thus possible for the first time to make a simple check on the age of natural wines at present up to 12 years old.

[*] Dipl.-Chem. R. L'Orange, Priv.-Doz. Dr. K. Wagener, and Prof. Dr. K. E. Zimen
Hahn-Meitner-Institut für Kernforschung
Glienicker Str. 100
1 Berlin 39 (Germany)

Molecular Structure and Magnetic Anisotropy of Amides

By *K. Todt* and *H. Paulsen*[*]

The action of the induced magnetic field of the amide group on adjacent protons has been studied in sterically fixed *N*-acylpiperidine derivatives. With a *cis* amide carbonyl group, the NMR signal of equatorial protons of the α-methylene group is shifted downfield (deshielding) and that of axial protons upfield (shielding). The magnetic field of the amide group therefore has different signs at the positions of these protons. The protons of freely-rotating *cis*-methyl groups of *N*-methylamides pass through alternating regions with deshielding and shielding magnetic fields; the observed shielding of these protons is an average value, which leads to further conclusions regarding the magnetic anisotropy of the amide group.

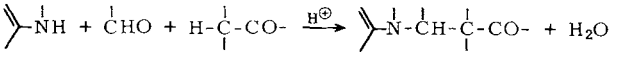
The knowledge gained concerning the magnetic action of the amide group in its environment can be utilized in two ways: If the position of a proton is known, its NMR signal, which is split when the rotation of the amide group is hindered, can be assigned to the rotational isomers on the basis of the chemical shift. Conversely, the position of a proton in relation to the amide group can be established by experimental determination (*e.g.* by the benzene dilution method) of whether it is in the deshielded or the shielded region, and can then be used to deduce the structure or the conformation of the amide. For example, the 2-methine proton of *N*-acetyl-2-methylpiperidine lies in the deshielded region; it follows that the compound has a chair conformation with an axial 2-methyl group. *N*-Acyl-2-methylpyrrolidine occurs in an envelope conformation in which the 2-methine proton is situated if the deshielded region. The isopropyl group in *N*-isopropyl-*N*-methylacetamide preferentially assumes a conformation in which the isopropyl methine proton is in the plane of the amide group.

[*] Dr. K. Todt and Doz. Dr. H. Paulsen
Institut für Organische Chemie der Universität
Papendamm 6
2 Hamburg 13 (Germany)

Synthesis and Reactions of Novel Carbonyl Compounds Containing Nitrogen

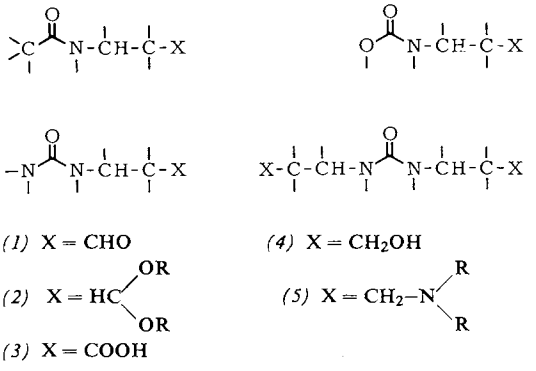
By *H. Petersen*[*]

Carbonyl compounds containing nitrogen are obtained by acidic condensation of an NH group of acyclic or cyclic ureas, amides, or carbamates with a carbonyl compound (particularly formaldehyde) and a CH-acidic aldehyde or ketone, in accordance with an α-ureidoalkylation principle[1,2].



This synthesis yields aldehydes *(1)* containing nitrogen, which can be converted *e.g.* into acetals *(2)* by reaction with monohydric or polyhydric saturated or unsaturated alcohols,

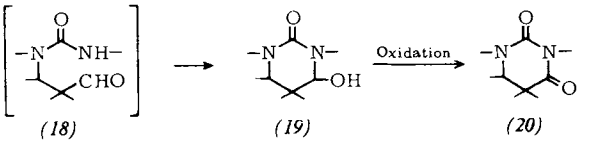
into monobasic or polybasic carboxylic acids *(3)* by oxidation, into monohydric or polyhydric alcohols *(4)* by hydrogenation, and into primary, secondary, or tertiary amines *(5)* of the ureas, amides, or carbamates by amination and hydrogenation. The compounds *(1)–(5)* are suitable for use *e.g.* in the synthesis of polycondensates and polymers, and can be converted into amino aldehydes, amino acids, amino alcohols, and polyfunctional amines by hydrolysis.



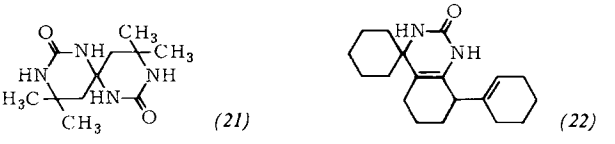
The amination and hydrogenation of the *N,N*-dialkylureido-*N'*-propionaldehydes *(6)* with secondary amines leads to 1-ureidopropylene-3-dialkylamines *(7)*, which can be quaternized at the basic nitrogen [*(8)*]. When heated, *(7)* give isocyanates [*(9)*], which react with H-acidic compounds to give a wide range of products.

The heterocycles *(11)*, *(12)*, *(14)*, and *(16)* can also be prepared in this way. For example, *N,N*-dialkylureido-*N'*-propionaldehydes *(6)* can be converted by hydrogenation into tetrahydro-*2H*-1,3-oxazin-2-ones *(11)*, by amination and hydrogenation with NH_3 or primary amines into hexahydropyrimidinones *(12)*, and by oxidation *via N,N*-dialkylureidopropionic acids *(13)* into tetrahydro-*2H*-1,3-oxazine-2,6-diones *(14)*. When *(13)* and *(14)* are heated, they give polyamides *(15)* and 2-azetidinones *(16)*, or, in the presence of water, β-amino acids *(17)*.

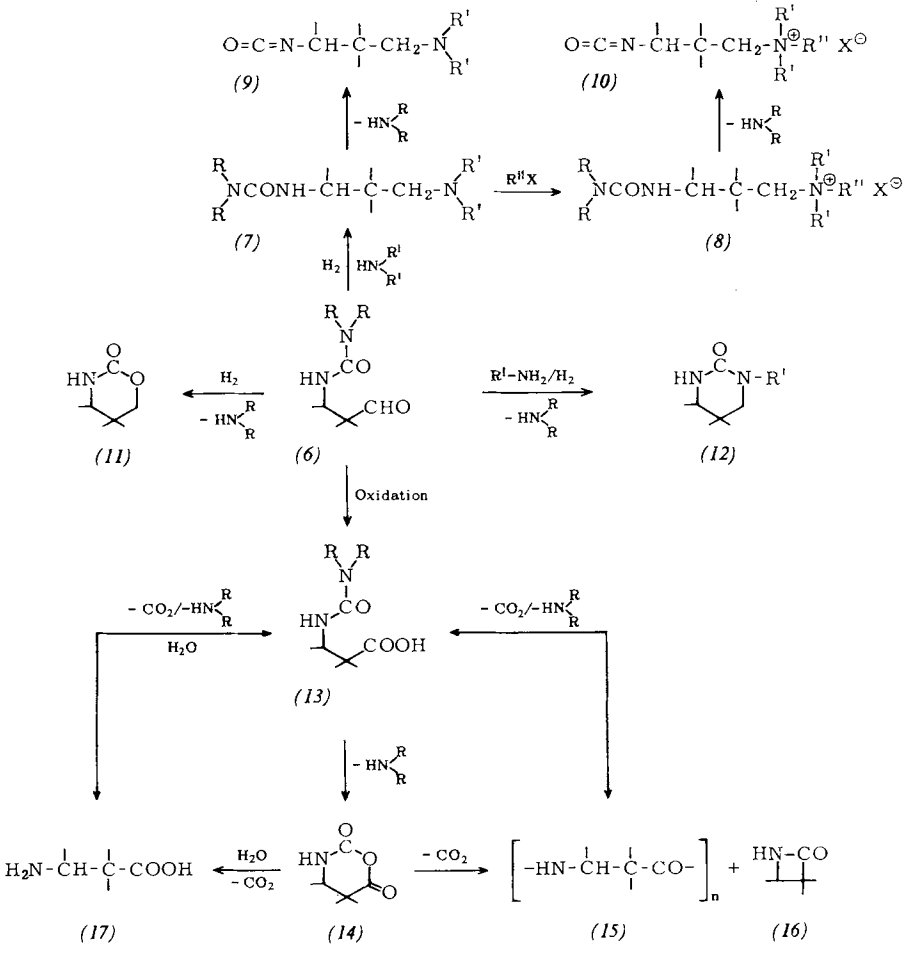
The acidic condensation of urea or its mono- or disubstituted derivatives with two moles of an aldehyde, of which at least one mole must exhibit CH-acidic character, leads formally *via (18)* to heterocycles of the 4-hydroxyhexahydro-2-pyrimidinone type *(19)* [2,3]. These heterocycles can be oxidized to hexahydro-2,4-pyrimidinediones *(20)*, which react with water to form β-amino acids or decompose when heated to form polyamides and cyanuric acid.



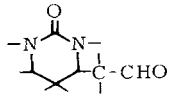
Polycyclic ureas are obtained in an analogous manner from ureas and CH-acidic ketones in the presence of acids. Recent investigations [2,4] have shown that the 'triacetonediurea' obtained by *Weinschenk* [5] from acetone and urea is a 4,4'-



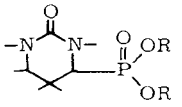
spirobi-(6,6-dimethylhexahydro-2-pyrimidinone) *(21)*. We obtained the polycyclic urea *(22)* from urea and cyclohexanone [4].



The heterocycles of the type *(19)* are cyclic α-alkylolureas, which condense with CH-acidic aldehydes to form 4-formyl-methylhexahydro-2-pyrimidinone *(23)* and with PH-acidic phosphorus compounds (*e.g.* dialkyl phosphites) to form dialkyl 2-oxohexahydropyrimidyl-4-phosphonates *(24)*.



(23)



(24)

The secondary reactions of *(19)* also include reactions with NH-acidic compounds, such as amines[2] and ureas[2,6,7], as well as with alcohols[2,8].

[*] Dr. H. Petersen
Badische Anilin- & Soda-Fabrik
Ammoniaklaboratorium
67 Ludwigshafen (Germany)

[1] *H. Petersen*: Festschrift „Carl Wurster". BASF, Ludwigshafen 1960; Textil-Rdsch. *16*, 646 (1961); Melliand Textilber. *43*, 380 (1962).

[2] *H. Petersen*, Angew. Chem. *76*, 909 (1964).

[3] *H. Petersen, H. Brandeis*, and *R. Fikentscher*, German Pat. 1230805 (1962), BASF.

[4] *H. Petersen*: Festschrift BASF. Ludwigshafen 1965, p. 123.

[5] *A. Weinschenk*, Ber. dtsch. chem. Ges. *34*, 2185 (1901).

[6] *H. Brandeis, H. Petersen*, and *R. Fikentscher*, German Pat. 1244207 (1962), BASF.

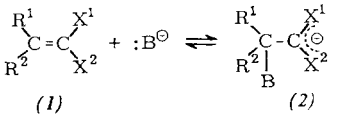
[7] *G. Zigeuner, E. A. Gardziella*, and *G. Bach*, Mh. Chem. *92*, 31 (1961).

[8] *H. Petersen, H. Brandeis*, and *R. Fikentscher*, German Pat. 1231247 (1962), BASF.

Reversibly Titratable Organic Lewis Acids

By *O. E. Polansky*[*]

Unsymmetrically substituted ethylenes *(1)*, in which X^1 and X^2 are strong electron-acceptor groups and R^1 and R^2 are weak acceptor or donor groups or H, have a relatively large partial positive charge on the C atom carrying R^1 and R^2. The Lewis-acid character of these compounds can be seen from the fact that bases are accepted reversibly at the position shown:



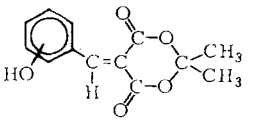
(1) *(2)*

The compounds *(1)* can accordingly be reversibly titrated in aqueous or aqueous-organic media, and have p*K* values of weak to medium-strong acids.

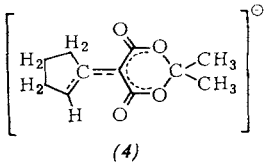
The UV spectra of the Lewis acid-base adducts *(2)* show superposition of the UV spectra of the chromophores R^1 and R^2, possibly of B, and of the anion $CHX^1X^{2\ominus}$, and thus prove structure *(2)*. Further evidence of the existence of *(2)* is provided by comparison of the NMR spectra of *(1)* and *(2)*, particularly when R^2 = H.

Corresponding to their Lewis-acid character, the olefins *(1)* very readily undergo nucleophilic attack at the C atom carrying R^1 and R^2, whereas the other C atom [even in *(2)*] is only slightly or not at all nucleophilic. The olefins *(1)* consequently do not enter appreciably into cycloadditions with diazoalkanes; instead, they react (probably in several steps) to form cyclopropanes, dihydrofurans, *etc.* The olefins *(1)*, as expected from their Lewis-acid character, catalyse the etherification of alcohols by diazoalkanes.

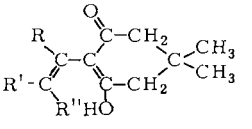
If the substituents R^1 and R^2 contain functional groups that can be acidified, the Brønsted-acid character becomes apparent, depending on the position of this group in relation to the double bond; *p*-hydroxybenzylidenemeldrum acid *(3a)* reacts as a Brønsted acid, while the *m*-hydroxy derivative *(3b)* reacts as a Lewis acid. The Lewis-acid character of the olefins *(1)* is occasionally suppressed by steric effects or by a tendency toward enolization. Thus the reaction of cyclopentylidenemeldrum acid with bases leads preferentially to the mesomeric anion *(4)*; the 2-alkylidenedimedones generally exist as the enol *(5)* if the alkylidene group contains β′-H atoms.



(3a): *p*-OH
(3b): *m*-OH



(4)



(5)

The p*K* values estimated by the HMO method exhibit a good agreement with the experimental values.

[*] Prof. Dr. O. E. Polansky
Lehrkanzel für Theoretische Organische Chemie
an der Universität
Währingerstr. 38
A-1090 Wien (Austria)
and
Max-Planck-Institut für Kohlenforschung
Stiftstr. 32–34
433 Mülheim/Ruhr (Germany)

Use of Some Short-Lived Radionuclides for Activation Analysis by Irradiation with the Fast Neutrons of a Swimming-Pool Reactor

By *H.-J. Born* and *E. Pfeffermann*[*]

Swimming-pool reactors moderated with light water have a high proportion of fast fission neutrons, as well as thermal neutrons, close to the core. These fission neutrons, like the 14 MeV neutrons of an accelerator, are suitable for use in neutron activation analysis. The flux of fast neutrons from a reactor is mainly characterized by its high constancy and its high neutron intensity between 1 and 10 MeV. The threshold values of the desired nuclear reactions should lie below 10 MeV, since the flux of higher-energy neutrons is appreciably lower.

Of the (n,p), (n,α), (n,2n), and (n,n′) nuclear reactions that could be considered, some short-lived reaction products were studied in detail by means of their gamma spectra. The reactions studied were $^{16}O(n,p)^{16}N$, $^{89}Y(n,n')^{89m}Y$, $^{207}Pb(n,n')^{207m}Pb$, and $^{11}B(n,p)^{11}Be$. Owing to the short half-lives (1–16 sec), rapid transport from the irradiation position to the measurement position is necessary. A pneumatic tube with flight times of 1 sec is used in the research reactor at Munich. It is important to separate the sample container from the transport container (rabbit), so that only the sample falls directly into the measuring chamber. Because of this automatic ejection device, the rabbit can be fitted with a cadmium filter. This permits a marked reduction of parasitic activities induced by thermal neutrons. Measurement of the γ-activity of the samples is carried out with a 3″×3″ NaI(Tl) crystal.

The effective cross-sections for the flux spectrum at the irradiation position were first determined for the nuclear

reactions mentioned above. The reactions are suitable for the detection of oxygen, yttrium, and lead[1] by neutron activation analysis.

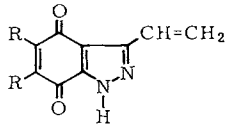
[*] Prof. Dr. H.-J. Born and Dipl.-Ing. E. Pfeffermann
Institut für Radiochemie
der Technischen Hochschule München
8046 Garching bei München (Germany)

[1] For sample weights of 100–500 mg the detection limits are 250 μg for oxygen, 1–10 μg for yttrium, and 500 μg for lead.

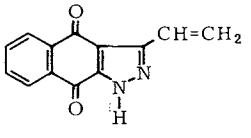
Vinylpyrazoloquinones

By *G. Manecke, G. Ramlow, W. Storck,* and *W. Hübner*[*]

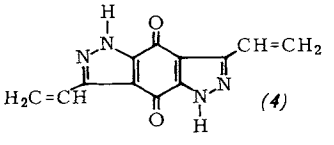
Whereas vinyl-substituted quinones have until now been obtainable only with difficulty, the vinylpyrazoloquinones *(1)* to *(4)* could be readily obtained by 1,3-dipolar addition of the diazoalkene vinyldiazomethane to quinones.



(1) R = CH_3
(2) R = Cl



(3)

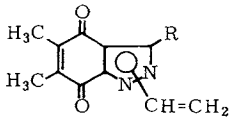


(4)

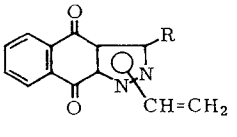
Apart from the dichloro compound *(2)*, whose redox potential is so high that it inhibits self polymerization, all these compounds are polymerizable. If *(2)* is converted into the hydroquinone diacetate, polymerization again becomes possible.

Alkylations on the pyrazole ring yield mixtures of isomers, which can be separated by column chromatography. The main product is the N^1 isomer. If the pyrazoloquinone has H instead of a vinyl group in position 3, the N^2 isomer is formed in a higher yield. This effect is intensified with increasing size of the substituents in the order $CH_3 < CH = CH_2 < (CH_2)_nSO_3H$. In the sulfalkylation of 3-vinylpyrazoloquinones, the steric effects are so great that only the N^1 isomers are formed. The methyl isomers are obtained by methylation with dimethyl sulfate. *N*-Vinylpyrazoloquinones are formed in the mercury acetate-catalysed reaction with vinyl acetate, and sulfalkylated water-soluble pyrazoloquinones result from the reaction of the *N*-alkali metal salts with sultones.

The *N*-vinylpyrazoloquinones *(5)–(12)* were prepared with vinyl acetate.



(5) 1-vinyl, R = H
(6) 2-vinyl, R = H
(7) 1-vinyl, R = vinyl
(8) 2-vinyl, R = vinyl



(9) 1-vinyl, R = H
(10) 2-vinyl, R = H
(11) 1-vinyl, R = vinyl
(12) 2-vinyl, R = vinyl

Only the *N*-vinyl groups of the pyrazolonaphthoquinones *(9)–(12)* were polymerizable. The *N*-vinylpyrazoloquinones could not be polymerized, even as derivatives of the corresponding hydroquinones. On the other hand, the 5,6-epoxy derivatives of the compounds *(5)–(8)* could be very readily polymerized.

Since the polymeric epoxy compounds could also be converted back into the quinones with potassium iodide in acetic acid/water, redox polymers could be obtained in this way.

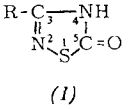
[*] Prof. Dr. G. Manecke, Dipl.-Chem. G. Ramlow,
Dr. W. Storck, and Dipl.-Chem. W. Hübner
Fritz-Haber-Institut der Max-Planck-Gesellschaft und
Institut für Organische Chemie der Freien Universität
Thielallee 63–67
1 Berlin 33 (Germany)

Contribution to the Chemistry of Substituted Δ^2-1,2,4-Thiadiazolin-5-ones

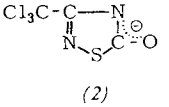
By *R. F. W. Rätz* and *H. D. Hoberecht*[*]

The Δ^2-1,2,4-thiadiazolin-5-ones are a class of reactive compounds, of which the few known members were previously regarded as 5-hydroxy-1,2,4-thiadiazoles. Chemical reactivity and spectroscopic data indicate that these compounds exist, both as the solid and in solution, in the lactam form *(1)*. Their acidity makes them capable of salt formation with inorganic and organic bases. These salts are so stable that they can be used as nucleophiles in a number of acylation reactions.

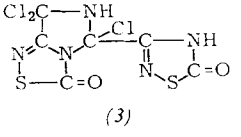
In aqueous solution, the anion *(2)* forms a dimer, which reacts with ammonia to form the previously unknown 5,7,7-trichloro-6,7-dihydro(5-oxo-Δ^2-1,2,4-thiadiazolin-3-yl)-3*H*,5*H*-imidazo[5,1-*c*][1,2,4]thiadiazol-3-one *(3)*. The compound was characterized by elemental analysis and by IR and mass spectroscopy.



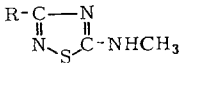
(1)



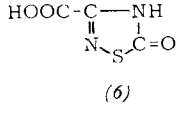
(2)



(3)



(4), R = Cl_3C-
(5), R = CH_3NH-C(=O)-



(6)

Attempts to obtain an analogous *N*-methylated compound by treatment of the dimer with methylamine instead of with ammonia were unsuccessful. Solutions of the compound *(1)*, R = Cl_3C, have a ketonic character in aqueous methylamine; the compounds *(4)* and *(5)* are formed.

In the presence of an excess of sodium hydroxide, *(1)*, R = Cl_3C, is converted into the disodium salt of the acid *(6)*. The free acid melts at about 140 °C with decarboxylation to give the parent substance of this series.

[*] Dr. R. F. W. Rätz and H. D. Hoberecht
Olin Mathieson Chem. Corp.
New Haven, Conn. 06504 (U.S.A.)

Electrochemical Studies on the Electron and Ion Defect State in α-Silver Selenide

By *D. O'Briain* and *H. Rickert*[*]

The relationship between the chemical potential of silver in α-silver selenide and the deviation from the ideal stoichiometric composition was determined by an electrochemical titration with the aid of the solid cell Ag/AgI/Ag_2Se at 200 °C. Owing to the highly imperfect arrangement of the silver ions in Ag_2Se, its chemical potential may be assumed to be constant. When the stoichiometric composition is

changed, the chemical potential of the silver depends only on the change in the concentration of the quasi-free ions and defect electrons. The thermodynamic behavior of the electrons in Ag_2Se can be quantitatively described by the application of Fermi-Dirac statistics, *i.e.* by taking into account the degeneracy of the electrons. The electrochemical thermodynamic method provides a means for the determination of the band gap in Ag_2Se. The partial conductivity of the silver ions was also studied as a function of the stoichiometric composition. In agreement with the lattice defect model, the partial conductivity σ is independent of the chemical potential of the silver, and can be expressed as a function of temperature by the following equation:

$$\sigma_{Ag^+} = 11.4 \exp(-1180\ \text{cal}/RT)\ \text{ohm}^{-1}\ \text{cm}^{-1}$$

The self-diffusion coefficient D of silver is also independent of the stoichiometric composition:

$$D_{Ag} = 7.95\times10^{-8}\ T \exp(-1370\ \text{cal}/RT)\ \text{cm}^2\ \text{sec}^{-1}$$

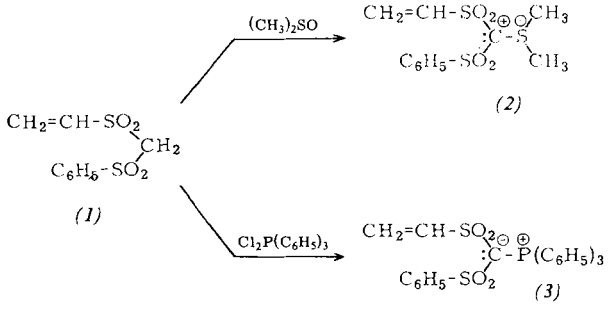
Comparison of the partial conductivity and the self-diffusion coefficient of silver ions gives a correlation factor of 0.36 at 300 °C for the self-diffusion. Conclusions regarding the diffusion mechanism can be drawn from this result.

[*] Dr. C. D. O'Briain and Doz. Dr. H. Rickert
Lehrstuhl und Abteilung für Elektrochemie der Universität
Kaiserstr. 12
75 Karlsruhe (Germany)

Investigation of *S*-Vinylsulfonylylides

By *H. Diefenbach*, *H. Ringsdorf*, and *R. Wilhelms* [*]

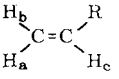
Dimethylsulfonium phenylsulfonylvinylsulfonylmethylide *(2)* and triphenylphosphonium phenylsulfonylvinylsulfonylmethylide *(3)* were prepared by condensation of phenylsulfonylvinylsulfonylmethane *(1)* with dimethyl sulfoxide and with triphenylphosphine dichloride respectively.



Elemental analyses and the fragments and maximum masses (*m/e* 306 and 506, respectively) in the mass spectrum confirm the compositions and molecular weights of *(2)* and *(3)*. The two unsaturated ylides can be recrystallized from water, and cannot be further acylated with benzoyl chloride.

The predominance of the indicated ylide structure over a possible ylene structure is confirmed by the UV spectrum of *(2)* (in 95% ethanol). In contrast to *(1)*, the spectrum of *(2)* no longer exhibits the fine structure due to an aromatic system. The spectrum, which contains a broad, intense band at $\lambda_{max} = 248$ nm ($\log \varepsilon_{max} = 3.93$) is similar to that of the bis-(phenylsulfonyl)methane anion ($C_6H_5-SO_2-\overset{\ominus}{C}H-SO_2C_6H_5$).

The ylide carbanion is stabilized by the adjacent SO_2 groups. The SO_2 stretching vibrations occur accordingly at lower wavelengths than in *(1)* (cf. displacement of the carbonyl frequency in acylylides). An increase in the electron densities on the phenyl and vinyl groups is also to be expected from the delocalization of the electron pair on the ylide carbanion. This is confirmed by the position of the signals due to the phenyl and vinyl protons in the NMR spectrum (measured in $(D_3C)_2SO$, TMS as internal standard).



	τ_a	τ_b	τ_c	τC_6H_5
(1)	3.64	3.68	2.91	2.1
(2)	4.23	4.03	3.07	2.3
(3)	4.37	4.73	2.94	2.4

Compounds *(2)* and *(3)* undergo free-radical polymerization to form macromolecular ylides. Copolymerization experiments with styrene show that the reactivity of the vinylsulfonylylides corresponds roughly to that of vinylphenylsulfone.

[*] Dr. H. Diefenbach, Doz. Dr. H. Ringsdorf, and
Dipl.-Chem R. Wilhelms
Institut für Polymere der Universität
Marbacher Weg 15
355 Marburg (Germany)

Stability and Properties of the Complexes of Hexavalent Actinides with Pyridine-2-carboxylic Acids and Quinaldic Acid

By *W. Robel* and *S. H. Eberle* [*]

Chelates of hexavalent uranium, neptunium, plutonium, and americium with pyridine-2-carboxylic acid (HAPA), 6-methylpyridine-2-carboxylic acid (HMAPA), and quinaldic acid are obtainable by precipitation from aqueous solution. Compounds of the types MO_2L_2, $MO_2L_2{\cdot}2H_2O$, and $MO_2L_2{\cdot}HL$ (solvated complexes) are formed. Depending on the precipitation conditions, it is possible to isolate *e.g.* $UO_2(APA)_2$ or $H[UO_2(APA)_3]$. The solvated complex has the properties of a difficulty soluble acid. Extraction of the hexavalent actinide from aqueous solution is possible *via* its chloroform-soluble tetraphenylarsonium salt.

Thermogravimetric studies show that the solvated compounds change into the normal compounds with loss of a ligand molecule by sublimation at *ca.* 200 °C.

Potentiometric, and in the case of Pu(VI) spectrophotometric, titrations indicate the stepwise formation of 1:1 and 1:2 complexes in aqueous solution. The stability constants can be calculated from the formation curves, *e.g.* Pu–HAPA $\log \beta_1 = 4.8$, Pu–HMAPA $\log \beta_1 = 2.5$.

[*] W. Robel and Dr. S. H. Eberle
Lehrstuhl für Radiochemie, Universität Karlsruhe, and
Institut für Radiochemie, Kernforschungszentrum
75 Karlsruhe (Germany)

Exchange Reactions and the Annealing of Nuclear Recoil Defects in Crystalline Co-, Rh-, and Ir-Amine Complexes

By *K. Rössler* and *W. Herr* [*]

The radionuclides formed in complexes of the types $[M(en)_2X_2]X$ and $[M(NH_3)_5X]X_2$ (M = Co, Rh, Ir; X = Cl, Br) by neutron capture can be separated on the basis of their modified chemical state. The specific activities that can be reached are limited by the degree of annealing by heat and γ-rays, by exchange reactions, and by the tendency of the compound to be decomposed by radiation. We found that transition reactions in particular have to be taken into ac-

count in these amine complexes even when there was no reactor radiation.

First-order exchange curves were obtained for the ^{36}Cl and ^{82}Br isotope exchange between ionically and covalently bonded halogen atoms in labeled crystalline *cis*- and *trans*-$[Co(en)_2X_2^*]X$ and *trans*-$[Rh(en)_2Cl_2^*]Cl$:

$k_1 = 10^{12} \exp(-32 \text{ kcal mole}^{-1}/RT)\ (\text{sec}^{-1})$ [Co complexes; for ^{36}Cl and ^{82}Br]

$k_1 = 10^{8} \exp(-30 \text{ kcal mole}^{-1}/RT)\ (\text{sec}^{-1})$ [Rh complex]

For example, ligand exchange in *trans*-$[Co(en)_2Cl_2^*]Cl$ is accelerated by a factor of 2 to 40 by previous irradiation with X-rays or with ^{60}Co-γ-rays (2×10^4 to 2×10^7 rad). The activation energy $E_A = 31$ kcal/mole is almost identical with that for samples that have not been irradiated. It is concluded that halogen exchange takes place *via* the defect sites (anion vacancies) already present in the lattice as well as those produced by radiation. This exchange is probably favored by an intermediate reduction of the central atom.

Conductivity measurements on *trans*-$[Co(en)_2Cl_2]Cl$ show a relationship with the exchange behavior.

In the Co-, Rh-, and Ir-pentammine complexes, the exchange leads to plateau values, the position of which depends on the temperature and on previous irradiation. Thus solid $[Co(NH_3)_5Cl]Cl_2^*$ exhibits a maximum of only 6% ^{36}Cl exchange at 150 °C, with a half-life of $t_{1/2} = 140$ min, whereas after X-ray irradiation (dose = 1.75×10^6 rad) it exhibits about 30% ^{36}Cl exchange and $t_{1/2} = 108$ min.

In crystalline *trans*-$[Co(en)_2Cl_2]Cl$, the exchange between the central atom and absorbed $^{60}Co^{2+}$ ions was also studied. This exchange obeys first-order kinetics and is appreciable even at 170 °C ($t_{1/2} = 100$ min).

We concluded from the results that, in the systems studied, the annealing can be largely understood on the basis of the high mobility of the ligand and central atoms, *i.e.* by simple exchange mechanisms.

[*] Dipl.-Chem. K. Rössler and Prof. Dr. W. Herr
Institut für Kernchemie der Universität
Zülpicher Str. 47
5 Köln (Germany)

Electrochemical Determination of the Specific Surface Area and the Activity of Porous Platinum

By *H. Binder, A. Köhling, K. Metzelthin, G. Sandstede,* and *M. L. Schrecker*[*]

The specific surface area of porous platinum that has been precipitated on an electrically conducting support can be determined by cathodic adsorption of hydrogen or by anodic desorption (oxidation) of adsorbed hydrogen atoms, with the aid of the potentiostatic triangular voltage sweep method. Owing to surface diffusion, the entire surface of the platinum is determined.

Electrochemical determination of the surface area has an advantage over the gas adsorption methods, not only because of its speed, but also because the platinum catalysts do not age as a result of elevated temperatures. The surface area depends on the nature of the platinum catalyst, *e.g.* whether platinum black or Raney platinum is used. In the case of Raney platinum, the specific surface area increases with increasing Al/Pt ratio in the aluminum alloy used, from about 7 m²/g (Al/Pt = 1) to about 37 m²/g (Al/Pt = 6). The specific surface area can decrease by up to 30% as a result of aging of the catalyst during the operation of the electrode. The ratio of the various crystal faces to one another also changes. The proportion of faces with higher indices is greater in fresh catalyst samples than in aged samples. This can be shown by the determination of the ratio of the BET surface area to the electrochemically determined surface area at various stages of aging.

The activity of the catalysts was determined from galvanostatic current-voltage curves, which were recorded during the anodic oxidation of methanol in dilute sulfuric acid. The activity of the platinum catalyst is not a simple function of the specific surface area. The activity depends in a characteristic manner *e.g.* on the Al/Pt ratio of the Raney alloy.

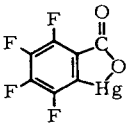
[*] Dr. H. Binder, Ing. A. Köhling, K. Metzelthin,
Dr. G. Sandstede, and M.-L. Schrecker
Battelle-Institut e.V.
Postfach 1337
6 Frankfurt/Main (Germany)

Chemistry of Perfluorinated Aromatic Mono- and Dicarboxylic Acids

By *P. Sartori*[*]

In the thermal decomposition of aliphatic perfluoroacyloxy compounds of Group IV elements (salts of aliphatic perfluorocarboxylic acids), two paths were found to exist for the decomposition of the molecule and the subsequent stabilization of the perfluoroalkyl residue: 1. Decarboxylation and removal of fluoride with formation of perfluoroolefins and 2. decarboxylation, decomposition of the perfluoroalkoxide into fluoride and the fluoride of a perfluorocarboxylic acid having one less C atom in the chain [1]. Neither reaction is possible with derivatives of pentafluorobenzoic acid. Various pyrolysis products are formed, depending on the central atom: octafluoroxanthone, decafluorobenzophenone, decafluorobiphenyl, pentafluorophenylmetal compounds, pentafluorobenzene, and pentafluorobenzoic anhydride[2].

Tetrafluorophthalic acid can be obtained from octachloronaphthalene by halogen exchange with KF in sulfolane and oxidation of the resulting octafluoronaphthalene with concentrated nitric acid. Reaction of its alkali metal or silver salts with alkylchlorosilanes yields perfluoroacyloxysilane derivatives. Unlike $TiCl_4$, $SiCl_4$ does not react completely with tetrafluorophthalic acid. The pyrolysis of Hg or Ag tetrafluorophthalate leads to *(1)* or octafluorobiphenylene and octafluorofluorenone.



(1)

[*] Doz. Dr. P. Sartori
Institut für Anorganische Chemie und Elektrochemie
der Technischen Hochschule
Templergraben 55
51 Aachen (Germany)

[1] *P. Sartori* and *M. Weidenbruch*, Chem. Ber. *100*, 2049 (1967).
[2] *P. Sartori* and *M. Weidenbruch*, Chem. Ber. *100*, 3016 (1967).

Experiments on the Poisoning of Catalysts used in the Synthesis of Ammonia

By *R. Brill, H. Schaefer,* and *G. Zimmermann*[*]

The poisoning by H_2S, S_2N_2, and thiophene of non-promoted and Al_2O_3-promoted iron catalysts for the ammonia synthesis was investigated in order to obtain information about the adsorption of sulfur on iron surfaces, the role of the promoter Al_2O_3 in relation to the tolerance for poisons, the effect of the poison on the ammonia synthesis, and the energy state of the catalytically active surface.

The iron surface of these catalysts chemisorb a maximum of 0.5 mg of sulfur/m² (corresponding to a monolayer). This

monolayer is retained even when the catalyst is treated with H_2 at 620 °C, whereas FeS formed on poisoning with high concentrations of H_2S can be reduced by H_2 above 300 °C. However, 0.16–0.25 mg of sulfur/m² is sufficient for complete poisoning of an iron catalyst. These experiments would suggest that only one or a few crystallographic surfaces are catalytically active and react preferentially with sulfur. On the other hand, in view of the vigorous reaction of sulfur, it is not impossible that the sulfur reacts nonspecifically in poisoning both by H_2S and by thiophene. However, experiments conducted with the field electron microscope[1] show that the activation of nitrogen is determined by the 111 face, so that the poisoning of this face will be important.

The adsorbed sulfur accelerates the sintering of the iron catalysts at high temperatures. The promoter Al_2O_3 hardly adsorbs sulfur. It increases the tolerance of iron catalysts by inhibition of sintering even in the partly poisoned state.

[*] Prof. Dr. R. Brill, Dr. H. Schaefer, and
Dipl.-Chem. G. Zimmermann
Fritz-Haber-Institut der Max-Planck-Gesellschaft
Faradayweg 4–6
1 Berlin 33 (Germany)

[1] *R. Brill, E.-L. Richter,* and *E. Ruch,* Angew. Chem. *79*, 905 (1967); Angew. Chem. internat. Edit. *6*, 882 (1967).

Torsional Vibration Measurements on Copolymers of Methyl Methacrylate and (Tri-n-propyl)tin Methacrylate

By *E. E. Schäfer* and *G. Rehage*[*]

The storage modulus G' and the loss modulus G'' [**] of copolymers and mixtures of polymers of methyl methacrylate and (tri-n-propyl)tin methacrylate were determined with a very sensitive torsion pendulum at a frequency of about 1 Hz and between −190 and 150 °C. It was found that the product was a true copolymer, a mixture of homopolymers, or a mixture of homopolymer and copolymer, depending on the polymerization conditions. The polymers prepared purely thermally, without the addition of a catalyst, consisted of a mixture of pure poly(tri-n-propyl)tin methacrylate and a copolymer of the two components. Similar heterogeneous products were also obtained when the temperature of polymerization was varied. However, when the polymerization was carried out in the presence of a catalyst (about 0.02-% of benzoyl peroxide) we obtained a true copolymer. Unlike the mixture, this did not solidify at two temperatures, but at a single point situated between that of pure poly(tri-n-propyl)tin methacrylate (−18 °C) and that of pure polymethyl methacrylate (about 120 °C).

Owing to its bulky side group, the poly(tri-n-propyl)tin methacrylate had a relatively low glass transition temperature, and so acted as an internal plasticizer on copolymerization with methyl methacrylate. It is therefore possible to determine by torsional-vibration measurements whether a product is a copolymer, a homopolymer mixture, or a mixture of homopolymer and copolymer, as is also shown by measurements reported by *Herwig*[1], *Oberst*[2], and *Heinze*[3].

[*] Dr. E. E. Schäfer and Prof. Dr. G. Rehage
Physikalisch-Chemisches Institut der Technische Hochschule Clausthal
Adolf-Römer-Str. 2A
3392 Clausthal-Zellerfeld (Germany)

[**] G' is the real component and G'' is the imaginary component of the complex shearing modulus $G^* = G' + iG''$. For viscoelastic materials formally there is a more complex shearing modulus, since the shearing strain and shear are displaced with respect to each other by the phase angle δ.

[1] *E. Jenckel* and *H. U. Herwig,* Kolloid.-Z. *148*, 7 (1956).

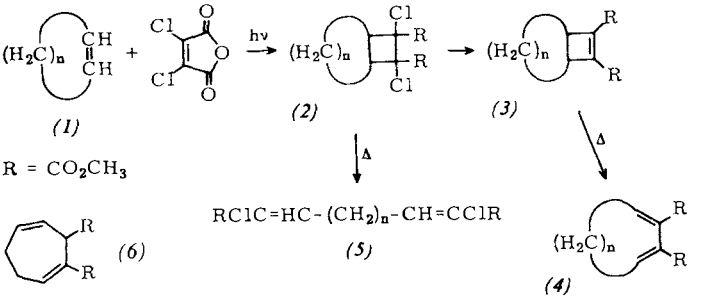
[2] *H. Oberst,* Ber. Bunsenges. physik. Chem. *70*, 375 (1966).

[3] *D. Heinze,* Makromolekulare Chem. *101*, 166 (1966).

Synthesis and Thermal Ring Cleavage of Bicyclic Cyclobutane Derivatives

By *H.-D. Scharf, M. Gallus,* and *F. Korte*[*]

The bicyclo-[*n*.2.0]alkane derivatives *(2)* are prepared by photocycloaddition (followed by hydrolysis and esterification) of dichloromaleic anhydride to cyclic olefins *(1)*, n = 3, 4, 5, 10. The steric course of the benzophenone-sensitized reaction, is being studied for various values of n.



(1) *(2)* *(3)* *(4)* *(5)* *(6)*

In the bicyclic compounds *(2)* thus obtained, the chlorine atoms are vicinal and *cis* to each other. Zinc and nickel are used to eliminate the chlorine to form *(3)*. The electrocyclic ring cleavage of *(3)* on thermal excitation is also being studied and the stereochemistry of the cyclic dienes *(4)* is considered on the basis of the Woodward-Hoffman rules. Results:

a) *(3)*, n = 3, is cleaved at 360 °C with simultaneous hydrogen shift to give *(6)*.

b) *(3)*, n = 5, yields the *cis-cis*-cyclononadiene derivative *(4)*, n = 5, as sole product when heated to 300 °C.

c) *(3)*, n = 10, with the *trans*-fused bicyclo[10.2.0]tetradecene system undergoes a smooth reaction at 120 °C to give the *trans-trans*-cyclotetradecadiene derivative *(4)*, n = 10.

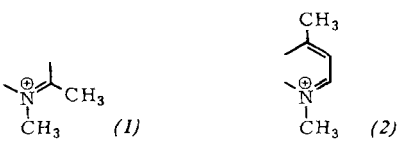
The thermal cleavage of the bicyclic compounds *(2)* leads to open-chain unsaturated dicarboxylic acids *(5)*. This reaction also proceeds stereoselectively.

[*] Dr. H.-D. Scharf, Dr. M. Gallus, and Prof. Dr. F. Korte
Organisch-Chemisches Institut der Universität
Meckenheimer Allee 168
53 Bonn (Germany)

N- and *O*-Heterocyclic Spiro Compounds

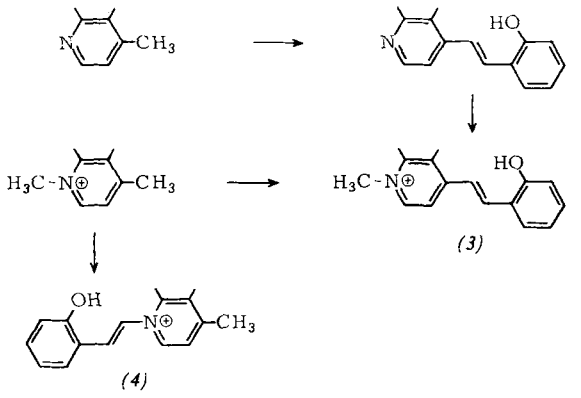
By *C. Schiele*[*]

In an examination of literature data on the synthesis of *N*- and *O*-heterocyclic spiranes, it was found that our observations[1] did not always agree with the literature reports. We therefore tried first to clarify the course of the condensation of *N*-heterocyclic methyl-substituted compounds of the types *(1)* and *(2)* with salicylaldehyde and 2-hydroxy-1-naphthalenecarb-



(1) *(2)*

aldehyde. In the case of dinuclear heteroaromatics, we synthesized an *N*-alkylated (*o*-hydroxy)styryl compound *(3)* by the route methyl-substituted heteroaromatic compound → (*o*-hydroxy)styryl compound, whereas condensation according to *Wizinger*[2] gave the product *(4)*[3]. This observation is supported in particular by the IR spectra. It can be seen from the formulae that cyclization to form the spirane



(3)

(4)

can be expected only with condensation products of the type *(3)*; however, their formation has not been observed in such systems.

[*] Dr. C. Schiele
AEG-Telefunken, Forschungsinstitut
Postfach 627
79 Ulm (Germany)

[1] *C. Schiele, M. Ruch,* and *D. Hendriks,* Tetrahedron *23,* 3733 (1967).

[2] *R. Wizinger* and *H. Wenning,* Helv. chim. Acta *23,* 247 (1940).

[3] *C. Schiele* and *D. Staudacher,* Tetrahedron, in press.

Calculation of Substituent Constants from Spectroscopic Data

By *G. P. Schiemenz* [*]

The σ constants of the Hammett relation are measures of the overall electronic effect of substituents X on the aromatic ring. They are obtained from the logarithms of the equilibrium constants (log *K*) or rate constants (log *k*) of reactions on a second substituent Y, *i.e.* from differences involving the properties of two species (educt and product or educt and transition state). The Hammett relation assumes that X has a similar influence on both species. It must then also be possible to obtain σ values for X from the properties of the groups Y in only one species. The position of an IR stretching band or of an NMR signal of Y has repeatedly been used for this purpose [1], a linear relationship being postulated between $\tilde{\nu}$ or δ and σ of X. However, the plots for *p*-X-substituted benzoic acids [2, 3], their esters [3] and nitriles [2–4], as well as benzaldehydes [3] and nitrobenzenes [3] do not give straight lines over the whole σ range.

The numerical values of σ are so chosen that the inductive and mesomeric effects, by definition, have equally strong influences on log *K*(*k*). This cannot be stipulated for other quantities. +M substituents have a different (stronger) influence on the bond order, and hence on the wave number $\tilde{\nu}$ of a stretching band of – M substituents than groups that have only an inductive effect, to which the –M substituents are adjacent. If one assumes that $\tilde{\nu}$ depends linearly, but to different degrees, on the partial terms σ_{+M}, σ_{-M}, and σ_I of the constant σ, then $\tilde{\nu}$ can be expressed by equation *(1)*, where $a > b \approx c$.

$$\tilde{\nu} = a\sigma_{+M} + b\sigma_{-M} + c\sigma_I + d \qquad (1)$$

For $\sigma < 0$ we have $\sigma_{-M} = 0$, and except for alkyl groups, $|\sigma_{+M}|$ is usually greater than $|\sigma_{-I}|$, *i.e.* $|a\sigma_{+M}| \gg |c\sigma_{-I}|$. σ_{-I} has a similar magnitude for common +M/–I groups, and can therefore be broken down into a constant component and a smaller, variable component ($\sigma_{-I} = \sigma_I^\circ + \Delta\sigma_I$); σ_I° is defined as the average of all σ_{-I} values, so that the sign of $\Delta\sigma_I$ changes. Eq. *(1)* then takes the form

$$\tilde{\nu} = a\sigma_{+M} + c\Delta\sigma_I + c\sigma_I^\circ + d$$

$c\sigma_I^\circ$ may be included in the constant *d*, and $c\Delta\sigma_I$ is negligible in relation to the much larger $a\sigma_{+M}$. Thus for $\sigma < 0$, a straight line of slope *a* is to be expected, except in the case of alkyl groups. The conditions for $\sigma > 0$ ($\sigma_{+M} = 0$, $b \approx c$, $\sigma_{-M} + \sigma_I = \sigma$) give, as an approximation, the equation $\tilde{\nu} = b\sigma + d$, *i.e.* a straight line having slope *b*. For the halogens, $\sigma_{+M} < \sigma_{-I}$, and consequently $a\sigma_{+M} \approx c\sigma_{-I}$, so that $\tilde{\nu}$ should be particularly low. The derivation therefore requires a steep straight line in the region $\sigma < 0$ and a shallower straight line for $\sigma > 0$, the two lines intersecting at about $\sigma = 0$; the points for the halogens lie appreciably below the lines, and those of alkyl groups slightly below. This picture is substantially in agreement with experimental findings (with individual values of *a* and *b* for each class of substances). The same is true of NMR signals.

[*] Priv.-Doz. Dr. G. P. Schiemenz
Institut für Organische Chemie der Universität
Olshausenstr. 40–60
23 Kiel (Germany)

[1] See, for example, *H. H. Jaffé,* Chem. Reviews *53,* 191 (1953); *C. N. R. Rao* and *R. Venkataraghavan,* Canad. J. Chem. *39,* 1757 (1961) (IR spectra); *R. E. Klinck* and *J. B. Stothers,* Canad. J. Chem. *40,* 1071 (1962) (NMR spectra).

[2] *M. S. C. Flett,* Trans. Faraday Soc. *44,* 767 (1948).

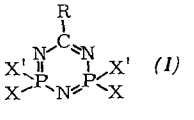
[3] *G.P. Schiemenz,* Lectures at Clausthal (Germany) on June 12, 1965, at Mülheim/Ruhr (Germany) on April 30, 1966, and at Halle/Saale (Germany) on Nov. 25, 1966.

[4] *O. Exner* and *K. Boček,* Tetrahedron Letters *1967,* 1433.

Substituted Diphospha-1,3,5-triazines

By *A. Schmidpeter, J. Ebeling,* and *N. Schindler* [*]

p-Alkyl- and aryl-substituted diphospha-1,3,5-triazines *(1)* are obtained by cyclocondensation of imidodiphosphinic trichlorides with amidinium chlorides [1] or by transamination of diphenylamidines with aminodiphosphazenes [2]; tetrachloro-substituted diphosphatriazines are best obtained by fusion or sintering of bis(trichlorophosphorus)nitride hexachlorantimonates *(2)* with an excess of amidinium chloride.



(1)

(a) X = X′ = Cl; R = alkyl, aryl
(b) X = X′ = OR′; R = alkyl, aryl
(c) X = R = C_6H_5; X′ = Cl

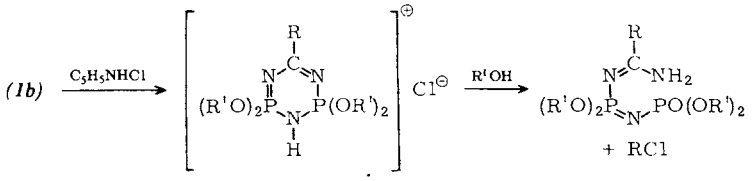
$$[N(PCl_3)_2]SbCl_6 + 2\ [RC(NH_2)_2]Cl \rightarrow 4\ HCl + [RC(NH_2)_2]SbCl_6 + \textit{(1a)}$$

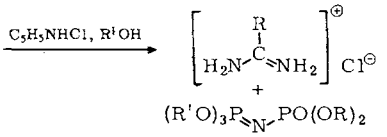
(2)

The ring skeleton *(1)* is stable to nucleophilic attack; the chlorine atoms on the phosphorus can be replaced with amino, alkoxy, or aryloxy groups by treatment with amines or alkoxides. Alcoholysis of the ring may occur during substitution with alcohol/pyridine. The first step is a proton transfer from pyridinium chloride.

The various substituted derivatives of *(1)* all appear to be protonated in position 3; in any case, the ^1H- and ^{31}P–NMR spectra show that the diphospha-1,3,5-triazinium ions are symmetrical. The kinetically controlled methylation, on the other hand, regularly takes place in position 1.

(1c) is formed as a mixture of the *cis*- and *trans*-forms on cyclocondensation. On nucleophilic substitution, the isomer ratio generally remains the same, within the limits that can be recognized by NMR spectroscopy. The substitution therefore takes place by a uniform mechanism.





The shielding of the phosphorus, which decreases in the order $R = H > CH_3 > C_6H_5CH_2 > C_6H_5 > N(CH_3)_2 > NH_2$, evidently is determined mainly by an anisotropy term due to the ring system.

[*] Dr. A. Schmidpeter, Dipl.-Chem. J. Ebeling, and Dipl.-Chem. N. Schindler
Institut für Anorganische Chemie der Universität
Meiserstr. 1
8 München 2 (Germany)

[1] *A. Schmidpeter* and *J. Ebeling*, Angew. Chem. *79*, 100 (1967); Angew. Chem. internat. Edit. *6*, 87 (1967).

[2] *A. Schmidpeter* and *J. Ebeling*, Angew. Chem. *79*, 534 (1967); Angew. Chem. internat. Edit. *6*, 565 (1967).

Adenosyl-B_{12}: Enzymatic Synthesis and Function

By *R. R. Schmidt*[*]

The results of recent investigations of the enzymatic synthesis of adenosyl-B_{12}[**] from vitamin B_{12} or hydroxocobalamin (B_{12a}) indicate the intermediate formation of the extremely nucleophilic hydridocobalamin (B_{12s}). This is then adenosylated by ATP in a second step to form adenosyl-B_{12}. Model investigations, which were closely based on the enzymatic findings, were carried out to study the mechanism of the enzymatic reduction of vitamin B_{12} or B_{12a} to B_{12s}. The main object of the investigations was to establish whether the reduction of B_{12a} (oxidation state of Co = +3) to B_{12s} (oxidation state of Co +1) proceeds as a one-step reaction with simultaneous transfer of two electrons by the reducing agent, or as a two step reaction in which only one electron is transferred in each step. In the latter case, reduced cobalamin (B_{12r}, oxidation state of Co = +2) would occur as an intermediate. The reduction was carried out *inter alia* with thiols, which act as reducing agents in enzymatic systems[1]. We found that the reduction proceeds as a one-step reaction. Thus the reduction of B_{12a} to B_{12s} with thioredoxin[2] and other biochemical reducing systems[3] does not occur in nature.

The function of adenosyl-B_{12} in enzymatic synthesis is still uncertain. Investigations on modified cobalamins should provide clues for the mechanistic interpretation of coenzyme B_{12}-catalysed reactions. Since the Co–C bond joining the adenosyl residue to the Co, and the 5′-hydrogen atoms of the adenosyl residue, play a central role in the mechanistic interpretation, 5′-modified adenosine derivatives were synthesized in order to convert them into suitably modified adenosyl-B_{12} and to examine their enzymatic behavior.

[*] Dr. R. R. Schmidt
Institut für Organische Chemie der Universität
Azenbergstr. 14/16
7 Stuttgart 1 (Germany)

[**] α-(5,6-Dimethylbenzimidazolyl)deoxyadenosylcobamide.

[1] *G. A. Walker, S. Murphy, R. R. Schmidt,* and *F. M. Huenneckens*, Federat. Proc. *26*, 343 (1967).

[2] *H. Weissbach, N. Brot,* and *W. Lovenberg*, J. biol. Chemistry *241*, 317 (1966).

[3] *E. Vitols, G. A. Walker,* and *F. M. Huenneckens*, Biochem. biophysic. Res. Commun. *15*, 372 (1964).

Ternary Alkali Metal and Alkaline Earth Fluorides of Neptunium, Plutonium, and Americium

By *H. Schmutz, M. Salzer,* and *C. Keller*[*]

Ternary fluorides of the trivalent and tetravalent actinides neptunium, plutonium, and americium having various compositions and structures were prepared by solid-phase reactions and precipitation reactions. The starting materials were the binary fluorides, carbonates, or oxides. The reactions were carried out at 350 to 1000 °C in a current of HF/N_2, to which H_2 or O_2 was added in some cases in order to obtain compounds of trivalent or tetravalent actinides, respectively.

As expected, the compounds such as $NaAmF_4$, $KAmF_4$, KAm_2F_7, and the corresponding plutonium compounds found in the systems $MF–MF_3$ (M^I = Na, K; M^{III} = Pu, Am) were found to be isostructural with the ternary fluorides of the lighter rare earth metals with the same formula. Attempts to prepare the analogous Np(III) compounds were unsuccessful, since oxidation of Np(III) to Np(IV) could not be prevented. The Np(IV) double fluorides $LiNpF_5$, Na_2NpF_6, $M_7Np_6F_{31}$, (M^I = Na, K, Rb) and the analogous Pu(IV) compounds were obtained in the pure state by direct synthesis. These compounds are isostructural with the similar ternary fluorides of thorium and uranium. The molar volume of the compounds prepared increases with increasing atomic number of the actinide.

The double fluorides of the type $M^{II}M^{IV}F_6$ (M^{II} = Ca, Sr, Ba, Pb and M^{IV} = Np; or M^{II} = Ca, Sr and M^{IV} = Pu) crystallize in the hexagonal LaF_3 lattice with random distribution of M^{II} and M^{IV}. Investigations on the systems $SrF_2–SrM^{IV}F_6$ (M^{IV} = Np, Pu) at 950 °C showed that 26 to 27 mole-% of SrF_2 dissolve in $SrM^{IV}F_6$, with formation of anion defects in the lattice. The solubility of SrF_2 in $SrM^{IV}F_6$ is practically independent of the M(IV) cation. Precipitations from aqueous solutions always yielded the stoichiometric compounds.

[*] Dr. H. Schmutz, Dr. M. Salzer, and Priv.-Doz. Dr. C. Keller
Lehrstuhl für Radiochemie, Universität Karlsruhe und
Institut für Radiochemie, Gesellschaft für Kernforschung, Kernforschungszentrum
75 Karlsruhe (Germany)

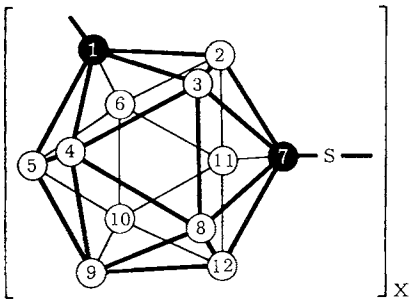
Carboranebis(sulfenyl chlorides) in Polymerization Reactions[**]

By *N. S. Semenuk, S. Papetti,* and *H. A. Schroeder*[*]

We attempted to use carboranes having a $B_{10}C_2$ skeleton (icosahedral) as structural units for thermally stable plastics. For example, polymers in which *m*-carborane units are linked by single carbon or phosphorus atoms were prepared.

Carborane polymers with sulfur bridges, which are derived from *m*-$B_{10}H_{10}C_2(SCl)_2$, have now been obtained for the first time. The bis(sulfenyl chloride) is readily obtainable by chlorination of *m*-$B_{10}H_{10}C_2(SH)_2$, and can be used for the preparation of several polymer systems, since the chlorine atoms can be readily replaced in nucleophilic reactions. It can be converted into polysulfides $(-CB_{10}H_{10}C–S–)_x$ *(1)* and polydisulfides $(-S–CB_{10}H_{10}C–S–)_x$ *e.g.* by reaction with the bifunctional *m*-$B_{10}H_{10}C_2Li_2$, or simply by heating in alcohol. Properties of the polysulfides: microcrystalline, $x \cong 30$, m.p. 219–222 °C. Properties of the polydisulfides: $x \cong 8$, m.p. 307–310 °C.

(1)



In addition to these polymers, the interesting bis(sulfonyl chloride) *m*-$B_{10}H_{10}C_2(SO_2Cl)_2$ was also prepared. Properties: colorless crystals, m.p. 62–63 °C.

[*] Dr. N. S. Semenuk, Dr. S. Papetti, and Dr. H. A. Schroeder
Olin Research Center, Chemicals Group
275 Winchester Avenue
New Haven, Conn. 06504 (U.S.A.)

[**] We are grateful to the Office of Naval Research for their financial support of this work.

The Reaction of Azides with Organometallic Compounds

By *H. Schumann* and *S. Ronecker*[*]

When refluxed in tetrahydrofuran, phenyl azide reacts with trimethylstannyllithium with liberation of nitrogen and formation of lithium *N*-phenyltrimethylstannylamide:

$$(CH_3)_3SnLi + C_6H_5N_3 \longrightarrow N_2 + (CH_3)_3Sn\text{-}N(C_6H_5)Li$$

Intermediate formation of a triazene can be ruled out on the basis of IR measurements.

In the reaction of phenyl azide with triphenylsilyl-, triphenylgermyl- triphenylstannyl-, and triphenylplumbyllithium, the reaction rate increases from the silicon to the lead derivative. The analogous reaction of trimethylstannane with phenyl azide leads to trimethylstannylphenylamine, which is stable at room temperature. Trimethylsilane and trimethylgermane react only at higher temperatures, and organometallically substituted amines containing NH functions cannot be isolated.

Hydrazoic acid and trimethylstannane react slowly at −78 °C to form trimethylstannylamine; however, owing to its extreme instability, this product can be detected only spectroscopically in solution, and attempts to isolate it yielded only tris(trimethylstannyl)amine.

Organometallic azides such as trimethylsilyl, trimethylgermyl, trimethylstannyl, or dibutylboron azide react only at high temperatures with organometallic lithium compounds or organometallic hydrides with replacement of the azide group. The lithium organometalamides isolated can be used as starting materials for the synthesis of organometalamides with mixed substituents.

[*] Doz. Dr. H. Schumann and Dipl.-Chem. S. Ronecker
Institut für Anorganische Chemie der Universität
Röntgenring 11
87 Würzburg (Germany)

The Search for New Neutron Emitters Among the Fission Products of Uranium-235

By *H.-D. Schüssler, W. Grimm,* and *G. Herrmann*[*]

The contributions of known and hitherto unknown neutron emitters to the groups exhibiting delayed neutron emission which are produced in the fission of uranium-235 by thermal neutrons were measured with the aid of a pneumatic tube conveyor installed in the Mainz reactor and automatically controlled separating apparatus. This permits transport times of 0.12 sec and separation times of 1 to 2 sec. The elements in question were isolated by ion or isotope exchange on preformed precipitates, *i.e.* iodine on silver iodide, iodine and bromine together on silver chloride, rubidium and cesium on ammonium molybdato- or thallium tungstatophosphate, and strontium and barium, accompanied by yttrium, zirconium, niobium, and the rare earths on barium sulfate, barium carbonate, and strontium carbonate; solvent extraction in bis-(2-ethylhexyl)orthophosphoric acid on polytrifluoromonochloroethylene powder was used for zirconium, niobium, and yttrium. Chemical yields and impurities were determined and corrected using long-lived radioisotopes. In this way nuclides having half-lives of less than a second, *e.g.* ^{140}I with $\tau_{1/2} = 0.8$ sec, can still be detected after pulsed irradiation.

Measurements for the fission of ^{235}U show contributions to the 22 sec group of 64.6 ± 2.2 % (± 2σ) for ^{137}I and 35.4 ± 2.3 % for ^{88}Br; the relative neutron intensities found are 1(^{137}I), 0.5(^{138}I), 0.8(^{139}I) and ≈ 0.5(^{140}I), and 0.4(^{87}Br), 1(^{88}Br), 1.7(^{89}Br) and 1.4(^{90}Br).

The components of the halogen nuclides are therefore: in the 6 sec group 33 % of ^{138}I and 67 % of ^{89}Br, in the 2 sec group 21 % of ^{139}I and 28 % of ^{90}Br, and in the 0.6 sec group ≈ 60 % of ^{140}I. Comparison of neutron-decay curves of the halogen fraction with analogous curves of unseparated samples shows that nonhalogens contribute < 5 % to the 22 sec group, 18 ± 5 % to the 6 sec group, and 50 ± 10 % to the 2 sec group. In the 6 sec group this contribution is due to ^{93}Rb, which is responsible for 22 ± 5 % of the neutron intensity of this group. The alkali metals (^{94}Rb, ^{142}Cs, ^{143}Cs) contribute 20 ± 6 % to the 2 sec group; there are also about 10 % each of the elements that are separated with alkaline earth precipitates and bis-(2-ethylhexyl)orthophosphoric acid, and (according to *del Marmol*[1]) of ^{85}As.

The percentages of the nuclides can be converted into absolute yields (neutrons per fission) with the aid of the known group yields. Comparison with estimated fission yields then gives the following neutron emission probabilities: 2.2 % (for ^{87}Br), 4.0 % (^{88}Br), 7.7 % (^{89}Br), 12 % (^{90}Br), 5.1 % (^{137}I), 2.8 % (^{138}I), 6.4 % (^{139}I), ~13 % (^{140}I), and 1.6 % (^{93}Rb).

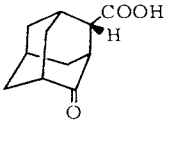
[*] Dipl.-Chem. H.-D. Schüssler, Dipl.-Chem. W. Grimm, and Prof. Dr. G. Herrmann
Institut für Anorganische Chemie und Kernchemie
der Universität
Johann-Joachim-Becher-Weg 24
65 Mainz (Germany)

[1] *P. del Marmol* and *M. Nève de Mévergnies*. J, inorg. nuclear Chem. *29*, 273 (1967).

Synthesis and Circular Dichroism of Optically Active Adamantane Derivatives

By *G. Snatzke, G. Eckhardt,* and *B. Ehrig*[*]

The dextrorotatory enantiomer of 4,8-dioxoadamantane-2-carboxylic acid was prepared with cinchonine, and the levorotatory enantiomer with cinchonidine. Partial reduction of one keto group with $NaBH_4$ followed by Clemmensen reduction and reoxidation leads to the 4-oxoadamantane-2-carboxylic acid *(1)* having an equatorial arrangement of the carboxyl group in relation to the ring containing the carbonyl group. Partial dithioketalization with ethanedithiol followed by Mozingo reduction yields the "axial" epimer of *(1)*. In all three acids, the carboxyl group could be replaced by Br or I in good yields by the Hunsdiecker method. Exchange of



(1)

bromine for chlorine took place with LiCl in DMF, for fluorine with AgF in chlorobenzene, and for azide with NaN_3 in DMF.

The carboxyl group of the "equatorial" keto acid was reduced to the primary alcohol after ketalization of the carbonyl group with glycol. The $-CH_2OH$ group could be converted, *via* the *p*-toluenesulfonate, into a methyl group by means of $LiAlH_4$.

The circular dichroism of "equatorial" β-methyladamantanone depends relatively strongly on the solvent, though the molecule is rigid. Thus the reduced rotatory strengths in cyclohexane, dioxane, and ethanol are 1.76, 2.23, and 2.52 biots, respectively; according to *Weigang*, this variation is due to the different refractive indices of the solvents. While the adamantanones with "equatorial" COOR or bromine follow the octant rule, the axial epimers exhibit "antioctant" behavior. This explains *e.g.* why 5,6β-dibromo-5α-cholestan-3-one gives a negative Cotton effect, contrary to the octant rule, a phenomenon that previously had to be attributed to a boat form of ring A.

The circular dichroism of the β-"equatorially" substituted halogenoadamantanones is unusually high, but this is because the dipole strength of the R band of these ketones is much greater than usual (*e.g.* $\varepsilon = 144$ for the bromine compound, $\varepsilon = 510$ for the iodine compound). The "axial" epimers, on the other hand, behave normally.

[*] Dr. G. Snatzke, Dipl.-Chem. G. Eckhardt, and Dipl.-Chem. B. Ehrig
Organisch-Chemisches Institut der Universität
Meckenheimer Allee 168
53 Bonn (Germany)

Photocatalysis by Semiconductors on Metal Supports. Photosensitized Oxidation of CO with Co_3O_4, NiO, and ZnO on Silver Supports [1]

By *F. Steinbach* [*]

In experiments carried out in the study of the mutual effects of metal and oxide in mixed catalysts, a photocatalytic reaction on a semiconducting layer in the immediate vicinity of a metal-semiconducting boundary layer is interpreted in terms of the internal photovoltaic effect.

An Ag layer (2000 Å) is vapor-deposited on quartz, and a semiconductor oxide suspended in acetone is painted on the silver (thinner than 1000 Å). The transparent double layer catalyst is irradiated from the Ag side with UV light; the reaction mixture has access to the oxide side. The kinetics and activation energy (kcal/mole) are determined. NiO: dark, $< 200\,^\circ C$ 40.0, $> 250\,^\circ C$ 21.0, light 10.0 NiO/Ag: dark, $< 280\,^\circ C$ 80.0, $> 300\,^\circ C$ 11.4, light 15.4. ZnO: dark, $> 400\,^\circ C$ 41.0, light 16.6. ZnO/Ag: dark, $> 370\,^\circ C$ 18.0, light 41.0. Co_3O_4: dark, $> 150\,^\circ C$ 18.8, light 8.8. Co_3O_4/Ag: dark, $> 150\,^\circ C$ 7.0, light 3.0. Ag: dark, $> 300\,^\circ C$ 14.6, light 6.25.

All the changes in activation energy due to the silver carrier and UV irradiation can be explained by changes in the distance between the Fermi level and the valence band ($E_V - E_F$) in the p-type semiconductor or the conduction band ($E_F - E_C$) in the n-type semiconductor. This distance is the principal parameter determining the activation energy. A common Fermi potential is assumed for the catalyst and the reaction mixture at thermal equilibrium. The catalysis consists in lowering of the energy threshold that has to be overcome in the electronic regrouping during the product formation. The conduction or valence band of the catalyst provides an energetically favorable transition level for the electrons of the substrate, the energy of which is characterized by the Fermi potential. Corresponding to the difference in the work function, electrons flow in the dark from the Ag into NiO and ZnO. The space charge layer in the oxide extends over the entire oxide layer, owing to its thinness. The activation energy on p-conducting NiO/Ag is increased, corresponding to an increase in ($E_V - E_F$), while that on n-conducting ZnO/Ag is decreased corresponding to a decrease in ($E_F - E_C$). Electron-hole pairs formed in light are separated by the electrostatic field at the Ag-oxide interface, leading to a flow of electrons back into the Ag. The bending of the bands becomes less, and the activation energy becomes smaller on the p-type oxide and greater on the n-type oxide. Co_3O_4 evidently has a smaller work function than Ag. Electrons flow into the Ag, even in the dark, with the result that the activation energy decreases. This tendency is intensified by the photoeffect.

The results for NiO with and without a support clearly show for the first time the proportionality between ($E_V - E_F$) and the activation energy. Dark reaction and conductivity measurement both give an Arrhenius diagram with four activation energies in four temperature ranges. In both cases the activation energies are in the ratio 4:2:0:1.

The catalytic photoeffects are reversible; light and dark measurements can be reproduced in any sequence. The advantage of this method of investigation is the possibility of a definite assignment of the observed catalytic action to the change in the electron distribution caused by photoexcitation.

[*] Dr. F. Steinbach
Physikalisch-Chemisches Institut der Universität
Sophienstr. 11
8 München 2 (Germany)

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Hydrogen Replacement by Recoil Tritium in Simple Aliphatic Compounds

By *G. Stöcklin* and *R. Cipollini* [*]

"Hot" tritium atoms were produced *in situ* by the $^3He(n,p)T$ or $^6Li(n,\alpha)T$ nuclear processes in simple aliphatic compounds of the type RX [R = CH_3, C_2H_5, C_3H_7; X = F, Cl, OH, NH_2, SH]. The reaction products were determined by radio-gas chromatography.

Comparative studies on binary CH_3X systems containing radical scavengers show a pronounced increase in the radiochemical yield of the H-substitution product CH_2TX with increasing C–X bond energy [C–SH < C–NH_2 < C–Cl < C–OH < C–F]. It is assumed that the primary substitution step by high-energy tritium atoms (eq. (1))

$$CH_3X + [T] \rightarrow [CH_2TX]^* + H \qquad (1)$$

is practically unaffected by chemical factors, but that the substitution product formed possesses a considerable excitation energy, and the resulting possibility of rupture of the weakest chemical bond (eq. (2b)) determines the yield.

$$[CH_2TX]^* \xrightarrow{a} \xrightarrow{+M} CH_2TX \qquad (2)$$
$$\xrightarrow{b} \cdot CH_2T + X\cdot$$

In the presence of iodine, the CH_2T radical can be scavenged as CH_2TI. The assumption of a highly excited primary substitution product, which either decomposes or is stabilized by collision, can be confirmed by pressure and phase effects; the yield of CH_2TX increases with increasing pressure and is greatest in the liquid phase.

As in the hydrocarbons, a distinct decrease in the H-substitution yield per C–H bond is observed in the series CH_3X, C_2H_5X, n-C_3H_7X. This can partly be explained by steric effects on the basis of 'the impact model' [1].

[*] Priv.-Doz. Dr. G. Stöcklin and Dr. R. Cipollini
Institut für Radiochemie der Kernforschungsanlage Jülich und Institut für Kernchemie der Universität Köln
Postfach 365
517 Jülich (Germany)

[1] For a review, see *R. Wolfgang* in *G. Porter*: Progress in Reaction Kinetics. Pergamon Press, London 1965, Vol. 3.

The Crystal Structure of Vanadium Chlorimide Trichloride Cl_3VNCl

By *J. Strähle* and *H. Bärnighausen*[*]

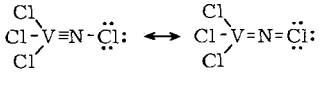
The triclinic unit cell of vanadium chlorimide trichloride[1] (a = 7.64, b = 7.14, c = 5.91 Å, α = 112.4°, β = 94.9°, γ = 107.8°) contains two molecules Cl_3VNCl in a centrosymmetric arrangement (space group $P\bar{1}$).

The structure was deduced from three-dimensional Patterson and Fourier syntheses and refined by the method of least squares. When the thermal anisotropy was taken into account, the reliability index R for the structure factors of the 1297 reflections evaluated was 6.5 %; when isotropic atomic vibrations were assumed (see table), R was 10.7 %.

Atomic coordinates and isotropic temperature parameters.

Atom	x	y	z	B(Å²)
V	0.1485	0.5020	0.2665	1.19
Cl(1)	0.4034	0.7585	0.5479	2.10
Cl(2)	0.0483	0.2917	0.4775	1.54
Cl(3)	0.1548	0.7204	0.0446	1.68
Cl(4)	0.3411	0.1970	−0.0947	2.80
N	0.2542	0.3515	0.0923	1.50

The Cl_3VNCl molecules have an approximately trigonal-pyramidal shape. A short distance (0.36 Å) above the base, which is formed by the atoms Cl(1), Cl(2), and Cl(3), is the V atom, followed by N and Cl(4). The VNCl grouping is almost linear (angle VNCl(4) = 175.2°), and is approximately perpendicular to the base. A careful analysis of the intramolecular atomic distances (V-Cl(1) = 2.204 ± 0.020, V-Cl(2) = 2.298 ± 0.008, V-Cl(3) = 2.383 ± 0.007, V-N = 1.642 ± 0.009, N-Cl(4) = 1.588 ± 0.009 Å) indicates that the bonding can be satisfactorily represented by the following resonance forms:



The distances V-Cl(2) and V-Cl(3) are greater than the distance V-Cl(1). This is connected with the fact that the atoms Cl(2) and Cl(3) act as "bridges" to vanadium atoms of adjacent molecules (intermolecular distances: Cl(2)....V′ = 2.600 ± 0.012, Cl(3)....V″ = 2.463 ± 0.020 Å). This gives a quasi-octahedral environment of Cl atoms for the V atoms. These "Cl octahedra" are joined by shared edges to form an infinite one-dimensional zigzag chain along [001].

[*] Dr. J. Strähle and Dr. H. Bärnighausen
Chemisches Laboratorium der Universität
Albertstr. 21
78 Freiburg/Br. (Germany)

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Protactinium-238, a New Nuclide, and its Role in the Formation of Heavy Transuranium Elements by Multiple Neutron Capture in Uranium-238

By *N. Trautmann*, *R. Denig*, and *G. Herrmann*[*]

In nuclear explosions, transuranium nuclides with mass numbers of up to 257 are formed by multiple neutron capture in $^{238}_{92}U$. The quantities decrease roughly exponentially with increasing mass number; nuclides with even mass numbers are formed preferentially. However, the odd mass numbers predominate among the heaviest nuclides. According to *Bell*[1] this could be explained by the formation of $^{238}_{91}Pa$, from which the heaviest nuclides are built up; the reaction $^{238}U(n,p)^{238}Pa$ would in this case have to proceed with an effective cross section of about 10 mbarn at a neutron energy of 14 MeV[1].

^{238}Pa is prepared by bombardment of natural uranium with 14 MeV neutrons. It is separated from the strongly predominating fission products by removal of the halogens by exchange on AgCl, the protactinium then being extracted from 9N HCl/0.1M oxalic acid in 2,6-dimethyl-4-heptanol and re-extracted with 12N HCl/0.5N HF.

The β- and γ-decay curves give a half life of 2.3 ± 0.1 min. The element assignment is confirmed by the X-ray spectrum, which shows the uranium lines at 13.6 (L_α), 17.0 (L_β), and 20.2 keV (L_γ) in a xenon proportional counting tube. β transitions with energies of 2.9 (about 20 %), 2.1 (40 %), and 1.4 MeV (40 %) are found with a plastic scintillator. More than 30 γ peaks are observed with a Ge(Li) semiconductor detector, the strongest peaks being at 103 (relative intensity 15), 448 (70), 548 (45), 583 (39), 635 (100), 679 (80), 686 (42), 805 (67), 863 (69), 884 (51), 1013 (80), 1059 (31), and 1082 keV (49). It follows from these results and from the γ-γ sum spectrum that levels up to about 2.0 MeV are filled in ^{238}U; bands based on octupole vibrations predominate. The effective cross section of the reaction $^{238}U(n,p)^{238}Pa$ with 14.6 MeV neutrons is found to be 1.3 ± 0.2 mbarn.

In order to evaluate these measurements, a number of isotopes formed in side reactions are studied, these isotopes being produced by $^{235}U(n,p)^{235}Pa$ and $^{236}U(n,p)^{236}Pa$ with 14 MeV neutrons and by $^{238}U(\gamma,p)^{237}Pa$ with 20 to 100 MeV γ rays. The half-life of 24.4 ± 0.5 min and the β energy of 1.41 ± 0.05 MeV are confirmed for ^{235}Pa[2]; a γ radiation with energies of 165 and 320 keV and 3 % intensity is also observed. The half-life of 9.0 ± 0.3 min and the β energy of 2.1 MeV found for ^{236}Pa differ from the values reported so far[3]; in addition, ^{236}Pa is found to emit γ rays of 642 and (weaker) 310 keV energy. No 39 min ^{237}Pa[4] is observed, but a nuclide having a half-life of 9.1 ± 0.2 min[5] is found, with β transitions at 2.3, 1.4, and 1.1 MeV and with its strongest γ rays at 529 (49), 540 (24), 688 (15), 852 (100), and 864 keV (41).

[*] Dipl.-Chem. N. Trautmann, Dipl.-Chem. R. Denig, and Prof. Dr. G. Herrmann
Institut für Anorganische Chemie und Kernchemie
der Universität
Johann-Joachim-Becher-Weg 24
65 Mainz (Germany)

[1] *G. J. Bell*, Physic. Rev. *139*, B 1207 (1965).
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[3] *G. Wolzak* and *H. Morinaga*, Radiochim. Acta *1*, 225 (1963).
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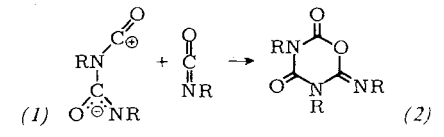
Cycloadditions of Isocyanates

By *H. Ulrich*[*]

The base-catalysed dimerization and trimerization of isocyanates, which lead to carbodiimides and isocyanurates, proceeds *via* the linear allophanate ion. The course of the reaction can be controlled by the use of sterically hindered catalysts.

The linear 1:1 adducts *(1)* of the aryl isocyanates are intermediates in the formation of the asymmetric trimers *(2)*, which have not yet been described. (Examples of *(2)*: R = C_6H_5, m.p. 222–224 °C; R = 2-CH_3–C_6H_4, m.p. 287–288 °C; and R = 4-Cl–C_6H_4, m.p. 308 °C.)

Dipolar intermediates of the type *(1)* were detected by IR spectroscopy and intercepted as 2:1 adducts with 6-membered rings in the reaction of arylsulfonyl isocyanates and carbodiimides, which leads to the formation of cyclic 1:1 adducts.



(1) *(2)*

This proves conclusively that the cycloaddition of arylsulfonyl isocyanates and carbodiimides is a stepwise process, and not synchronous.

[*] Dr. H. Ulrich
The Upjohn Company
North Haven, Conn. (U.S.A.)

Investigations on the Mechanism of the Degradation of Polycaprolactam by Thermal Oxidation

By *G. Valk* and *H. Krüssmann*[*]

We were able to show in an earlier publication[1] that the primary attack in the degradation of polycaprolactam by thermal oxidation, as in photooxidation[2], takes place on the *N*-vicinal methylene group. After hydrolysis of the degraded material, adipic acid can be isolated as the principal product. Preferential reaction at this point can be readily explained by the greater stability of the intermediate radical as a result of participation in the amide resonance. At the same time, the chain conformation of the polymer leads to interaction of the protons of the *N*-vicinal methylene group with the π-electron system of the carbonamide group, with a resulting increase in the reactivity of these hydrogen atoms[3]. In addition to adipic acid, the lower dicarboxylic acids and the monocarboxylic acids up to n-valeric acid (which is the main component of this fraction) are also formed.

However, other reaction paths also appear to exist. The caprolactam group must be attacked from the acid side as well as from the amine side, since it would otherwise be impossible to explain the formation of the homologous ω-amino acids up to ε-aminocaproic acid, which were detected as their *N*-trifluoroacetyl methyl esters. In contrast to the mono- and dicarboxylic acids, all the amino acids are formed in almost equal quantities, since none of the methylene groups is attacked in preference to the others. This agrees with the results obtained by *Pritzkow*[4], who reported a statistical attack on the methylene groups in the degradation of methyl caproate by thermal oxidation. The alkylamines resulting from decarboxylation of the amino acids could be identified. Once again, there was no preferential formation of any of the homologous amines.

Other degradation products formed are carbonyl compounds, including acetaldehyde and traces of propionaldehyde and butyraldehyde, as well as cyclopentanone, which probably results from the cyclization of the principal degradation product, adipic acid. The carbonyl compounds were detected gas-chromatographically as the 2,4-dinitrophenylhydrazones.

To summarize, it can be said that the degradation of polycaprolactam by thermal oxidation is much more complicated than the photo-oxidative degradation studied by *Sharkey* and *Mochel*[2].

[*] Priv.-Doz. Dr. G. Valk and Dipl.-Chem. H. Krüssmann
Textilforschungsanstalt
Frankenring 2
415 Krefeld (Germany)

[1] *G. Valk*, *H. Krüssmann*, and *P. Diehl*, Makromolekulare Chem., *107*, 158 (1967).

[2] *W. H. Sharkey* and *W. E. Mochel*, J. Amer. chem. Soc. *81*, 3000 (1959).

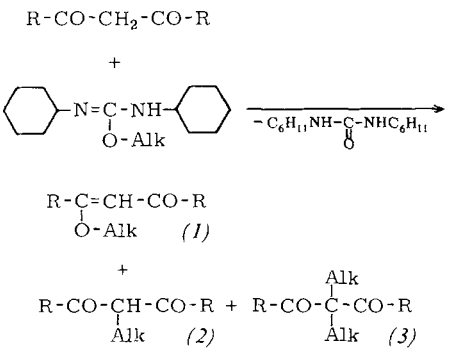
[3] *G. Heidemann* and *H. Zahn*, Makromolekulare Chem. *62*, 123 (1963).

[4] *W. Pritzkow* and *K. Dietzsch*, Chem. Ber. *93*, 1733 (1960).

Alkylations with *O*-Alkyl-*N,N'*-dicyclohexylisoureas

By *E. Vowinkel* and *H. Kruse*[*]

β-Diketones react with *O*-alkyl-*N,N'*-dicyclohexylisoureas to form keto enol ethers *(1)*, 2-alkyl-1,3-diketones *(2)*, and/or 2,2-dialkyl-1,3-diketones *(3)*.

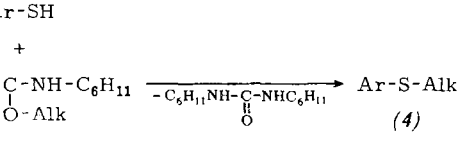


The ratio of *O*- to *C*-alkylation is determined, not only by the reactivity of the *O*-alkylisourea, but also by the acidity of the β-diketone used. *O*-Alkylation is favored by β-diketones having high acidities; the proportion of *C*-alkylation increases with decreasing acidity. Thus the reaction of dibenzoylmethane leads to the enol ether *(1)*, whereas acetylacetone gives both *O*- and *C*-alkylated products.

Since the acidity of the β-diketones is decreased by the introduction of an alkyl group on the central C atom, progressive alkylation favors *C*-alkylation with formation of *(3)*.

The *O*-alkyl products *(1)* do not rearrange into *C*-alkyl products *(2)* under the conditions of the reaction.

Thiophenols react with *O*-alkyl-*N,N'*-dicyclohexylisoureas to form aryl alkyl sulfides *(4)*.



Other functional groups do not affect the course of the reaction. Thus the formation of thioethers is not affected *e.g.* by unprotected amino groups, since it is faster than any transamidation of the isourea ether. There is no danger of competitive reactions even when free phenol and carboxyl groups are present; the alkylation of the thiol group predominates in every case because of its pronounced nucleophilicity. As is shown by the reaction with thiosalicylic acid, the thiol group is selectively alkylated when equimolar quantities of reactants are used.

The isourea ethers with primary and secondary alkyl groups all give very good yields with thiophenols. *O*-t-Butyl-*N,N'*-dicyclohexyl-isourea gives only a small quantity of thioether, together with appreciable quantities of isobutylene. In this case a t-butylcarbenium ion is first splitt off from the protonated isourea ether in an S_N1 reaction; this carbenium ion then either reacts with the thiophenolate anion to form the thioether or loses a proton to form isobutylene.

In some reactions, small quantities of diaryl disulfide and bis(arylthio)methane (which always occur together) are obtained as byproducts. These are formed in a combined oxidation-reduction reaction of the thiophenols with *S*-aryl-*N,N'*-dicyclohexylisothioureas, which are formed from the *O*-alkylisoureas by transetherification during the alkylation.

[*] Dr. E. Vowinkel and H. Kruse
Institut für Organische Chemie der Universität
Olshausenstr. 40–60
23 Kiel (Germany)

Kinetic Investigations of Substitution Reactions of Metal Carbonyl-Carbene Complexes

By *H. Werner*, *V. Kiener*, and *H. Rascher*[*]

Metal carbonyl-carbene complexes $M(CO)_5C(OCH_3)R$ (M = Cr, Mo, W; R = CH_3, C_6H_5) react with phosphines PR'_3 (R' = C_2H_5, n-C_4H_9, C_6H_{11}, *p*-$CH_3C_6H_4$) and phosphites

$P(OR'')_3$ ($R'' = C_2H_5$, C_6H_5) even under very mild conditions to form respectively the compounds $M(CO)_4(PR'_3)C(OCH_3)R$ and $M(CO)_4[P(OR'')_3]C(OCH_3)R$, which are very stable to oxidation and heat. Kinetic investigations based on IR spectroscopic and photometric measurements suggest that the rate-determining step in these substitutions is the initial elimination of a carbonyl group:

$$M(CO)_5C(OCH_3)R \rightarrow M(CO)_4C(OCH_3)R + CO$$

The activation energy is 28.2 ± 0.4 kcal/mole for M = Cr and R = CH_3, and 27.4 ± 0.6 kcal/mole for M = Cr and R = C_6H_5. These values are more than 10 kcal/mole lower than the activation energy for the elimination of a CO group from chromium hexacarbonyl.

The rate of formation of the compounds $Cr(CO)_4(PR'_3)C(OCH_3)CH_3$ ($R' = C_6H_{11}$, p-$CH_3C_6H_4$) does not vary considerably with the solvent. The first-order rate constants in di-n-butyl ether at 58.8 °C and in dioxane exceed those in saturated hydrocarbons (*e.g.* n-decane) only by about 15 and 30 %, respectively.

The reaction between the metal carbonyl-carbene complexes $M(CO)_5C(OCH_3)R$ and tertiary aliphatic phosphines PR'_3 is accompanied by the formation of the phosphine-metal carbonyls $PR'_3M(CO)_5$ [by the displacement of the carbene ligand from $M(CO)_5C(OCH_3)R$] and $(PR'_3)_2M(CO)_4$ [by the displacement of the carbene ligand from $M(CO)_4(PR'_3)C(OCH_3)R$] as by-products. These reactions most probably proceed *via* an S_N2 mechanism, with a direct attack by the phosphine on the formally divalent carbon atom of the carbene ligand. The fact that the $M-C(OCH_3)C_6H_5$ bond is cleaved much more easily than the $M-C(OCH_3)CH_3$ bond is in full agreement with concepts of the nature of this bond, developed by *E. O. Fischer et al.*[1].

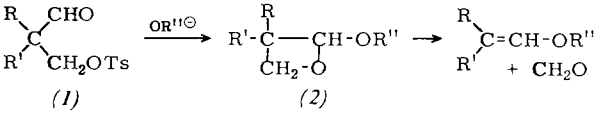
[*] Doz. Dr. H. Werner, Dipl.-Chem. V. Kiener, and H. Rascher
Anorganisch-Chemisches Laboratorium
der Technischen Hochschule
Arcisstr. 21
8 München 2 (Germany)

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Solvolysis Reactions of β-Tosyloxy Aldehydes

By *P. Weyerstahl*[*]

While the reaction between β-iodo- and β-trialkylammonium aldehydes and alkoxy ions $OR^{\ominus}$ leads to fragmentation, in the case of β-tosyloxy aldehydes *(1)* this reaction generally remains in the background (R = CH_3, C_2H_5, C_4H_9, R′ = CH_3, C_2H_5), for these compounds give instead cyclic acetals *(2)*, which may decompose into enol ethers and formaldehyde.



(1) *(2)*

When R″ is a primary alcohol residue, compound *(2)* is relatively stable and, under suitable conditions, represents the only product. When R″ is a secondary or a tertiary alcohol residue, the stability of *(2)* rapidly decreases and enol ether is formed in increasing amounts. Enol ethers are also formed when the stable acetal having a four-membered ring is boiled with traces of acids, or else as a result of surface catalysts. Secondary β-tosyloxy aldehydes undergo fragmentation (R = R′ = CH_3).

2-Methyl-2-formylcyclohexyl tosylate was prepared in two isomeric forms *(3)* and *(4)* in order to study the effect of steric factors on the reactions.

These structures were assigned on the basis of comparing them with four isomeric 4-t-butyl-2-methyl-2-formylcyclo-



(3) *(4)*

hexyl tosylates whose configurations were known; (these compounds were so prepared that their configuration was assignable in an unambiguous manner).

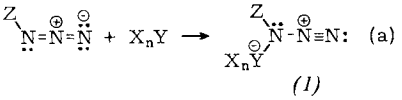
The solvolysis of *(3)* and *(4)* gave no four-membered acetal ring. The tosylate *(4)* gave the fragmentation product 1-methylcyclohexene in an almost quantitative yield; the tosylate *(3)* gave 26 % of 1-methylcyclohexene, 35 % of 2-methylcyclohexane carboxylic acid, 17 % of 3-methyl-3-formylcyclohexene, and 7 % of 2-hydroxymethylcyclohexanecarbaldehyde dialkylacetal.

[*] Dr. P. Weyerstahl
Lehrstuhl für Theoretische Organische Chemie
der Technischen Universität
Strasse des 17. Juni Nr. 115
1 Berlin 12 (Germany)

Structure and Reactivity of the *N*-Diazonium Group $\backslash\ddot{N}-N\equiv N:$

By *N. Wiberg*, *W.-Ch. Joo*, and *K. H. Schmid*[*]

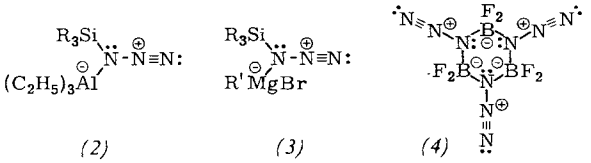
Compounds of the general formula *(1)*, containing an *N*-diazonium group are prepared by the addition of Lewis acids X_nY to azides ZN_3 (Reaction (a)):



(a)

(1)

For example, the Lewis acids $X_nY = (C_2H_5)_3Al$ and R′MgBr (R′, R = organic group) add to silyl azide $ZN_3 = R_3SiN_3$ [cf. *(2)*, *(3)*], and difluoroborazide, acting as a Lewis acid, can add to the azide group of a second molecule of difluoroborazide [$X_nY = F_2(N_3)B$, $ZN_3 = F_2BN_3$; cf. *(4)*].

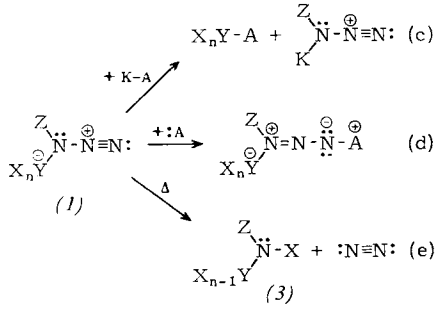


(2) *(3)* *(4)*

The preparation of *(4)* and other inorganic halogeno-element azides or organo-element azides with *N*-diazonium groups (*e.g.* $[Cl_4SbN_3]_2$, $[Cl_2Sn(N_3)_2]_n$, $[(CH_3)_2AlN_3]_3$) is carried out in the simple manner shown in Scheme (b):

$$Z-Hal + R_3Si-N_3 \rightarrow Z-N_3 + R_3Si-Hal \quad (b)$$

The chemical behavior of the *N*-diazonium group is characterized by three types of reaction: 1) Compounds K–A with a highly polar bond between K and A (*e.g.* $Na^{\oplus}N_3^{\ominus}$,



(c)

(d)

(e)

(1) *(3)*

$(CH_3)_3Si-Cl$) or bases:A (*e.g.* tetrahydrofuran) can split the bridging bond Y—N in *(1)* [cf. (*c*); *e.g.* reaction of $Cl_2Sn(N_3)_2$ with $(CH_3)_3SiCl$[1]); 2) Bases:A (*e.g.* $(C_6H_5)_3P$:) can add on to the terminal nitrogen in *(1)* [cf. (*d*); *e.g.* reaction of $(Cl_4SbN_3)_2$ with $(C_6H_5)_3P$[2]); and 3) Heating leads to the elimination of N_2 from *(1)* [cf. (*e*)].

Kinetic studies show that the thermal stability of *(3)* increases with decreasing Lewis acidity of R'MgBr, decreasing tendency to migration of the ligands R', and with increasing bulk of the R_3Si group.

[*] Priv.-Doz. Dr. N. Wiberg, Dr. W.-Ch. Joo, and Dr. K. H. Schmid
Institut für Anorganische Chemie der Universität
Meiserstr. 1
8 München 2 (Germany)

[1] *N. Wiberg* and *K. H. Schmid*, Chem. Ber. *100*, 748 (1966).
[2] *N. Wiberg* and *K. H. Schmid*, Angew. Chem. *79*, 938 (1967); Angew. Chem. internat. Edit. *6*, 953 (1967).

^{18}O-Isotope Exchange between TcO_4^- and ReO_4^- Ions and Water

By *A. Wiechen, W. Herr, B. Hess,* and *H. H. Pieper*[*]

The oxygen exchange

$$M^{18}O_4^- + H_2{}^{16}O \rightleftharpoons M^{16}O_4^- + H_2{}^{18}O$$

was investigated for the TcO_4^- and ReO_4^- ions as a function of the temperature, the H^+ activity, the concentration, and the added salt content. The effect of ionizing radiation on the exchange kinetics was of particular interest.

The oxo anions were labeled with $H_2{}^{18}O$ enriched by a factor of 8 to 10, and were precipitated at 0 °C as sparingly soluble $AgTcO_4$ and $AgReO_4$.

After the thermal decomposition of the silver salts at about 1000 °C, the O-isotope analysis was carried out mass spectrometrically by measuring the ratio $^{34}O_2/^{32}O_2$.

In the case of both oxo anions, the normal thermal oxygen exchange was found to be first order with repect to the MO_4^- concentration, and second order with respect to the H^+ activity. The reaction rate R in media with pH < 4 can be expressed as

$$R = k\,[H_2O]\,[MO_4^-]\,[H^+]^2$$

where $k = 1.2\times10^2$ l^3 mole^{-3} min^{-1} for $NaTcO_4$ and $k = 2.95\times10^3$ l^3 mole^{-3} min^{-1} for $NaReO_4$ (at 30 °C in both cases). The determination of the temperature-dependence of R in the range 10–75 °C gives activation energies of 8.4 and 8.20 kcal/mole for $NaTcO_4$ and $NaReO_4$, respectively.

The following reaction scheme may be assumed:

$$MO_4^- + 2\,H^+ \overset{\text{fast}}{\rightleftharpoons} H_2OMO_3^+$$

$$H_2OMO_3^+ + H_2O \overset{\text{slow}}{\rightleftharpoons} H_2OMO_3^+ + H_2O$$

The O-exchange of ReO_4^- ions induced by ^{60}Co-γ-radiation is accelerated by a factor of 10^2 to 10^3, according to the experimental conditions. The observation that electron-acceptors and hydrogen-radical acceptors (*e.g.* O_2 and acetone) act as inhibitors, while hydroxyl ion acceptors (*e.g.* H_2 and methanol) act as accelerators provides evidence concerning the mechanism of the radiation-induced exchange. The appearance of lower oxidation states indicates the participation of reducing species.

The radiation-induced exchange may consequently proceed according to the scheme:

$$Re^{VII}O_4^- + e_{aq} \rightarrow Re^{VI}O_4^{2-}$$
$$Re^{VI}O_4^{2-} + H_2O \rightarrow Re^{VI}O_3 + 2\,OH^-$$
$$\text{or } Re^{VII}O_4^- + H \rightarrow Re^{IV}O_3 + OH^-.$$

The OH radicals may partly re-oxidize lower oxidation states:

$$Re^{VI}O_3 + OH \rightarrow Re^{VII}O_4^- + H^+.$$

[*] Dr. A. Wiechen and Prof. Dr. W. Herr
Institut für Kernchemie der Universität
Zülpicher Str. 47
5 Köln (Germany)
Dipl.-Phys. B. Hess and Dipl.-Phys. H. H. Pieper
Arbeitsgruppe „Institut für Radiochemie"
der Kernforschungsanlage Jülich
517 Jülich (Germany)

Apparatus for Measuring the Natural Optical Activity and the Faraday Effect in the UV and the Visible Regions

By *J. Winkler*[*]

The effects of magneto-optical activity have recently once more acquired interest, owing to the development of equipment that permits the measurement of the optical activity as a function of the wavelength. As in the case of natural optical activity, one must distinguish between magneto-optical rotation (MOR, Faraday effect) and magnetic circular dichroism (MCD, Cotton-Scherer effect). Both effects are proportional to the applied magnetic field intensity, the thickness of layer penetrated by the radiation, and – in the case of solutions – the concentration. The lines of force of the magnetic field must be parallel to the light beam, and therefore a hole must be drilled in a permanent magnet or an electromagnet with an iron core. The advantage of a solenoid is obvious and the development of superconducting magnets now places intense fields at our disposal.

The chief difficulty in MOR measurements is that the solution and the cell window have a considerably greater effect than the solute. A way of overcoming this difficulty lies in the use of two magnets with opposing lines of force and in the insertion of a cell with the solvent into one field and a second cell with the solution into the other field. The unwanted effects then cancel out, and the rotation of the solute can be directly recorded.

In the case of the Faraday effect, the measurement of circular dichroism is to be preferred to measuring the rotation even more than in the case of natural optical activity since the solvent and the cell window have no effect here.

The MOR is best measured with a spectropolarimeter whose cell volume is sufficiently large for housing a permanent double magnet or a suitable superconducting magnet. Adaption to fit a large electromagnet does not seem to be advantageous, because the accuracy and the sensitivity of the apparatus are generally greatly reduced on rearrangement of the setup. By contrast, the measurement of circular dichroism does not require high-precision mechanical construction, since, unlike in rotation, the measurement is carried out in an electro-optical manner. The sensitivity of an apparatus that we constructed from commercially available units was found to be 10^{-5} extinction units.

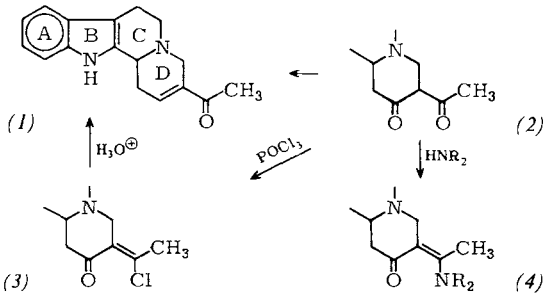
[*] Dr. J. Winkler
Arbeitsgemeinschaft für Strukturchemie
der Technischen Hochschule
Steinheilstr. 1
8 München 2 (Germany)

Investigations of Syntheses in the Indole Series

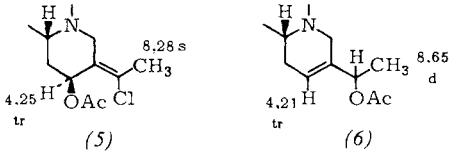
By *E. Winterfeldt* and *H. Radunz*[*]

The α,β-unsaturated ketone *(1)* seems to be a suitable starting material for the construction of ring E in heterocyclic indole alkaloids. After an improved method had been found

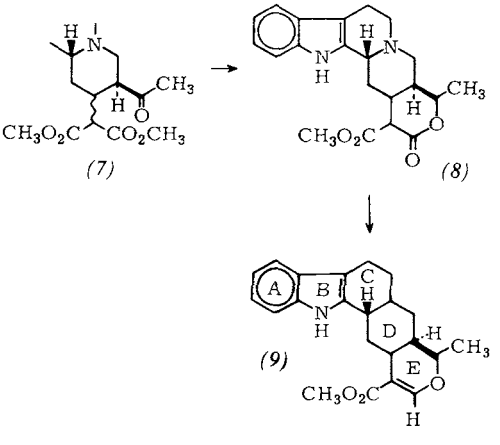
for the synthesis of the diketone *(2)*, it became possible to prepare *(1)* by selective reactions involving the β-dicarbonyl system of *(2)*.



Although the reactions of *(2)* with primary and secondary amines are selective, they lead exclusively to the enamine *(4)* which is of no use in this work. However, as the NMR data for enamines and their reduction products show, this selectivity may be utilized to prepare the chloride *(3)*. The structure of this compound is established by reduction and hydrolysis to the ketone *(1)*, as well as by reduction to alcohol, characterized as the acetate *(5)*. (The numbers in *(5)* and *(6)* refer to the NMR spectra).



The position of the functional groups in *(1)* has similarly been established by reduction and conversion into the acetate *(6)*. Furthermore, hydrogenation gives two epimeric saturated ketones. The Michael addition with malonic ester leads from *(1)* to the diester *(7)*, which can be converted into the lactone *(8)*.



[*] Priv.-Doz. Dr. E. Winterfeldt and H. Radunz
Organisch-Chemisches Institut der Technischen Universität
Strasse des 17. Juni Nr. 115
1 Berlin 12 (Germany)

Note added in proof: In the meantime, starting with stereochemically pure lactones, the borohydride reduction to the corresponding cyclosemiacetals and subsequent acid catalysed dehydration to yield structures of type *(9)* has been accomplished.

A Study of Primary Recoil Effects by Means of the Mössbauer Effect

By *J. Klöckner, P. Rother, F. Wagner,* and *Ursel Zahn*[*]

Products formed after nuclear transformations in a solid can be studied in favourable cases by Mössbauer effect measurements. The isomer shift and the quadrupole splitting of recoilless γ-lines yield information about the electron density and the electric field gradient at the nucleus. The emitted spectrum is therefore characteristic for the electron configuration of an atom after a nuclear transformation during the time of γ-emission. In contrast to radiochemical and mass spectrometric methods, Mössbauer spectroscopy allows an investigation of the electronic state of the atom 10^{-7} to 10^{-9} sec after the nuclear event without chemical analysis.

Using the method described we studied the formation of different valence states of iridium after the β^--decay of ^{193}Os in potassium hexachloroosmate(IV), K_2OsCl_6, at 4.2 °K. Well defined isomer shifts have been observed for the 73 keV transition in ^{193}Ir in Ir metal and various Ir(IV) and Ir(III) compounds. The shift of -2.4×10^{-7} eV of Ir^{3+} with respect to Ir^{4+} and the equally large shift between Ir^{4+} and Ir metal can be interpreted using a calibration scheme deduced from optical isotope shift data. The isomer shift between Ir^{3+} and Ir^{4+} with electron configurations $5d^6$ and $5d^5$ is attributed to the shielding effect of the sixth 5d electron. Isotope shift measurements on 5d elements show that the shielding effect of one 5d electron depends but little on the number of the other 5d electrons present. Using this calibration scheme one can predict the isomer shifts expected for valence states chemically less stable than Ir^{3+} and Ir^{4+}. The recoilless emission spectrum of a K_2OsCl_6 source yields a number of lines which can be attributed to different valence states of Ir atoms. Besides lines of Ir^{4+} and Ir^{3+} a strong line characteristic for Ir^{2+} was observed. Several weak lines may belong to higher valence states of Ir but cannot be assigned unequivocally. An attempt is made to interpret the high yield of Ir^{2+}, observed after the β^--decay during the lifetime of the Mössbauer level ($\tau = 5.8$ nsec) as a consequence of the secondary ionization processes following the change in nuclear charge.

K_2OsCl_6 sources synthesized from radioactive Os metal and sources prepared by direct neutron activation of K_2OsCl_6 yield similar Mössbauer spectra. Some additional weak lines in the emission spectrum of the directly neutron activated K_2OsCl_6 could be due to radiation damage.

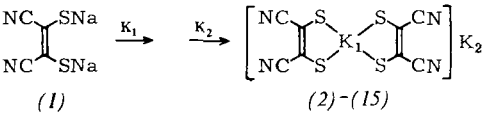
[*] J. Klöckner, P. Rother, Dr. F. Wagner, and Dr. Ursel Zahn
Physik-Department der Technischen Hochschule
Arcisstr. 21
8 München 2 (Germany)

Semiconducting Properties of Some Nitriles and their Polymers with a Porphyrazine Structure

By *G. Manecke* and *D. Wöhrle*[*]

Disodium 1,2-dicyanoethylene-1,2-dithiolate *(1)* reacts with metal ions (K_1) such as Cu^{2+}, Ni^{2+}, Co^{2+}, Fe^{2+}, and Fe^{3+} to form bis-(1,2-dicyano-ethylene-1,2-dithiolo)metal chelates. These complexes contain a second, ionically bonded, cation (K_2). Compounds *(4)–(10)*, *(12)*, and *(15)* have now been prepared for the first time. Adducts formed with the solvent may arise during synthesis and purification.

The d-c conductivities of the chelates (measured on tablets under 1500 kg/cm², between 20 and 120 °C) lie between

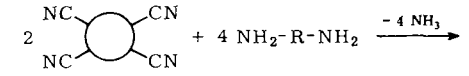


(1) *(2)–(15)*

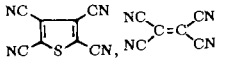
	K_1	K_2		K_1	K_2
(2)	Cu^{2+}	$[N(CH_3)_4]_2^+$	*(9)*	Cu^{2+}	Co^{2+}
(3)	Cu^{2+}	$[N(CH_3)_4]_2^+$	*(10)*	Co^{2+}	Cu^{2+}
(4)	Cu^{2+}	H_2^+	*(11)*	Ni^{2+}	$[N(CH_3)_4]_2^+$
(5)	Cu^{2+}	Ag_2^+	*(12)*	Ni^{2+}	Cu^{2+}
(6)	Cu^{2+}	$Ag^+[N(CH_3)_4]^+$	*(13)*	Fe^{2+}	$[N(CH_3)_4]_2^+$
(7)	Cu^{2+}	Cu^{2+}	*(14)*	Fe^{3+}	$[N(CH_3)_4]^+$
(8)	Cu^{2+}	Ni^{2+}	*(15)*	Fe^{3+}	H^+

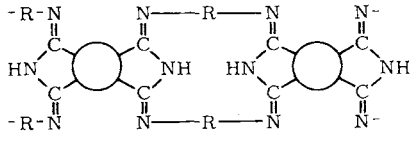
5.6×10^{-2} and 1.8×10^{-14} ohm^{-1} cm^{-1}. The thermal activation energies, calculated from $\sigma = \sigma_0 \exp(-E/2kT)$ extend down to 0.05 eV.

Polymers with a tetraazadiarylenediisoindolenine type structure *(16)* were prepared by reacting *(2)*, *(4)*, *(5)*, *(7)*, *(8)*, *(11)–(14)*, tetracyanothiophene, and tetracyanoethylene with 2,6-diaminopyridine, and by reacting tetracyanothiophene and tetracyanoethylene with *p*-phenylenediamine at elevated temperatures, with the liberation of NH_3. The structure of the black, insoluble polymers was determined by elemental analysis and IR spectroscopy. The conductivities of the polymers vary between 2.3×10^{-4} and 7.2×10^{-14} ohm^{-1} cm^{-1}. Autocondensation of 2,5-diaminodicyanothiophene, with and without $CuCl_2$, leads to black polymers having conductivities between 7.1×10^{-3} and 7.1×10^{-8} ohm^{-1} cm^{-1}.

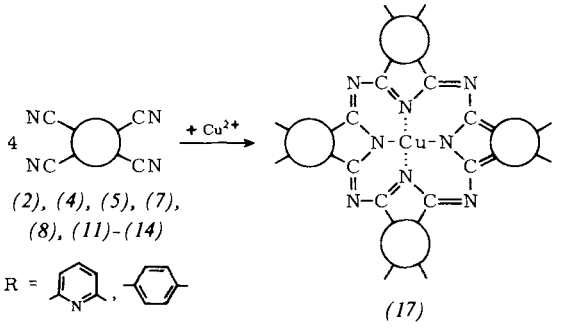


(2), (4), (5), (7), (8), (11)-(14)





(16)



(2), (4), (5), (7), (8), (11)-(14)

(17)

Polymers with a phthalocyanine type structure *(17)* have been obtained by reacting *(2)*, *(4)*, *(5)*, *(7)*, *(8)*, and *(11)* to *(14)* with acetylacetonatocopper at elevated temperatures. The resulting polymers are black and insoluble; their conductivities vary between 3.2×10^{-3} and 3.2×10^{-8} ohm^{-1} cm^{-1}.

[*] Prof. Dr. G. Manecke and Dipl.-Chem. D. Wöhrle
Fritz-Haber-Institut der Max-Planck-Gesellschaft
Faradayweg 4–6
1 Berlin 33 (Germany)

Comparative Determination of the Structure of Gaseous Molecules by Electron Diffraction and Microwave Spectroscopy

By *W. Zeil*[*]

Difficulties of a theoretical nature arise when we attempt to increase the accuracy of the determination of distances in gaseous free molecules by microwave spectroscopy and electron diffraction beyond 0.01 Å. These difficulties are due to the fact that the molecules are never rigid bodies. Even when the molecules are in the vibrational ground state, the calculated distances are unsharp because of zero-point vibration. Furthermore, the electron diffraction method averages over r the atomic coordinates which vary in time because of the vibrations, whereas the microwave spectroscopic method averages over $1/r^2$ both in the vibrational ground state and in the excited vibrational states.

These relationships are still manageable with diatomic and triatomic molecules, but virtually no comparative data obtained with these two methods have yet been published for larger molecules. – And it is precisely for these larger molecules that, in general, neither method alone can guarantee a complete determination of the structure.

The present aim was to combine the two methods for the determination of the structure of larger molecules, so as to obtain maximum information. Another aim was to establish the extent, in the combined method, of uncertainties pertaining to the structure and caused by the physical phenomena mentioned above. Investigations by this combined method on the molecules $(CH_3)_3CCl$, $(CH_3)_3SiCl$, $(CH_3)_3C-C\equiv C-Cl$, $(CH_3)_3Si-C\equiv C-Cl$, and COS have shown that the agreement between the two methods improves with the size and weight of the molecules.

[*] Prof. Dr. W. Zeil
Lehrstuhl für Physikalische Chemie der Universität Ulm
Present address:
Bau 35
Hertzstr. 16
75 Karlsruhe (Germany)

Further Investigations on the Isotope Fractionation of Alkali Metal Ions by Filtration through Biological Membranes

By *K. Wagener* and *U. Zimmermann*[*]

Highly active ion pumps operate in most animal and plant membranes, and they can effect an intensive demixing of components. Such stationary demixing states may be connected with isotope fractionation whose extent is a function of the type of the ion pump. This fact may be utilized to elucidate the transport mechanism.

Having previously found no enrichment of potassium isotopes in measurements with an accuracy of 0.1 %, we have now attempted to intensify any isotope bias that may be present. This was best done with the isotopes of a physiologically suitable rare element.

In measurements involving potassium in the marine algae *Valonia macrophysa* and *Chaetomorpha linum*, these algae were allowed to grow in sea water in which all or part of the potassium had been replaced by rubidium. After a stationary rubidium distribution between the medium and the cell fluid had been reached, we extracted the cell fluid and used it to prepare a new culture medium for a second series. After a stationary rubidium distribution between the medium and the cell fluid had been reached, we again isolated the cell fluid to prepare a third culture medium, *etc.* If there is an isotope separation at all, such a treatment will intensify it several fold. If the enrichment factor between Rb in the cell fluid and Rb in the medium is $(1 + \varepsilon)$ for each step, the enrichment factor between the cell fluid of the n-th step and the medium of the first step is $(1 + \varepsilon)^n$.

A shortcoming of this technique is that the rubidium is progressively diluted in each successive preparation of the culture medium (this must be compensated by the addition of potassium). This effect is fast, and after 5–10 steps the concentration of rubidium is down to the detection limit. After the medium has been modified, the new stationary state is reached in about six days, but we invariably allowed eight or nine days to elapse before extracting the cell fluid. In the first fifteen days, rubidium caused no changes in the cells.

The isotope enrichment factor for rubidium in the cell fluid was determined mass spectrometrically, and the following

values were obtained (figures in brackets refer to the number of measurements):

Step 1	2.612 ± 0.005	(2)
Step 2	2.610 ± 0.006	(4)
Step 3	2.610 ± 0.005	(5)
Step 4	2.611 ± 0.006	(3)
Step 5	2.612 ± 0.004	(4)

The corresponding value for the first step in the culture medium was 2.613 ± 0.005 (4). This fivefold potentiation indicates that the isotope effect between the cell fluid and the medium must be smaller than 0.05 %. The transport models for single-file diffusion and kinetics of complexes on carriers are, in their present form, not compatible with this result[1].

[VB 103 IE]

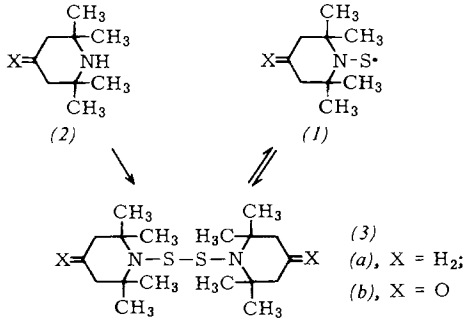
German version: Angew. Chem. *79*, 983 (1967)

[*] Priv.-Doz. Dr. K. Wagener and Dipl.-Chem. U. Zimmermann
Hahn-Meitner-Institut für Kernforschung
Glienicker Str. 100
1 Berlin 39 (Germany)

[1] *K. Wagner* and *U. Zimmermann*, Ber. Bunsenges. physik. Chem., in press.

SELECTED ABSTRACTS

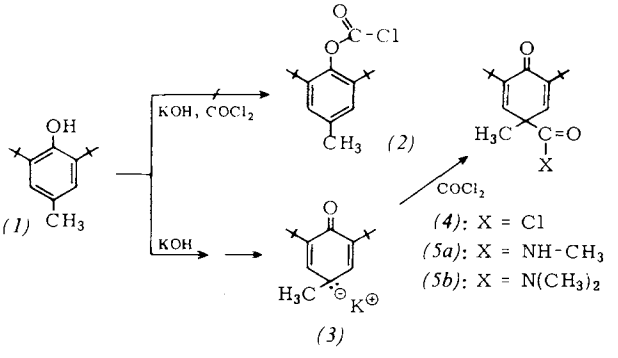
2,2,6,6-Tetramethylpiperidinothiyl *(1a)*, a new stable radical, has been synthesized by *J. E. Bennett*, *H. Sieper*, and *P. Tavs*. Reaction of the piperidines *(2a)* and *(2b)* with SCl_2 in DMF at −40 °C gave bis(2,2,6,6-tetramethylpiperidine) disulfide *(3a)* (66 %) or bis(2,2,6,6-tetramethyl-4-oxopiperidine) disulfide *(3b)* (81 %). When the disulfides were heated, alone or in solution, to 90–200 °C, an ESR spectrum with three lines was observed; this indicates homolysis of the S–S bond to give the 2,2,6,6-tetramethylpiperidinothiyl *(1a)* or 2,2,6,6-tetramethyl-4-oxopiperidinothiyl radicals *(1b)*.



/ Tetrahedron *23*, 1697 (1967) / −Ma. [Rd 702 IE]

A new dehydrogenation reaction with diethyl azodicarboxylate has been described by *F. Yoneda*, *K. Suzuki*, and *Y. Nitta*. The ester reacts selectively with primary or secondary alcohols to give aldehydes and ketones. The reaction is carried out in alcohol at room temperature in the dark over a period of 1 to 3 days. Alternatively, the starting materials may be refluxed in anhydrous benzene for 0.5 to 10 hours. The diethyl azodicarboxylate is hydrogenated to diethyl hydrazodicarboxylate. The yields are generally about 60–80 %. Thiols, *p*-anisidine, and hydrazobenzene are dehydrogenated to give disulfides, 4,4′-azodianisole, and azobenzene, respectively. The advantages of this dehydrogenation are the mild conditions used and the fact that after the dehydrogenation, there is no oxygen present to cause further oxidation. / J. org. Chemistry *32*, 727 (1967) / −WG. [Rd 712 IE]

The preparation of new oxocyclohexadienecarboxamides *(5)* is described by *H. A. Stansbury* and *R. F. Cantrell*. The reaction of 2,6-di-t-butyl-4-methylphenol *(1)* with KOH and phosgene leads, not to the chloroformate *(2)*, but by a novel reaction *via* the corresponding potassium phenoxide to a ketone *(3)*, which then reacts with phosgene to give 3,5-di-t-butyl-1-methyl-4-oxo-2,5-cyclohexadienecarbonyl chloride *(4)*.



(4) condenses with methylamine and with dimethylamine to give the crystalline amides *(5a)* (m.p. 98–99 °C) and *(5b)* (m.p. 84–86 °C) respectively, these amides being obtained in a very pure state. The yield of *(4)*, based on the quantity of phenol used, is 54 %. *(4)* can be quantitatively converted into *(5a)*. If *(4)* is not isolated, *(5b)* can be obtained in an overall yield of 84 %. / J. org. Chemistry *32*, 824 (1967) / −WG

[Rd 713 IE]

Alkali metal alkynides in dimethyl sulfoxide, can be obtained in almost quantitative yield from (methanesulfonyl)methyllithium or -sodium and the appropriate 1-alkynes, according to *J. Kříž*, *M. J. Beneš*, and *J. Peška*. Alkyl halides, dialkyl sulfates, aldehydes, ketones, and esters react directly with these solutions in accordance with equation (a) or (b) at 20 to 30 °C under argon (molar ratio ≈ 1.1 : 1; yield 70–90 %).

$$RC{\equiv}CM + R^1X \rightarrow RC{\equiv}CR^1 + MX \quad (a)$$

$$RC{\equiv}CM + R^2R^3CO \rightarrow RC{\equiv}C{-}CR^2R^3\,(OM) \quad (b)$$

M = Li, Na; R = H, CH_3, $CH_3(CH_2)_2$, C_6H_5
R^1X = $(CH_3)_2SO_4$, CH_3I, $CH_3(CH_2)_nBr$ (n = 2,3);
R^2R^3CO = CH_3CHO, CH_3COCH_3, $C_6H_5COCH_3$, cyclohexanone

The alkali metal alkynides generally react with 1-alkynes to give 1:1 adducts (also > 1:1 for R=H, CH_3), which are probably charge-transfer complexes of the alkynide anion and the 1-alkyne (λ_{max} = 480 to 350 nm). / Collect. czechoslov. chem. Commun. *32*, 398 (1967) / −Jg. [Rd 732 IE]

Cu^{II} exists in square-planar coordination in the well known Egyptian blue, $CaCuSi_4O_{10}$ (4 oxygen atoms arranged in a square around the Cu atom at a distance of 1.19 Å). *A. Ludi* and *R. Giovaloni* have studied the relationships between light absorption and coordination. In the ligand field of

symmetry D_{4h}, the ^2D term of the Cu^{II} splits into four terms, giving rise to three absorption bands. The broad band with $\lambda_{max} = 16000\ cm^{-1}$ can in fact be resolved into three bands: 12900 ($d_{xy} \rightarrow d_{x^2-y^2}$), 15900 ($d_{xz}$, $d_{yz} \rightarrow d_{x^2-y^2}$), and 18800 cm^{-1} ($d_{z^2} \rightarrow d_{x^2-y^2}$). Comparison with other complexes in which Cu^{II} is coordinated with oxygen shows:

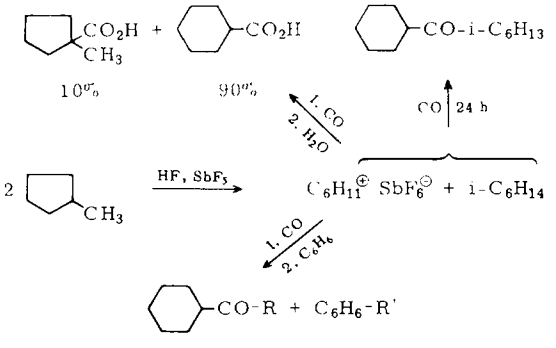
tetragonally distorted octahedron → square planar

$Cu_{0.1}Mg_{0.9}O$	$Cu(OH)_2$	$CaCuSi_4O_{10}$
$\lambda_{max} = 12$	$\lambda_{max} = 14.3$	$\lambda_{max} = 16 \times 10^3\ cm^{-1}$

violet shift

Naturwissenschaften *54*, 88 (1967) / –Jg. [Rd 733 IE]

The carbonylation of aliphatic hydrocarbons in liquid hydrogen fluoride proceeds simply and in very good yields by a process described by *R. Paatz* and *G. Weisgerber*, in which SbF_5 is added to the solution. At 0 to 20 °C and at 1 atm of CO, the solution takes up a quantity of CO equivalent to the SbF_5 within a few minutes. Carbenium hexafluoroantimonate is probably formed first in every case, with disproportionation in the case of cycloalkanes (*e.g.* cyclopentane, cyclohexane, methylcyclopentane, and methylcyclohexane; open-chain saturated hydrocarbons being formed in a quantity equivalent to the quantity of SbF_5) and with evolution of H_2 in the case of alkanes (*e.g.* isopentane). The final products are carboxylic acids, esters, or simple or mixed ketones, depending on whether the primary product is solvolysed with H_2O or alcohol or allowed to react with a hydrocarbon for a long time, *e.g.*



R = C_6H_5, c-C_6H_{11}, C_6H_4-c-C_6H_{11}; R' = c-C_6H_{11}, C_6H_5

/ Chem. Ber. *100*, 984 (1967) / –Jg. [Rd 751 IE]

Uncharged fragments of aromatic molecules produced by electron impact were detected by *H. Genzel* and *O. Osberghaus*. The vapor of the substance under investigation (benzene, toluene, fluorobenzene, iodobenzene, azobenzene, anisole, biphenyl) is introduced into a vacuum chamber (10^{-4} to 10^{-6} mm Hg) as a molecular beam, and the molecules are fragmented by an electron beam (200 eV, approx. 10 mA) entering at right angles to the molecular beam. Some of the fragments pass into the ion source (where there is a second electron beam, 50 eV) of a mass spectrometer. Grids at a suitable potential prevent ions or electrons from passing from the electron-impact chamber into the ion source. The first electron beam is rectangularly modulated at 32 Hz. This enables the primarily formed neutral fragments to be distinguished from the particles formed in the ion source from the gas molecules. The ionization potentials of the neutral fragments C_6H_5, C_6H_4, and C_6H_2 were found to be 9.35 ± 0.15 eV, 9.50 ± 0.15 eV, and 9.85 ± 0.15 eV respectively. / Z. Naturforsch. *22a*, 331 (1967) / –Hz. [Rd 710 IE]

Pyruvate:ferredoxin oxidoreductase has been concentrated to a purity of about 90 % by *K. Uyeda* and *J. C. Rabinowitz* from *Clostridium acidi urici*. The enzyme catalyses the reaction

$$\text{pyruvate} + \text{CoA} + \text{X} \rightleftharpoons \text{acetyl-CoA} + CO_2 + XH_2.$$

X is ferredoxin, which may be replaced by rubredoxin, FAD, FMN, and artificial electron acceptors such as benzylviologen. The enzyme also catalyses the CoA-dependent $^{14}CO_2$-pyruvate exchange and the formation of acetoin from pyruvate (in the absence of electron acceptors); it is probably a TPP-enzyme. When substrate quantities of enzyme are used in the presence of CoA, the reduction of an enzyme chromophore at 410 nm is observed, with formation of acetyl-CoA. The reduced chromophore can be reoxidized by ferredoxin or FAD. The reactions are assumed to proceed as follows:

1. Pyruvate + TPP-enzyme$_{ox}$ ⇌ hydroxyethyl-TPP-enzyme$_{ox}$ + CO_2

2. Hydroxyethyl-TPP-enzyme$_{ox}$ + CoA ⇌ TPP-enzyme$_{red}$ + Acetyl-CoA

3. TPP-enzyme$_{red}$ + X ⇌ TPP-enzyme$_{ox}$ + XH_2

/ Federat. Proc. *26*, 561 (1967) / –Hö. [Rd 714 IE]

An enzyme-substrate intermediate of D-amino-acid oxidase was stabilized by *L. Hellerman* and *D. S. Coffey* by reduction with $NaBH_4$. The enzyme catalyses the oxidation of D-amino acids with oxygen to give α-keto acids and ammonia, the cofactor being FAD. On aerobic incubation of D-amino-acid oxidase, FAD, [^{14}C]-D-alanine, and $NaBH_4$, the enzyme becomes radioactive. After total hydrolysis of the protein, it was found that radioactive ε-*N*-(1-carboxyethyl)-L-lysine had been formed. When radioactive FAD and unlabeled D-alanine are used, no radioactivity is incorporated into the protein. The results are interpreted by assuming that a primary oxidation product of D-alanine containing an imino function (in the hydrophobic zone that almost certainly exists around the FAD) is aminolysed by the ε-amino group of a lysine residue bound to the enzyme. Subsequent hydrolysis releases ammonia, the amino group of the lysine, and the reaction product, *i.e.* pyruvate. When $NaBH_4$ is added, a hydrolysis-resistant secondary amine is formed. Radioactive pyruvate is not bound to the enzyme under any conditions. / J. biol. Chemistry *242*, 582 (1967) / –Hö. [Rd 715 IE]

The primary structure of yeast phenylalanine-tRNA has been established by *U. L. RajBhandary et al.* (*H. G. Khorana*'s research group). The tRNA contains 76 nucleosides including 1 thymidine, 2 pseudouridine, 2 dihydrouridine, 2 methylcytidine, 1 2′-*O*-methylcytidine, 1 methyladenosine, 1 2-methylguanosine, 1 dimethylguanosine, 1 2′-*O*-methylguanosine (2′OMeG) and 1 7-methylguanosine. The last two were isolated from a tRNA for the first time. An unidentified base was also found. The most likely anticodon is 2′-OMeG–A–A. The sequence contains no A–A–A-trinucleotide. In attempts to find a secondary structure by the principle of the maximum number of base pairs, the resulting structure largely corresponds to those of the tRNA's elucidated so far (for alanine, serine, and tyrosine, all from yeast). The assumed anticodon is present in the same place in all these hypothetical secondary structures. / Proc. nat. Acad. Sci. USA, *57*, 751 (1967) / –Hö. [Rd 716 IE]

In the reaction of liquid barium/sodium solutions with nitrogen, *C. C. Addison, B. M. Davies, R. M. Lintonbon,* and *R. J. Pulham* found rules that are valid for metal melts in general (*e.g.* for Li/Na + N_2, Li/Hg + N_2, Pb/Na + C_2H_5Cl). If the binary melt has discontinuities in its liquidus curve or in its electric conductivity at any composition, the composition of the reaction product changes at these points of discontinuity. Thus on reaction until all the barium has been consumed, a Ba/Na melt gives Ba_3N (melts with $>$ 8.5 atoms-% of Ba), Ba_2N (melts with $>$ 3.5 atoms-% of Ba), and Ba_3N_2 (melts with $<$ 3.5 atoms-% of Ba). The chemical reactivity depends less on the electropositivity (which is approximately the same for Na and Ba) than on the structure of the short-range order zones. / Chem. Commun. *1967*, 211 / –Jg. [Rd 737 IE]

Mercury derivatives of decaborane containing Hg—B σ bonds have been synthesized for the first time by *N. N. Greenwood* and *N. F. Travers*. Whereas $HgCl_2$ and $HgBr_2$ are reduced by decaborane $B_{10}H_{14}$ in tetrahydrofuran, $HgCl_2$ metalates decaborane in ether:

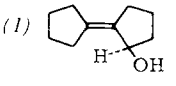
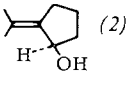
$$B_{10}H_{14} + n\,HgCl_2 \rightarrow B_{10}H_{14-n}(HgCl)_n + n\,HCl \quad (n = 7, 8)$$

CH_3HgX (X=Cl, Br, I) reacts with $B_{10}H_{13}Na$ in ether to give the mercury derivative $B_{10}H_{13}HgCH_3$ in yields of 50 to 80 %. The reaction of CH_3MgX with decaboranylmagnesium iodide (order of reaction rates: Cl > Br $\gg$ I) leads to the complexes $Mg[(B_{10}H_{12})_2Hg] \cdot 5\,MgX_2 \cdot n$ ether, *e. g.* $Mg[(B_{10}H_{12})_2Hg] \cdot 5\,MgCl_2 \cdot 11$ether, which dissolve in water without decomposing. The anion $[(B_{10}H_{12})_2Hg]^{2-}$ could be precipitated as the orange tetramethylammonium salt. The asymmetric M–B stretching vibrations due to the tetrahedral structures (MB_4) can be detected for the complexes $[(B_{10}H_{12})_2M]^{2-}$ in the long-wave IR region (Hg–B: 225; Cd–B: 235; Zn–B: 278 cm^{-1}). / Chem. Commun. *1967*, 216 / –Jg. [Rd 738 IE]

The stereoselective efficiency of hydrogenation catalysts has been studied by *T. J. Howard* and *B. Morley*. The hydrogenolysis of substituted benzyl alcohols on Raney nickel catalysts always leads to retention, and hydrogenolysis on Pd catalysts to inversion. This is explained by the difference in orientation of the OH groups, which are turned toward the surface of the catalyst in one case and away from the surface in the other. However, the hydrogenation (110 atm; 20 °C) of allyl alcohols such as *(1)* and *(2)* (see table) leads more or less

	Yield of *trans*-hydrogenation product (%) with:					
	Ni	Ni_2B	Ru/C	Pt	Rh/C	Pd/C
(1)	98	92	90	87	82	85
(2)	97	91	89	88	86	81

predominantly to *trans*-alcohols (identified as phenylurethanes). This suggests coordination of the OH group with the catalyst surface, *i.e.* interaction with the π-electrons of the double bond and the lone electrons the oxygen; partial inversion appears to occur only as a secondary process (the ability to isomerize generally increases in the order Ni<Ru<Pt<Rh<Pd).

(1)  *(2)* 

/ Chem. and Ind. *1967*, 73 / –Jg. [Rd 739 IE]

BOOK REVIEWS

Natürliche Proteinasen-Inhibitoren. (Natural Proteinase Inhibitors). By *Rosemarie Vogel, I. Trautschold,* and *E. Werle*. From the series "Biochemie und Klinik". Edited by *G. Weitzel* and *N. Zöllner*. Georg Thieme Verlag, Stuttgart 1966. 1st Edit., xii, 108 pages, 4 figures, 20 tables, DM 29.70.

The present monograph presents the first German-language review of the now extensive field of natural proteinase inhibitors. The subject matter is divided according to the source of the proteinase inhibitors: plant (from Leguminosae, potatoes, grains, beets); microbial; animal and human proteinase inhibitors (from ascarides, egg-white, milk, blood serum, urine, organs, particularly endocrine glands such as the pancreas). Each chapter is subdivided into sections on isolation, properties, composition, and inhibition spectrum. The monograph is rounded off by an introductory chapter on determination methods and definitions, a concluding chapter on therapeutic possibilities, and an extensive bibliography.

The size of the bibliography is impressive and so far unequalled (more than 900 entries). The animal proteinase inhibitors, particularly those of the ox, and the serum proteinase inhibitors are discussed in great detail, considerable space being devoted to the work of the authors. The difficult characterization and differentiation of the proteinase inhibitors has been very successfully accomplished, though many simplifications in the case of the cattle proteinase inhibitors that have become widely used in therapy (*e.g.* the ox-organ inhibitor) make the dividing lines rather unclear. Research in this field is advancing so rapidly that the monograph can be recommended to all who are interested.

W. Appel [NB 618 IE]

Kunststoff-Handbuch. Band VI: Polyamide. Aufbau, Verarbeitung, Eigenschaften und Anwendung. (Handbook of Plastics, Volume VI: Polyamides. Constitution, processing, properties, and applications.) Edited by *R. Vieweg* and *A. Müller*. Carl Hanser-Verlag, Munich 1966. 1st Edit., xvi, 698 pp., 477 illustrations, 111 tables, DM 140.–; advance order DM 126.–; subscription price DM 112.–.

The present volume[*] about the polyamides demonstrates how necessary it is to present this class of compounds in a comprehensive handbook to all concerned with the subject. The field "polyamides" has assumed such proportions that it is difficult to be aware of all the relevant facts. For this reason, the present volume, with a good index and appendix tables, proves an excellent reference work and is also suited for the study of special points. The excellent subdivision of the material facilitates the search for answers to specific problems which are not listed as such in the index.

Following an introduction, which mentions such topics as history, nomenclature, and production, the book goes on to deal with the formation of polyamides by polymerization and polycondensation, their physical structure and melting behavior, as well as the synthesis of and production processes for polyamides in general. The next chapter describes the processing of polyamides, and includes an account of injection molding, screw extrusion molding, and casting. An account is also given of the processing of solutions and dispersions as well as forming, welding, adhesion, *etc.* The behavior of polyamides toward moisture and water, chemical reagents, and toward mechanical, thermal, and electrical influences is dealt with in a section which provides a transition to the

chapter headed "applications". A separate section is devoted to the identification and analysis of polyamides.

The volume presents information on the manufacture, properties, processing, and applications of polyamides to manufacturers, engineers, and constructors as well as to chemists, physicists, and students of these subjects. The reviewer feels that the application to textiles does not really belong in this volume but should be dealt with in a volume on textiles. To summarize, the volume is no less than excellent and can be whole-heartedly recommended. *O. Horn* [NB 621a IE]

[*] Cf. Angew. Chem. *78*, 832 (1966); Angew. Chem. internat. Edit. *5*, 855 (1966).

Kunststoff-Handbuch. Band VII: Polyurethane. Herstellung, Eigenschaften, Verarbeitung und Anwendung. (Handbook of plastics, Volume VII: Polyurethanes. Production, properties, processing, and applications.) Edited by *R. Vieweg* and *A. Hoechtlen*. Carl Hanser-Verlag, Munich 1966. 1st Edit., xix, 767 pp., 419 illustrations, 137 tables, DM 180.00: subscription price DM 144.00.

Polyurethanes are being used in ever increasing amounts, primarily as elastomers and as foams. The great difference between polyurethanes and other plastics, which are delivered as finished polymers and only have to be worked, lies in the fact that the former are actually produced on the premises of the user by polyaddition. Since it is up to the user to obtain a product of the desired properties by varying the types and amounts of the components, the publication of the present book is of great importance.

The work opens with an account of the chemistry and development of polyurethanes by their inventor *O. Bayer*. This is followed by a large chapter headed "starting materials" in which the components (polyesters, polyethers, as well as polyisocyanates) are dealt with, as are the auxiliary agents (accelerators, retarders, propellents, stabilizers, softeners, fillers, *etc.*). The next chapter is concerned with process plant, process technology, and methods of finishing; it contains much useful information for manufacturers.

The following chapters are devoted to the manufacture, technology, applications, and testing of elastomers and hard foams and soft foams; the text is well supported by illustrations. The volume closes with an account of the use of polyurethanes as adhesives, for injection molding, and for the finishing of textiles. A glossary of trade names facilitates use of the book.

The publication of each new volume underlines the value of this series, which contains such excellently presented information written by outstanding experts in the fields of construction, architecture, and engineering as well as chemistry. Following the appearance of this excellent volume, one can look forward with keen interest to the publication of further volumes of the series. The volume under review is an eminently successful work and can be warmly recommended to all who are interested in this field. *O. Horn* [NB 621b IE]

Lehrbuch der organischen Chemie (Textbook of Organic Chemistry). By *H. Beyer*. S. Hirzel Verlag, Leipzig 1966. 11th/12th Edit., xviii, 813 pages, 102 figures, 12 tables, DM 24.–.

In the reviewers opinion this textbook, which is now in its 11th/12th edition, owes its popularity among students to two factors: the first is its low price, and the second is the fact that in spite of its size and content, the book is laid out and written in a simple and readily understandable manner.

However, the frequent oversimplification can lead students to false conclusions. For example, the student must regard carbenes and nitrenes as isolable substances that exist as such, and not as reaction intermediates that cannot be isolated. In the formulation of onium (ammonium, oxonium) salts, the repeated insertion of a positive charge outside the (unnecessary) brackets as well as on the N or O atom, so that two positive charges are shown with only one negative charge, is misleading. Several other points that would not be difficult to improve could be mentioned. On the other hand, since new editions of the book are published in rapid succession, the author has been able to keep step with the results of research, as is particularly clear in the present edition. Many sections have been updated or rewritten to take into account developments in preparative and theoretical chemistry as well as in industrial chemistry, the chemistry of natural products, and biochemistry. The references to literature reviews and monographs may also prove very useful to the advanced reader. It is to be expected that the book will continue to enjoy a large readership.

F. Micheel [NB 610 IE]

Glycoproteins. Their Composition, Structure, and Function. Edited by *A. Gottschalk*. BBA Library, Vol. 5. Elsevier Publishing Company, Amsterdam 1966. 1st Edit., xvi, 628 pages, numerous figures and tables, Dfl. 100.–.

Our knowledge about the chemistry and biochemistry of the sugar-protein complexes, which, 10 years ago, was based on a few experimental observations, has grown enormously in the past decade. Findings concerning the chemical structure and biological function of glycoproteins have led to the appearance of several thousand publications. This first attempt to present a detailed survey of the present research position is therefore very welcome. The editor, *A. Gottschalk*, did not write the review himself, but divided the field into 12 sections, each of which was dealt with in a self-contained article by an appropriate specialist, though a few sections consist of subchapters.

Gottschalk himself contributes five sections, three in collabortation with other authors. Six contributions come from *A. Neuberger*'s research group. Authors of other chapters are: *R. W. Jeanloz, R. A. Gibbons, J. E. Eastoe, M. D. Melamed, P. Jollès, E. R. B. Graham, E. M. Press* and *R. R. Porter, A. G. Bearn* and *W. C. Parker, M. Maxfield, M. Watkins, M. T. McQuillan* and *V. M. Trikojus, H. Papkoff, E. Buddecke* and *L. Warren*. Thus the present work is not a detailed monograph, but is more of a handbook in which the specialist can find a wealth of methodic details. It is to the editor's credit that this did not become a pure collection of experimental procedures. Instead, authors of great experience in the field of glycoproteins discuss the scope and capabilities of selected methods, and the resulting book is of much more value to the reader. Most of the authors have also attempted to describe the chemical and biochemical reaction courses on which the methods are based in the light of the latest knowledge.

Special emphasis is placed on physicochemical methods, to which *R. A. Gibbons* devotes an entire chapter in connection with the determination of the purity, uniformity, and molecular size of glycoproteins. In addition to a general inventory interspersed with questions of nomenclature, the discussion includes the analysis of the various components of this class of compounds and of the functional groups, including amino-acid analysis and the bonding of the sugars to one another and to the peptide chain. Much space is also devoted to the amino acids and neuraminic acids, the glycoproteins, and the heterosaccharides that can be isolated from these. The last group of topics forms the subject of a very clearly written chapter by *L. Warren*. The reader who is particularly interested in the chemistry of the glycoproteins will find an article by *A. Neuberger, R. D. Marshall*, and *A. Gottschalk* on the conformation of the sugar components of this class of substances and the acid- and alkali-induced rearrangements of these carbohydrates; this is the only self-contained discussion of this subject that has been published so far.

Occasional overlapping is found in the treatment of similar topics, as *e.g.* in the case of the serum glycoproteins, which play an important part in the field of sugar-protein compounds; however this is practically unavoidable in a book written by several authors. The presentation is excellent, and the book offers the first self-contained survey of the field in question for the research worker who is interested in the biochemistry of the glycoproteins, a particularly valuable feature being the detailed critical appraisal and description of the methods used in this field.

H. Faillard [NB 602 IE]

Developments in Inorganic Nitrogen Chemistry. Edited by *Ch. B. Colburn*, Elsevier, Amsterdam-London-New York 1966. 583 pp., 180 s.

As a result of its many-sided nature the chemistry of nitrogen has always interested chemists in general. Developments in this branch of chemistry have by no means been neglected during the past decades, even if the results have not been and are not as spectacular as in other fields. Colburn suggested a discussion of the developments in the inorganic chemistry of nitrogen, and has now succeeded in persuading internationally famous authors to contribute to the individual fields.

In this first volume, *M. Green* discusses the results of MO and VB calculations for simple nitrogen-containing molecules in a section entitled "Bonding in nitrogen compounds" (71 pages). It becomes clear what difficulties must still be overcome before adequate agreement between calculated and experimental results is obtained. This exceptionally interesting and clear chapter is followed by a discussion of the chemistry of "Inorganic azides" (78 pages) by *A. D. Yoffe*, with emphasis on physical and physicochemical aspects.The chemical properties, particularly of the covalent azides, are dealt with too briefly, organometallic azides being almost entirely ignored. Nevertheless, *Yoffe*'s contribution contains perhaps unusual, but extremely useful, material for the chemist. *M. Becke-Goehring* and *E. Fluck* discuss in detail the chemistry of inorganic compounds with S–N bonds (92 pages). It is precisely in this field that substantial progress has been made and new knowledge gained during the past two decades. The contribution by *W. P. Griffith* (66 pages) on "Nitrogen ligands", *i.e.* transition metal complexes, in which the nitrogen atom behaves as a donor is necessarily restricted to a small range of selected examples As illustrations, the author has chosen NH_3, N_2H_4, NH_2OH, amide and imide, cyanate, fulminate, thiocyanate, selenocyanate, cyanide, alkylnitrile and alkyl cyanide complexes, with nitrido, azido, azo, nitrate, nitrite, NO, and NS complexes. Twenty pages are devoted to the chemistry of complexes with amines and heterocyclic bases.

A detailed though not very clearly arranged discussion of phosphorus-nitrogen compounds by *M. L. Nielsen* occupies 165 pages (without touching on the cyclic phosphorus nitrides). This work must be at present the most complete survey of compounds containing P–N bonds. The description by *J. K. Ruff* of the nitrogen compounds of boron, aluminum, gallium, indium, and thallium (51 pages) does less than full justice to boron-nitrogen chemistry (22 pages), but shows how quickly our knowledge of nitrogen compounds becomes scanty as soon as we pass on to the heavier elements of this group. In conclusion, *G. W.A.Fowles* gives a clear, very instructive summary on "Inorganic reactions in liquid ammonia" (54 pages). A very meager subject index is matched by the absence of an author index.

The book can serve as a very useful source of information for all those wishing to obtain a survey of the subject. Both the type of discussion and the level of the individual articles vary, and yet the book as a whole is surprisingly coherent. The price needs some consideration, especially in view of the fact that the literature considered does not as a rule extend beyond 1962.

H. Nöth [NB 642 IE]

Advances in Magnetic Resonance. Vol. 1. Edited by *J. S. Waugh*. Academic Press. New York-London 1966. 1st Edit., xi, 413 pages, numerous figures and tables, $ 15.00.

The first successful observations of magnetic resonance phenomena date back about twenty years. Developments in this field since then have been so extensive that it is practically impossible for the individual to obtain a full general picture. The appearance at this stage of progress reports on magnetic resonance methods is therefore very welcome. This thought has obviously been shared by others, since a similar work is to be published soon by Pergamon Press.However, it is clear from the list of forthcoming publications that there is little fear of excessive overlap in the near future.

The field covered by "Advances in Magnetic Resonance" is to be very wide, and in addition to nuclear spin resonance, electron spin resonance, and nuclear quadrupole resonance, it will also include related topics such as molecular beams, optical pumping, and microwave spectroscopy.

Each volume will contain five to ten review articles. Besides original theoretical articles, they will contain reports on speculative views or on individual phenomena, as well as accurate tables.

Volume 1 contains an article by *A. G. Redfield* on the "Theory of Relaxation Processes", which is essentially a revised and further annotated version of his paper in IBM J. Res. Develop. *1*, 19 (1957). In a chapter on "Chemical Rate Processes and Magnetic Resonance", *C. S. Johnson jr.* reports on the concepts and methods of this field, which is particularly important to nuclear magnetic resonance. A welcome article is the review by *D. R. Eaton* and *W. D. Phillips* on "Nuclear Magnetic Resonance of Paramagnetic Molecules", which shows what conclusions concerning the geometric and electronic structure of paramagnetic molecules and metal complexes can be drawn from the isotropic hyperfine contact and pseudocontact interaction between magnetic atomic nuclei and unpaired electrons.

The next two chapters form a well matched pair. In "Theory of Nuclear Spin-Spin Coupling", *M. Barfield* and *D. M. Grant* point out the difficulties and dangers of approximations (mainly VB and MO methods) for the calculation of nuclear spin coupling constants. This is followed by a valuable 120-page tabulation by *A. A. Bothner-By* of all that is known with certainty about "Geminal and Vicinal Proton-Proton Coupling Constants in Organic Compounds", with many structural formulae. Only 10% of the measurements that have been reported were accepted as sufficiently accurate. A short introduction gives rules for the estimation of the magnitude and sign of the coupling constants. The book closes with a useful tabulation by *K. W. Bowers* on "Electron Spin Resonance of Radical Ions", covering literature up to mid-1964. The table gives the empirical formula of the ion, name and structure of the neutral molecule, hyperfine splitting constants, solvent, and references.

The volume contains an author and subject index. It can be recommended in every respect.

R. F. Zürcher [NB 601 IE]

Bioorganic Mechanisms. By *T. C. Bruice* and *S. Benkovic*. From the series "Frontiers in Chemistry". W. A. Benjamin, Inc., New York-Amsterdam 1966. 1st Edit., Vol. 1, viii, 372 pp., numerous figures, bound $ 22.50. Vol. 2: viii, 419 pp., numerous figures, bound $ 25.00.

The reaction mechanisms of enzyme-chemical processes form an area between theoretical organic chemistry and biological chemistry, for which the new term "bioorganic mechanisms" has been coined. This new creation might lead one to think that it is associated with self-willed sensationalism. However, a perusal of the present two volumes shows that this is not so. This term describes exactly what is meant, *i.e.* the field in which enzyme reactions and enzyme mechanisms can be interpreted with the aid of more or less complete

models or in which the driving force of the transformations of biochemically important compounds and the function of the cofactors can be explained by theoretical considerations without the boundaries between enzymatically and chemically catalysed processes becoming blurred.

On closer examination, this work becomes even more deserving of the reader's admiration and gratitude. It is an excellent introduction for the advanced reader as well as a mine of information for the specialist, who will find the many references useful in dealing with his problems. The book is obviously based on a course of lectures, and anyone who is planning lectures on biochemical reaction mechanisms will find this carefully and intelligently written book full of extremely valuable information. Most biochemists lack the training required to tackle, without some help, the reaction-kinetic problems that arise. Two thoroughly experienced organic chemists, who are themselves working in this intermediate field, have now made an effort to help in this respect. The introductory chapter presents a perfectly clear and simple treatment of the basic views on acid-base catalysis. This chapter also includes a discussion of the concepts of neighborhood catalysis and of steric and polar effects on the hydrolysis of esters. This is the authors' own particular field, but this does not mean that they are any less careful or less critical in other sections. The excellent appraisal from the standpoint of the experienced theorist (they are by no means reticent with their judgement which is always fair) is particularly stimulating. Much of the work in this field the laws of which are only just starting to be recognized, is very deductive, and this is even openly stated Excessively speculative mechanisms are briefly dismiesed with a reference to the literature.

Further, in the first part, hydrolyses of esters and amides, the only biochemically important acyl cleavages, are discussed on the basis of the general point of view deduced previously. This is followed by an examination of the catalytic processes in various hydrolysis and transfer systems. These are the reactions of the thioesters and of the phosphate esters in the widest sense, and the mode of action of the cofactors thiamine, nicotinamide, folic acid, and biotin. Model reactions that take place under extreme conditions not found in biological systems are not considered. However, model reactions that have no precise physiological analogues, but that can contribute to an understanding of biochemical processes, are occasionally discussed. Though these two volumes already contain enough material with which the reader must become thoroughly acquainted, one still looks forward to the proposed third volume, which is to contain the mechanisms of the B_{12} coenzymes, the flavins, and the ribonucleases.

The thorough and critically compiled bibliography covers a wide field, ranging from a short historical introduction to completely new works. The presentation of the books is excellent and the printing of the text and of the formulae is outstanding and free from errors. The only unwelcome feature is the high price of the work, which can otherwise be recommended to anyone who is studying, or who wishes to study, enzyme mechanisms.

L. Jaenicke [NB 587 IE]

Adhesion and Adhesives. By *R. S. R. Parker* and *P. Taylor*. Pergamon Press, Oxford-London-Edinburgh-New York-Toronto-Paris-Frankfurt 1966. 1st Edit., vi, 142 pages, numerous figures, 25 s.

A great deal is still unknown about the process of adhesion, despite much fundamental research which has been conducted in an effort to answer the many open questions.

The authors begin with a historical survey ranging from the earliest adhesive processes of the distant past to the modern processes used, *e.g.*, in light-construction techniques, and including the technical principles underlying these processes. They then turn to the process of adhesion itself, which they describe as an exchange of secondary valences (van der Waals forces) and define accordingly. Other views such as the diffusion theory are discussed, but the magnitude of the adhesive force is mainly determined by wetting. Further chapters deal with the joint surface and its preparation as well as with the production and testing of adhesives and adhesive joints. The chemical and physical properties of polymers are then discussed, and the sources and applications of the principal adhesives are described in detail. Further sections deal with specific adhesives, such as the isocyanates and the cyanacrylates, and with their chemistry.

The book closes with a discussion of the cementing of reinforced plastics and of adhesive systems of various compositions. Adhesion to metals is mentioned only briefly.

Nonetheless, the book as a whole gives an impression of completeness, and provides an insight into a many-sided technology with a solid scientific foundation.

A. Matting [NB 611 IE]

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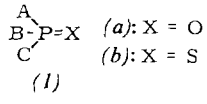
Nucleophilic Reactivity of the Thiophosphoryl Group

BY H. TEICHMANN AND G. HILGETAG [*]

The difference in the nucleophilic reactivities of the $\geq P{=}S$ and $\geq P{=}O$ groups can be satisfactorily explained on the basis of Pearson's acid-base concept [21]. The thiophosphoryl sulfur is a typical "soft base", and reacts preferentially with sub-group B metals, halogens, and sp^3 hybridized carbon, whereas it is largely inert to "hard acids" such as protons, carbonyl carbon, and tetrahedral phosphorus. Since a nucleophilic attack by the thiophosphoryl sulfur leads to a decrease in the charge density of the phosphorus atom, the latter (or the α-carbon atom in O-alkyl esters) becomes more open to nucleophilic attack. This reaction principle forms the basis of sulfur exchange, dealkylation, isomerization, and the Pistschimuka and Michalski reactions.

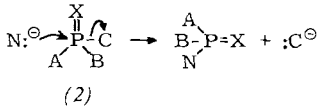
I. Introduction

Neutral phosphoryl and thiophosphoryl compounds *(1)* can react both as nucleophiles and as electrophiles. Apart from the reactivity of the substituents A, B, and



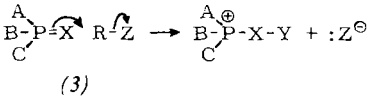
(1)

C (*e.g.* nucleophilic: PO-activated olefination [1]; electrophilic: dealkylation [2]), one can generally distinguish an electrophilic center at the phosphorus atom *(2)* and a nucleophilic center at the oxygen or sulfur atom *(3)*.



(2)

e.g. A,B = alkyl, alkoxy;
C = Cl; X = O,S; N = OH



(3)

e.g. A,B,C = alkyl; X = S;
RZ = CH_3I

Special attention has been paid in the past to the electrophilic center at the phosphorus atom, since this is the point of attack in such important reactions as hydrolysis [3] and phosphorylation [4]. The present article is confined to reactions in which the thiophosphoryl sulfur functions as a nucleophile. These are the reactions in which phosphoryl and thiophosphoryl compounds exhibit the greatest differences in behavior.

(1a) and *(1b)* differ:

1. in the electronegativities of oxygen (3.5) and of sulfur (2.5);

2. in the dissociation energy, which is 40–60 kcal/mole lower for the P=S bond (about 90 kcal/mole) than for the P=O bond (125–155 kcal/mole) [5];

3. in the extent of π bonding, which is lower for the P=S bond than for the P=O bond. This is shown by the force constants of the bonds [6], the difference in the shortening of the bond lengths [7], the difference between the dissociation

[*] Dr. H. Teichmann and Prof. Dr. G. Hilgetag
Institut für Organische Chemie
der Deutschen Akademie der Wissenschaften
An der Rudower Chaussee
DDR 1199 Berlin-Adlershof (Germany)

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energies of the single and double PX bonds [8], the difference in electronegativity between P and X [9], and the ^{31}P-NMR signals, which always occur at lower fields for *(1b)* than for *(1a)* [10, 11].

The P=O bond may be regarded as a semipolar bond on which is superimposed a p_π–d_π bond due to back-donation of p electrons from the oxygen atom to empty d orbitals of the phosphorus atom. Since the overlap of the p and d orbitals is greatest near the oxygen atom, the p_π–d_π bond of the P=O group is much more strongly polar than the p_π–p_π bonds usually encountered in carbon chemistry [12]. The p_π–d_π interaction, and hence the P=O bond order, increases with increasing electronegativity of the substituents A, B, and C; this is clearly shown by the position of the PO frequency, which shows a linear relationship to the sum of the electronegativities of the substituents A, B, and C [13, 14]. Calculations of the P=O bond order yield different values according to the methods used, but the results always show the same trend.

Table 1. Bond order N of the P=O bond as found (A) from the force constants [6], (B) by an MO calculation [15]. Σx = sum of the electronegativities of the substituents.

	F_3PO	Cl_3PO	Br_3PO	$(CH_3)_3PO$
Σx	12	9	8.4	6.0
N (A)	2.34	2.09	2.02	1.7
N (B)	2.98	2.19	1.96	1.0

A similar situation is to be expected for the P=S bond, the π-bond component in this case being smaller. The bonding again depends on the electronegativity of the substituents [14, 16, 17], but this dependence is less pronounced in the P=S frequency, owing to the mechanical coupling between the P=S and P(A,B,C) stretching vibrations [14, 17, 18]. The similarity of the P=O and P=S bonds is also evidenced by the fact that the frequency shifts on complex formation with acceptor molecules (cf. Section II) take place in the same direction.

Differences between *(1a)* and *(1b)* are also found:

4. in the availability of empty 3d orbitals of the thiophosphoryl sulfur, which may explain the greater stability of some thiophosphoryl complexes [19, 20].

The experimental data on the nucleophilic reactivities of phosphoryl oxygen and of thiophosphoryl sulfur can be largely explained by *Pearson*'s concept [21], according to which oxygen is a "hard base" and so reacts preferentially with "hard acids" (protons, A metals, carbonyl carbon, phosphoryl phosphorus), whereas sulfur is a "soft base" and reacts mainly with "soft acids" (B metals, tetrahedral carbon, halogens). This is illustrated by the following examples.

1. Phosphine oxides form stable salts with inorganic and organic acids [22], and can be titrated acidimetrically [23]. The only known salt of a phosphine sulfide is evidently a hydrobromide (an oil) [24]; attempted resolutions of chiralic phosphine oxides [25], but not of phosphine sulfides [26], by salt formation with optically active acids have been successful.

Similarly, the hydrogen bonding ability is strong in phosphoryl compounds but much weaker in thiophosphoryl compounds [27]; the resulting lower solubility in water and greater resistance to hydrolysis were deciding factors in the development of the thiophosphate insecticides [28].

2. Phosphoryl compounds are extremely useful for the extraction of many metal salts from aqueous solution [29], whereas the corresponding thiophosphoryl compounds have much poorer extraction properties [30]. The only ions that are extracted particularly well by thiophosphoryl compounds [32] are those of the B metals (mainly group I, II, and VIII transition elements that are rich in d electrons and form readily polarizable cations [31]).

3. Trialkyl phosphates *(4)* react with diester chlorides of phosphoric and thiophosphoric acids *(5)* to form pyrophosphates or pyrothiophosphates *(6)*; trialkyl phosphorothionates give the same reaction only in so far as they are converted into thiol compounds [33]. The phosphoryl oxygen is thus able to carry out a nucleophilic attack on the chloro(thio)phosphate [34],

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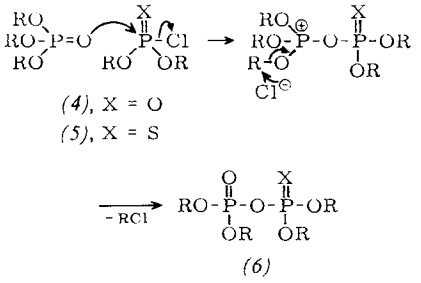
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which is impossible in the case of the thiophosphoryl sulfur.



(4), X = O
(5), X = S

(6)

4. Whereas phosphine sulfides can be alkylated even with alkyl halides to form alkylthiophosphonium salts [35], the analogous reactions of phosphine oxides take place only with stronger alkylating agents [25, 36]. O→S transalkylation is a characteristic of many esters of phosphorothionic and phosphonothionic acids (cf. Section V 2b).

5. The "soft acids" ICl, IBr, and I_2 [21] form more stable adducts with thiophosphoryl compounds than with phosphoryl compounds [27, 37]. Even the less "soft" and more strongly oxidizing halogens Br_2 and Cl_2 give characteristic reactions with thiophosphoryl compounds (cf. Section III).

These examples already indicate a classification of the types of electrophiles to be discussed according to metal salts, halogenating agents, carbonyl and phosphoryl compounds, and alkylating agents.

II. Reactions with Metal Salts [*]

The many crystalline addition products of phosphine oxides and phosphinic, phosphonic, and phosphoric acid derivatives, as well as the solvates present in solution in extractions with phosphoryl compounds, result from a donor-acceptor interaction between phosphoryl oxygen and metal. Even in systems such as $OPCl_3/SbCl_5$, in which chloride ion transfer according to (a) (solvent system concept) was at first regarded as more likely than adduct formation at the oxygen atom (b) (coordination model), (b) has proved to be more significant [38–41].

$$OPCl_2^{\oplus}\,SbCl_6^{\ominus} \xleftarrow{(a)} OPCl_3 + SbCl_5 \xrightarrow{(b)} Cl_5Sb{\leftarrow}OPCl_3$$

Apart from X-ray structure analysis [41], P=O-metal coordination can be deduced in particular from IR measurements. The formation of a coordinate bond from the oxygen to the metal weakens the back-donation of electrons from the oxygen to the phosphorus, and so reduces the P=O bond order; this leads to a strong bathochromic shift of the P=O frequency [42,43]. If the simultaneous decrease in the electron density on the phosphorus cannot be compensated by other substituents, this also results in a downfield shift of the ^{31}P resonance line [44,45].

Until recently, the only thiophosphoryl addition compounds known were a few metal salt adducts. However, several research groups have now described new compounds that seem to call for a revision of the earlier view that the donor character of the thiophosphoryl sulfur is insignificant. Nevertheless, the adducts of the phosphoryl compounds are generally much more stable than those of the thiophosphoryl compounds except for a few adducts of phosphorothionates [46,47] and phosphine sulfides [20], mainly with Ag and Hg(II) salts. A plausible explanation of this is offered by *Ahrland*'s view [48] that the coordinate bond between a "soft base" and a typical B metal can be strengthened by back bonding by d electrons of the metal to the ligand.

It has recently been shown that the P=S frequency also undergoes an appreciable bathochromic shift as a result of metal-sulfur coordination [20,49–51].

1. Thiophosphoryl Halides

Whereas *e.g.* very many phosphorus oxychloride adducts are known [41], the only thiophosphoryl halide adducts obtained so far are evidently [53–55]

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$SPCl_3 \cdot AlCl_3$ [52], $SPBr_3 \cdot AlBr_3$ [52a], $SPCl_3 \cdot SbCl_5$ [52–54], and $SPBr_3 \cdot SbCl_5$ [54]. $SPBr_3 \cdot SbCl_5$ decomposes at room temperature, and $SPCl_3 \cdot SbCl_5$ at temperatures above 140 °C [54]. The low stability and the results of calorimetric measurements [56] indicate a much weaker donor character for the sulfur in the thiophosphoryl halides than for the oxygen in $OPCl_3$.

According to ^{31}P–NMR and conductivity measurements, $SPCl_3 \cdot AlCl_3$ appears to exist in solution as the chloro complex $SPCl_2^{\oplus}$ $AlCl_2^{\ominus}$ [57]. However, X-ray structure investigations on comparable $OPCl_3$ adducts, which dissociate similarly in solution [40], have revealed unmistakable P–O-metal coordination [41]; no corresponding investigations on thiophosphoryl compounds have yet been reported.

2. Thiophosphoryl Amides

Adducts of thiophosphoryl tripiperidide and tripyrrolidide with $PdCl_2$, $CdBr_2$, and CdI_2 [49] and of thiophosphoryl trismethylamide, triscyclohexylamide, trimorpholide, and tripiperidide with $SnCl_4$ and $SnBr_4$ [58] have been obtained.

Metal-nitrogen coordination can be discounted for these compounds on the grounds of their IR spectra (the $CdHal_2$ adducts show bathochromic shifts of 20–40 cm^{-1} for the P=S frequency [49]; the P=S frequency of the triscyclohexylamide changes from 652 cm^{-1} to 610 cm^{-1} in the $SnCl_4$ adduct and to 607 cm^{-1} in the $SnBr_4$ adduct [58]).

3. Phosphine Sulfides and Diphosphine Disulfides

A compound of triethylphosphine sulfide with $PtCl_2$ was mentioned as early as 1857 [59]. With two exceptions, however, the phosphine sulfide adducts listed in Table 2 were obtained only in the last three years. Other attempted preparations have been unsuccessful [20,49,61,62].

The frequency shifts are of roughly the same order of magnitude as those for phosphine oxide adducts, confirming that the bonding is similar. However, no information about the stability of the complex can be deduced from the magnitude of $\Delta\nu_{P=S}$. Thus some of the adducts of the trialkylphosphine sulfides can be sublimed without decomposition [50], whereas those of triphenylphosphine sulfide generally decompose on heating [20]. The $SnHal_4$ adducts of the trialkylphosphine sulfides undergo complete ligand exchange with trialkyl phosphates or trialkyl phosphorothiolates:

$$[R'_3PS]_2SnHal_4 + 2\,(RO)_3PO \rightarrow 2\,R'_3PS + [(RO)_3PO]_2SnHal_4$$

Table 2. Addition compounds of tertiary phosphine sulfides. $\Delta\nu P{=}S$ = difference between the P=S frequencies in the free phosphine sulfide and in the adduct.

Compound	M.p. (°C)	$\Delta\nu P{=}S$ (cm^{-1})	Ref.
$2\,(CH_3)_3PS \cdot SnCl_4$	196–199	−36	[50]
$2\,(CH_3)_3PS \cdot SnBr_4$	182–184	−37	[50]
$2\,(CH_3)_3PS \cdot ZnI_2$	—	−30	[51]
$2\,(CH_3)_3PS \cdot CdI_2$	—	−27	[51]
$2\,(CH_3)_3PS \cdot HgCl_2$	—	−37	[51]
$4\,(CH_3)_3PS \cdot CuClO_4$	—	—	[63]
$2\,CH_3(C_2H_5)_2PS \cdot 3\,HgBr_2$	93	—	[64]
$(C_2H_5)_3PS \cdot 2\,HgCl_2$	—	—	[60]
$2\,(C_2H_5)_3PS \cdot SnCl_4$	194–196	−8	[50]
$2\,(C_2H_5)_3PS \cdot SnBr_4$	182–184	−13, −32	[50]
$2\,(n\text{-}C_3H_7)_3PS \cdot SnCl_4$	166–166.5	−25, −38	[50]
$2\,(n\text{-}C_3H_7)_3PS \cdot SnBr_4$	176–177	−30, −43	[50]
$2\,(n\text{-}C_4H_9)_3PS \cdot SnCl_4$	93–95	—	[50]
$2\,(n\text{-}C_4H_9)_3PS \cdot SnBr_4$	101–102	−48, −55	[50]
$2\,(CH_3)_2C_6H_5PS \cdot SnCl_4$	174–177	−44	[50]
$2\,(CH_3)_2C_6H_5PS \cdot SnBr_4$	155–157	−40	[50]
$2\,(C_6H_5)_3PS \cdot PdCl_2$	236	—	[61]
$(C_6H_5)_3PS \cdot AuCl_3$	~140	—	[65]
$(C_6H_5)_3PS \cdot AuCl$	>130	—	[65]
$4\,(C_6H_5)_3PS \cdot Hg(ClO_4)_2$	206–210	−52	[66]
$2\,(C_6H_5)_3PS \cdot HgBr_2$	—	−77 [*]	[49]
$(C_6H_5)_3PS \cdot HgCl_2$	225–226	−43	[20]
$(C_6H_5)_3PS \cdot AlBr_3$	93–95	−56	[20]
$2\,(C_6H_5)_3PS \cdot SnCl_4$	163–166	−55	[20]
$2\,(C_6H_5)_3PS \cdot TiCl_4$	88–90	−102	[20]
$(C_6H_5)_3PS \cdot 2\,TiCl_4$	85–88	−57	[20]
$(C_6H_5)_3PS \cdot TiBr_4$	240–250	−102	[20]
$(C_6H_5)_3PS \cdot SbCl_5$	72–73	−96	[20]
$(C_6H_5)_3PS \cdot NbCl_5$	128–130	−62	[20]
$(C_6H_5)_3PS \cdot TaCl_4$	202–205	−62	[20]
$2\,(C_6H_5)_3PS \cdot AgNO_3$	160	−32	[67]
$(C_6H_5)_3PS \cdot AgNO_3$	82–83	−51	[67]

[*] This value is probably too high, since $\nu P{=}S$ in $(C_6H_5)_3PS$ was given incorrectly.

Unlike the very unstable $SnCl_4$ adduct of triphenylphosphine sulfide, they are not decomposed by trialkyl phosphorothionates or by diethyl ether. The relative donor strengths toward tin(IV) halides thus decrease in the order $(RO)_3PO, (RO)_2(RS)PO > R_3PS > (RO)_3PS$, $R_2O > Ar_3PS$ [68].

Phosphine sulfides reduce Cu(II) to Cu(I) [63], and, to some extent, Fe(III) to Fe(II) [20]; $Hg_2(ClO_4)_2$ disproportionates on reaction with triphenylphosphine sulfide [66]. The resulting ions are always "softer" acids than the starting materials, and are therefore better suited for complex formation with the phosphine sulfide.

The following compounds have been prepared from diphosphine disulphides: $2\,R_2P(S)P(S)R_2 \cdot CuClO_4$ ($R = CH_3, C_2H_5$); $R_2P(S)P(S)R_2 \cdot CuCl$ ($R = CH_3$) [51]; and $R_2P(S)P(S)R_2 \cdot SnHal_4$ ($R = CH_3, C_2H_5$, n-C_3H_7, n-C_4H_9; Hal = Cl, Br) [50,58]. The Cu(I) adducts are formed from diphosphine disulfides and Cu(II) salts in ethanol. A chelate structure *(7)* was deduced from

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[63] *P. E. Nicpon* and *D. W. Meek*, 151th Meeting Amer. Chem. Soc. 1966, Abstracts H-63.

[64] *L. Maier*: Topics in Phosphorus Chemistry, Vol. 2, Interscience Publ., New York-London-Sydney 1965, p. 116.

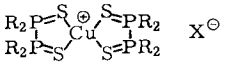
[65] *J. M. Keen*, J. chem. Soc. (London) *1965*, 5751.

[66] *R. A. Potts* and *A. L. Allred*, Inorg. Chem. *5*, 1066 (1966).

[67] *H. Teichmann*, *I. Schwandt*, and *G. Hilgetag*, unpublished.

[68] *H. Teichmann*, lecture to the 3rd All-Union Conference on the Chemistry and Application of Organophosphorus Compounds, Moscow, October 27th, 1965.

conductivity measurements[51]. The $SnHal_4$ compounds, some of which are extremely sparingly soluble, appear to have a different structure.



(7): X = ClO_4, $CuCl_2$

4. Phosphorothionates, Phosphonothionates, and Phosphinothionates

The reactions of these compounds clearly illustrate the difference in the behavior of "hard" and "soft" acids. While the metal-sulfur coordination is retained in the reaction products with soft acids, the A metals tend to loosen the metal-sulfur bond.

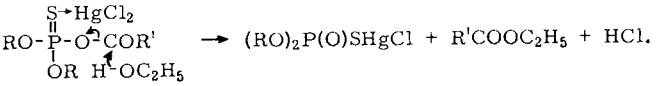
a) Reactions with "Soft" Acids

Solid adducts of triesters of phosphorothionic acid have been obtained with $HgCl_2$[47,69–71], $AuCl_3$, $PtCl_4$[69], $AgNO_3$[46,69], $AgNO_2$ and $AgBF_4$[46]. The formation of crystalline compounds of phosphorodithioates with Ag and Hg salts had been observed by *Carius*[72] as long ago as 1861. Phosphonothionates and phosphinothionates also give crystalline $AgNO_3$ adducts[73]. No corresponding compounds of esters of phosphoric acid are known; for example, triphenyl phosphate, unlike triphenyl phosphorothionate, does not react with $AgNO_3$[46].

The partial positive charge induced on the phosphorus atom by the sulfur-metal coordination makes either the phosphorus atom itself or (in alkyl esters) the α-carbon atom of an ester residue more open to nucleophilic attack. Consequently, the adducts of trialkyl phosphorothionates with B-metal salts are generally not very stable. Thus the $HgCl_2$ adducts *(8)* lose alkyl chloride, sometimes even during preparation, but in any case when heated[69,74]:

$$\underset{(8)}{(RO)_3PS\cdot 2\,HgCl_2} \rightarrow \underset{(9)}{(RO)_2P(O)SHgCl\cdot HgCl_2} + RCl$$

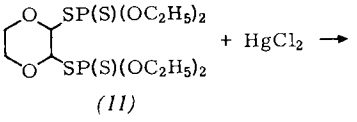
A series of dealkylation products *(9)* has been described[69]. Dialkyl phosphorochloridothioates and phosphorofluoridothioates react in the same way with mercury(II) chloride or acetate[75]. In dialkyl acyl phosphorothionates *(10)*, the acyl group is particularly readily removed, so that these compounds can



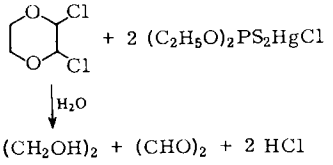
(10)

be determined alkalimetrically after addition of alcoholic $HgCl_2$ solution[76].

A similar reaction is used for the determination of the insecticide Delnav *(11)*[77].



(11)



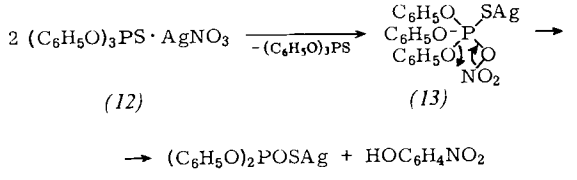
However, this reaction is not characteristic of thiophosphates, but is observed with mercaptals in general[78].

The very large increase in electrophilic reactivity of the phosphorus atom as a result of sulfur coordination is particularly obvious in the transesterification reactions of trialkyl phosphorothionates in the presence of $HgCl_2$, which proceed even at room temperature[79]:

$$(C_2H_5O)_3PS \xrightarrow[HgCl_2]{CH_3OH} (CH_3O)_3PS\cdot 2\,HgCl_2$$

The Cu-ion catalysed hydrolysis of *p*-nitrophenyl phosphorothionates and phosphonothionates[80] and the Ag-ion catalysed formation of 4-t-butylmethylenecyclohexane from dimethyl 1-hydroxy-4-t-butylcyclohexylmethylphosphonothionate[81] probably take place for the same reason.

Another unusual reaction is the smooth cleavage of triaryl phosphorothionates by silver nitrate[46,82], which is best explained by an attack on the phosphorus atom by the nitrate ion.



(12) *(13)*

$$\rightarrow (C_6H_5O)_2POSAg + HOC_6H_4NO_2$$

On the other hand, the corresponding reactions of the trialkyl phosphorothionates, which also proceed *via* addition compounds *(14)*[46], are evidently true dealkylations.

---

[69] *P. Pistschimuka*, Ber. dtsch. chem. Ges. *41*, 3854 (1908); J. prakt. Chem. [2] *84*, 746 (1911); J. russ. physic.-chem. Soc. *44*, 1406 (1912), especially p. 1448f.

[70] *W. G. Emmett* and *H. O. Jones*, J. chem. Soc. (London) *99*, 713 (1911).

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[77] *C. L. Dunn*, J. agric. Food Chem. *6*, 203 (1958).

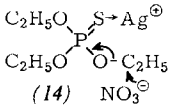
[78] *T. A. Mastryukova et al.*, Izvest. Akad. Nauk SSSR, Ser. chim. *1956*, 443; Chem. Abstr. *50*, 16662 (1956).

[79] *R. Donner*, *Kh. Lohs*, and *H. Holzhäuser*, Mber. dtsch. Akad. Wiss. Berlin *8*, 240 (1966); Z. anorg. allg. Chem. *347*, 156 (1966).

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[82] *G. Hilgetag*, *G. Lehmann*, *A. Martini*, *G. Schramm*, and *H. Teichmann*, J. prakt. Chem. [4] *8*, 207 (1959).



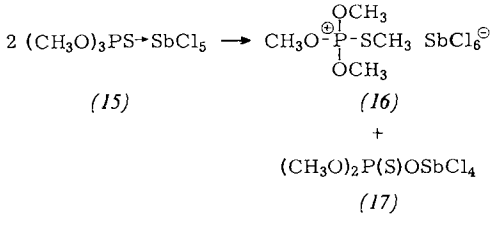
$\rightarrow (C_2H_5O)_2POSAg + C_2H_5ONO_2.$

(14)

The reactions of methyl diphenyl and of phenyl dimethyl phosphorothionates with $AgNO_3$ should otherwise yield nitrophenol in addition to methyl nitrate, but they do not [83].

b) Reactions with "Hard Acids"

Triesters of phosphorothionic acid react with metal halides of the type used as Friedel-Crafts catalysts, such as $SbCl_5$ [84,85], $SnCl_4$, $SnBr_4$ [86], $TiCl_4$, $AlCl_3$, and $FeCl_3$ [47], the ease with which the reaction takes place increasing with the alkylating power of the ester. However, there is no sulfur-metal coordination in any of the crystalline products isolated. The partial positive charge induced on the phosphorus atom by adduct formation again facilitates the heterolysis of an *O*-alkyl bond, but this, together with the highly nucleophilic character of the sulfur toward tetrahedral carbon and the tendency of the A metals to coordinate with "harder" bases, leads to the formation of thiol compounds. For example, trimethyl phosphorothionate and $SbCl_5$ give a 1:1 adduct *(15)* at −80 °C, which changes quantitatively, even below room temperature, into a quasiphosphonium hexachloroantimonate *(16)* and an unstable dealkylation product *(17)* [84].



$2\ (CH_3O)_3PS{\rightarrow}SbCl_5 \rightarrow CH_3O\text{-}P^{\oplus}(OCH_3)\text{-}SCH_3\ SbCl_6^{\ominus}$

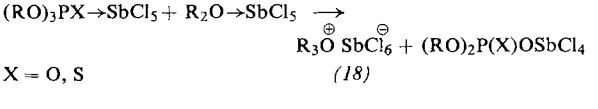
(15) (16)

+

$(CH_3O)_2P(S)OSbCl_4$

(17)

Trimethyl phosphate, on the other hand, gives a stable adduct $(CH_3O)_3PO{\rightarrow}SbCl_5$ [87]. The extremely powerful alkylating properties of this adduct, as well as those of *(15)*, can be used *e.g.* in a simple preparation of trialkyloxonium salts *(18)* [88].



$(RO)_3PX{\rightarrow}SbCl_5 + R_2O{\rightarrow}SbCl_5 \rightarrow R_3O^{\oplus}\ SbCl_6^{\ominus} + (RO)_2P(X)OSbCl_4$

X = O, S (18)

Since quasiphosphonium ions of the type *(16)* can be easily dealkylated, even by weak nucleophiles [89], to yield trialkyl phosphorothiolates, and since A metals generally favor coordination with oxygen rather than with chloride ions, reactions of phosphorothionates with most Lewis acids result in formation of phosphorothiolate adducts [47,85,86].



$[(RO)_3PS]_2SnCl_4 \rightarrow (RO)_3\overset{\oplus}{P}SR\ Cl_4Sn{\leftarrow}OP(OR)_2S^{\ominus} \rightarrow [(RO)_2(RS)PO]_2SnCl_4$

(For further details of this reaction, see Section V 2b.) A few phosphorothiolate adducts were prepared in this way some decades ago, but were wrongly regarded as phosphorothionate adducts [69] (starting from the isomeric thiolates identical adducts are obtained [47]).

The relationship between this type of isomerization and the alkylating power is clearly shown in the series

$$(CH_3O)_3PS > (CH_3O)_2CH_3PS > (CH_3O)(CH_3)_2PS.$$

Phosphonothionates are also isomerized (though much more slowly than phosphorothionate) into phosphonothiolate adducts by tin(IV) halides, but with phosphinothionates the reaction stops with the formation of the thiono ester adduct. This is the first case in which the thiono and thiolo esters give isomeric adducts instead of identical adducts [68]. In both isomeric series, strong bathochromic shifts of the P=O and P=S frequence indicate the bonding site [58] (cf. Table 3).

Table 3. Isomeric adducts of thiophosphinates.

Compound	M.p. (°C)	νP=O (cm^{-1})	νP=S (cm^{-1})
$(CH_3O)(CH_3)_2PS$	–	–	585
$[(CH_3O)(CH_3)_2PS]_2SnCl_4$	121–122	–	538
$[(CH_3O)(CH_3)_2PS]_2SnBr_4$	105–107	–	540
$(CH_3S)(CH_3)_2PO$	40	1190	–
$[(CH_3S)(CH_3)_2PO]_2SnCl_4$	127.5–129	1085–1125	–
$[(CH_3S)(CH_3)_2PO]_2SnBr_4$	116–118	1075–1105	–

III. Reactions with Halogenating Agents

The most important electrophiles in this class are the elemental halogens and sulfuryl chloride. Two types of reactions can be distinguished here even more clearly than in the reactions with metal salts. Thus if the phosphorus atom carries alkoxy (or OH or SH) groups, the secondary attack by a nucleophile is directed toward the alkyl residue (or toward the proton); otherwise the nucleophile attacks the phosphorus atom, with replacement of sulfur by halogen (or, particularly with thionyl chloride, by oxygen).

Halogens oxidize thiophosphoryl compounds in the presence of water to form phosphoryl compounds and sulfate; the oxidizing agents in this reaction are hypohalite ions, which are characterized by their high nucleophilicity toward tetrahedral phosphorus. In spite of their preparative [90] and analytical importance [91], these and similar oxidations will not be discussed here.

1. Phosphine Sulfides and Diphosphine Disulfides

Triarylphosphine sulfides form crystalline adducts with ICl, IBr, and I_2 [19,37,92,93]. These adducts are more stable than those of the corresponding phosphine

[83] *G. Hilgetag, I. Schwandt,* and *H. Teichmann,* unpublished.

[84] *H. Teichmann* and *G. Hilgetag,* Chem. Ber. *96,* 1454 (1963).

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[86] *H. Teichmann* and *G. Hilgetag,* Chem. Ber. *98,* 856 (1965).

[87] *G. Hilgetag, H. Teichmann,* and *M. Jatkowski,* unpublished.

[88] *G. Hilgetag* and *H. Teichmann,* Chem. Ber. *96,* 1446 (1963).

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[91] *K. Groves,* J. agric. Food Chem. *6,* 30 (1958).

[92] *R. A. Zingaro* and *E. A. Meyers,* Inorg. Chem. *1,* 771 (1962); *R. A. Zingaro* and *R. M. Hedges,* J. physic. Chem. *65,* 1132 (1961).

[93] *R. A. Zingaro,* Inorg. Chem. *2,* 192 (1963).

oxides [19, 37]. IR spectra [19, 23] and X-ray structure investigations [19] indicate sulfur-halogen coordination and rule out the possibility of interaction between the halogen and the aromatic nuclei.

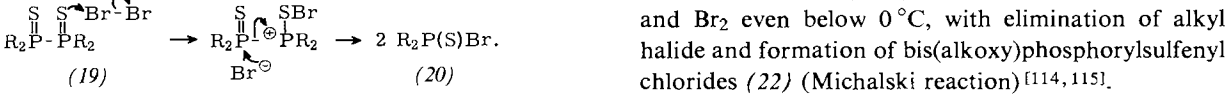
Table 4. Addition compounds $R_2R'PS$. Hal_2·$\Delta\nu P{=}S$ = difference between the P=S frequencies in the free phosphine sulfide and in the adduct.

R	R′	Hal_2	M.p. (°C)	$\Delta\nu P{=}S$ (cm^{-1})	Ref.
C_6H_5	C_6H_5	ICl	124	−38	[92,93]
C_6H_5	C_6H_5	IBr	151.5	—	[92,93]
1-Naphthyl	C_6H_5	IBr	137–140	−29	[19]
C_6H_5	C_6H_5	I_2 [*]	140	−37	[92,93]
C_6H_5	1-Naphthyl	IBr	155–156	−20	[19]
C_6H_5	1-Naphthyl	I_2	157–160	−12	[19]
1-Naphthyl	C_6H_5	I_2	117–120	−23	[19]
1-Naphthyl	1-Naphthyl	I_2	174–176	−32	[19]
C_6H_5	4-Methyl-1-naphthyl	I_2	161–166	−10	[19]
4-Methyl-1-naphthyl	C_6H_5	I_2	177–180	−13	[19]
4-Methyl-1-naphthyl	4-Methyl-1-naphthyl	I_2	233–245	−17	[19]

[*] This compound has the composition $2(C_6H_5)_3PS{\cdot}3\ I_2$.

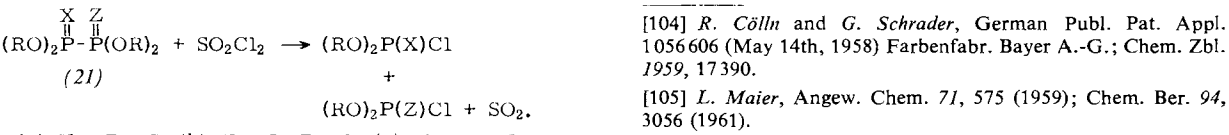
The reactions with Cl_2 and Br_2 do not stop with the formation of the adducts, but lead, by substitution at the phosphorus atom (which has acquired a partial positive charge), to halogenophosphoranes and sulfur halides. For example, diarylthiophosphinyl chlorides give diaryltrichlorophosphoranes [94]; the analogous chlorination of $SPCl_3$ to PCl_5 has been known for a long time [95].

The unusually easy cleavage of tetraalkyldiphosphine disulfides *(19)* by Cl_2 [96,97], Br_2 [96–98], or SO_2Cl_2 [97–99] to dialkylthiophosphinyl halides *(20)* can be explained in a similar manner [100]:



(19) *(20)*

In agreement with this view, dithio-*(21a)* [101] and monothiohypophosphates *(21b)* [102] are cleaved by SO_2Cl_2 in a strongly exothermic reaction even below 0 °C, whereas the sulfur-free compounds *(21c)* must be heated under reflux [103].



(a): X = Z = S; *(b)*: X = O, Z = S; *(c)*: X = Z = O

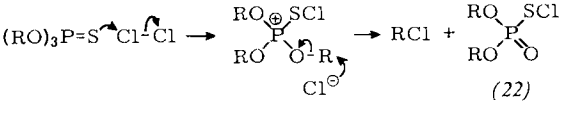
Since dialkylthiophosphinyl halides themselves react by the same principle with halogenating agents, the reaction of tetraalkyldiphosphine disulfides with an excess of Cl_2 or Br_2 yields dialkyltrihalogenophosphoranes [96], and the reaction with an excess of SO_2Cl_2 yields dialkylphosphinyl chlorides [98, 104]. When $SOCl_2$ is used instead of SO_2Cl_2, the intermediate thiophosphinyl chlorides, though detectable [105], can no longer be isolated [105–107].

Thiophosphonyl dihalides [107, 108] and phosphine sulfides [107–110] also form the corresponding phosphoryl compounds with $SOCl_2$. The determining factor in this reaction is the electron density, not at the phosphorus, but at the sulfur atom, as is shown by the marked decrease in reactivity in the order $(CH_3)_2P(S)Cl > (C_6H_5)CH_3P(S)Cl > C_6H_5P(S)Cl_2 > P(S)Cl_3$ [107]. A similar substituent effect is also observed in the reactions with SbF_3: phosphine sulfides and diphosphine disulfides give di- and trifluorophosphoranes respectively [111], trialkyl phosphorothionates do not react [111], and thiophosphonyl dichlorides [112] and thiophosphoramidic dichlorides [113] simply undergo halogen exchange.

2. Derivatives of Thiophosphoric, Thiophosphonic, and Thiophosphinic Acids

a) Esters, Ester Chlorides, and Ester Amides

Addition compounds of trialkyl phosphorothionates with I_2 have been detected in solution; they are more stable than the corresponding trialkyl phosphate adducts [27]. Trialkyl phosphorothionates react with Cl_2 and Br_2 even below 0 °C, with elimination of alkyl halide and formation of bis(alkoxy)phosphorylsulfenyl chlorides *(22)* (Michalski reaction) [114, 115].



(22)

[94] *W. G. Craig* and *W. A. Higgins*, US-Pat. 2727073 (Dec. 13th, 1955), Lubrizol Corp.; Chem. Abstr. *50*, 9445 (1956).

[95] *Chevrier*, C. R. hebd. Séances Acad. Sci. *68*, 1174 (1869).

[96] *W. Kuchen*, *H. Buchwald*, *K. Strolenberg*, and *J. Metten*, Liebigs Ann. Chem. *652*, 28 (1962).

[97] *R. Cölln* and *G. Schrader*, German Publ. Pat. Appl. 1054453 (Feb. 12th, 1958) Farbenfabriken Bayer A.-G.; Chem. Zbl. *1959*, 12696.

[98] *L. Maier*, Chem. Ber. *94*, 3051 (1961).

[99] *H. Schlör* and *G. Schrader*, German Publ. Pat. App. 1067021 (May 31st, 1958) Farbenfabr. Bayer A.-G.; Chem. Zbl. *1960*, 5319.

[100] *B. Miller*, Topics in Phosphorus Chemistry, Vol. 2, Interscience Publ., New York-London-Sydney 1965, p. 142.

[101] *L. Almasi* and *L. Paskucz*, Chem. Ber. *96*, 2024 (1963).

[102] *J. Michalski*, *W. Stec*, and *A. Zwierzak*, Bull. Acad. polon. Sci., Sér. Sci. chim. *13*, 677 (1965).

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[105] *L. Maier*, Angew. Chem. *71*, 575 (1959); Chem. Ber. *94*, 3056 (1961).

[106] *H. J. Harwood* and *K. A. Pollart*, US-Pat. 3104259 (July 20th, 1959) Monsanto Chem. Co.; Chem. Zbl. *1965*, 38-2479.

[107] *K. A. Pollart* and *H. J. Harwood*, J. org. Chemistry *27*, 4444 (1962).

[108] *H. J. Harwood* and *K. A. Pollart*, US-Pat. 3082256 (July 20th, 1959) Monsanto Chem. Co.; Chem. Zbl. *1964*, 46-2222.

[109] *H. J. Harwood* and *K. A. Pollart*, J. org. Chemistry *28*, 3430 (1963).

[110] *L. Maier*, Helv. chim. Acta *47*, 120 (1964).

[111] *R. Schmutzler*, Inorg. Chem. *3*, 421 (1964).

[112] *R. Schmutzler*, J. inorg. nucl. Chem. *25*, 335 (1963); *H. L. Boter* and *A. J. J. Ooms*, Recueil Trav. chim. Pays-Bas *85*, 21 (1966).

[113] *G. Schrader*, unpublished; cited in: Methoden der organ. Chemie (Houben-Weyl), 4th Edit., Georg Thieme-Verlag, Stuttgart 1964, Vol. XII/2, p. 753.

[114] *J. Michalski* and *A. Skowronska*, Chem. and Ind. *1958*, 1199.

[115] *J. Michalski*, *B. Pliszka-Krawiecka*, and *A. Skowronska*, Roczniki Chem. *37*, 1479 (1963).

Sulfuryl chloride is a better reagent than elemental halogen for the preparation of *(22)* [114–116]. Dialkyl ester amides, dialkyl aryl, and diaryl alkyl esters of thiophosphoric acid generally react in the same way [115]. However, conversion decreases rapidly in the order $(C_2H_5O)_3PS > (C_6H_5O)(C_2H_5O)_2PS > (4\text{-}O_2NC_6H_4O)(C_2H_5O)PS > (4\text{-}O_2NC_6H_4O)_2(C_2H_5O)PS$ (the ethyl bis-(4-nitrophenyl) ester does not react at all), again showing the effect of the substituents on the nucleophilic strength of the thiono sulfur [115]; the reverse order applies in the ease of dealkylation by nucleophilic attack at the α-carbon atom [2].

Since compounds *(22)*, like alkanesulfenyl chlorides, add to multiple bond systems [114–117], the Michalski reaction is of great preparative interest.

Dialkyl thiophosphoryl chlorides *(23)* also enter into this reaction [118].

$$(C_2H_5O)_2P(S)Cl + SO_2Cl_2 \rightarrow \underset{ClS\quad Cl}{\overset{C_2H_5O\quad O}{P}} + C_2H_5Cl + SO_2.$$

(23)

On the other hand, a different reaction course is reported [119] for esters of phosphonochloridothionic acids *(24)*, the nucleophilic attack in the second step taking place, not on the carbon, but on the phosphorus atom.

$$\underset{C_2H_5O\quad Cl}{\overset{C_2H_5\quad S}{P}} + SO_2Cl_2 \rightarrow \underset{C_2H_5O\quad O}{\overset{C_2H_5\quad SCl}{P}} + SOCl_2.$$

(24)

This type of reaction is necessarily also encountered with triphenyl phosphorothionate, which gives tris-(phenoxy)dichlorophosphorane (or ionic products having the same overall composition) with Cl_2 [115] or SO_2Cl_2 [115, 120].

The formation of methylphosphonochloridates from dialkyl phosphonothionates and thionyl chloride [121] may also proceed *via* a sulfenyl chloride, which splits off sulfur when heated.

The reaction of trialkyl phosphorothionates with alkanesulfenyl chlorides *(25)* [122] also follows the scheme of the Michalski reaction.

$$(CH_3O)_3PS + CH_3SCl \rightarrow (CH_3O)_3\overset{\oplus}{P}SSCH_3\ Cl^{\ominus} \rightarrow$$

(25)

$$\underset{CH_3O\quad SSCH_3}{\overset{CH_3O\quad O}{P}} + CH_3Cl$$

[116] *W. H. Mueller, R. M. Rubin,* and *P. E. Butler,* J. org. Chemistry *31*, 3537 (1966).

[117] *J. Michalski, B. Borecka,* and *S. Musierowicz,* Bull. Acad. polon. Sci., Sér. Sci. chim. *6*, 159 (1958); *B. Borecka, T. Kapecka,* and *J. Michalski,* Roczniki Chem. *36*, 87 (1962); *J. Michalski* and *S. Musierowicz, ibid. 36*, 1655 (1962).

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[120] *A. C. Poshkus, J. E. Herweh,* and *L. F. Hass,* J. Amer. chem. Soc. *80*, 5022 (1958).

[121] *Z. Pelchowicz,* J. chem. Soc. (London) *1961*, 238.

[122] *J. B. Douglass* and *W. J. Evers,* J. org. Chemistry *29*, 419 (1964).

b) Thioacids and Thioacid Anhydrides

Dialkyl phosphorothioic acids and their salts, like the triesters, react with Cl_2 [123] or SO_2Cl_2 [123, 124] to form sulfenyl chlorides *(22)*. However, the overall

$$(RO)_2P(S)OH + Cl_2 \rightarrow (RO)_2P(O)SCl + HCl$$

(22)

equation conceals the fact that *(22)*, as an extremely strong electrophile, immediately reacts with the dialkyl phosphorothioate, which is present in excess, to form the disulfide *(26)*, which is then chlorinated with cleavage to form *(22)* [123].

$$(RO)_2P(S)OH + (22) \xrightarrow[-HCl]{} (RO)_2P(O)SSP(O)(OR)_2$$

(26) $\xrightarrow{+Cl_2}$ 2 *(22)*

The alkylalkoxyphosphorylsulfenyl chlorides *(27a)*, which can be prepared in a similar manner, decompose readily with deposition of sulfur [125, 126], while the dialkyl- [125] and diarylphosphorylsulfenyl chlorides [127] *(27b)* decompose during attempts to prepare them.

$$\underset{A\quad SCl}{\overset{R\quad O}{P}} \rightarrow \underset{A\quad Cl}{\overset{R\quad O}{P}} + S$$

(27) (a): A = RO; *(b)*: A = R

The chlorination of dialkyl phosphorodithioates *(28)*, which is used for the preparation of dialkyl phosphorochloridothioates *(29)*, also proceeds through the stages sulfenyl chloride, disulfide, and sulfenyl chloride [71, 128, 129]; the bis(alkoxy)thiophosphoryl-

$$(RO)_2PS_2H \xrightarrow[-HCl]{+Cl_2} \underset{RO\quad SCl}{\overset{RO\quad S}{P}} \rightarrow \underset{RO\quad Cl}{\overset{RO\quad S}{P}} + S$$

(28) *(29)*

sulfenyl chlorides *(28)* have themselves only recently become available by another method [129, 130].

The chlorination of diaryldithiophosphinic acids yields diaryltrichlorophosphoranes [94, 131], and that of aryldithiophosphonic anhydrides *(30)* leads *via* isolable thiophosphonyl dichlorides *(31)* to tetrachlorophosphoranes *(32)* [132].

[123] *B. Lenard-Borecka* and *J. Michalski,* Roczniki Chem. *31*, 1167 (1957).

[124] *J. Michalski* and *B. Lenard,* Roczniki Chem. *30*, 655 (1956).

[125] *C. Borecki, J. Michalski,* and *S. Musierowicz,* J. chem. Soc. (London) *1958*, 4081.

[126] *J. Michalski* and *A. Ratajczak,* Chem. and Ind. *1959*, 539; Roczniki Chem. *36*, 911 (1962).

[127] *W. G. Craig,* US-Pat. 2724726 (Nov. 22nd, 1955) Lubrizol Corp.; Chem. Abstr. *50*, 10129 (1956).

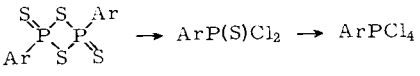
[128] *L. Malatesta,* Gazz. chim. ital. *81*, 596 (1951).

[129] *L. Almasi* and *L. Paskucz,* Chem. Ber. *98*, 3546 (1965).

[130] *L. Almasi* and *A. Hantz,* Chem. Ber. *97*, 661 (1964); *L. Almasi* and *L. Paskucz, ibid. 98*, 613 (1965).

[131] *W. A. Higgins, P. W. Vogel,* and *W. G. Craig,* J. Amer. chem. Soc. *77*, 1864 (1955); *C. Stuebe, W. M. LeSuer,* and *G. R. Norman, ibid. 77*, 3526 (1955).

[132] *H. Z. Lecher, R. A. Greenwood, K. C. Whitehouse,* and *T. H. Chao,* J. Amer. chem. Soc. *78*, 5018 (1956); *H. Z. Lecher* and *R. A. Greenwood,* US-Pat. 2870204 (Jan. 20th, 1959) Amer. Cyanamid Co.; Chem. Abstr. *53*, 11306 (1959).



(30) (31) (32)

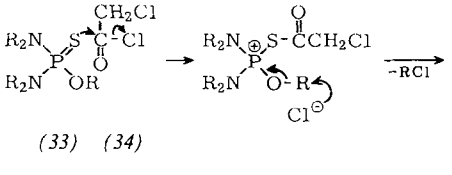
IV. Reactions with Carbonyl and Phosphoryl Compounds

As has been mentioned, the thiophosphoryl sulfur should not be very reactive toward the "hard" carbonyl carbon and phosphoryl phosphorus. Accordingly, only a few reactions with particularly reactive carbonyl groups have been reported, and most of these are not very characteristic.

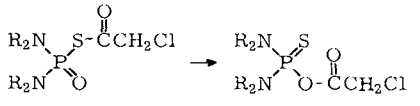
The replacement of carbonyl oxygen by sulfur[133], which has been used in preparative chemistry, and the more recently discovered, analogous replacement of phosphoryl oxygen by sulfur[134,135] with the aid of phosphorus(v) sulfide are of considerable importance. This reaction is only mentioned in passing, since it is not confined to thiophosphoryl sulfur, but even takes place with phosphorus sulfides, such as P_4S_3[136], which only contain P–S–P bonded sulfur.

1. Reactions with Carbonyl Compounds

The relatively smooth reaction of trialkyl phosphates with acyl chlorides to form dialkyl acyl phosphates[137] has evidently been achieved in the thiophosphate series only for a few diester monoamides and monoester diamides *(33)* with chloroacetyl chloride *(34)*[138].



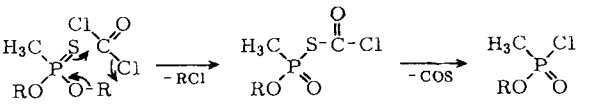
(33) (34)



(35) (36)

S-Acyl thiophosphates *(35)* rearrange to the more stable *O*-acyl derivatives *(37)*[76].

Dialkyl methylphosphonothioates *(37)*, like their oxygen analogues, react with phosgene[139] or oxalyl chloride[121] to form esters of phosphonochloridic acids *(38)*.



(37) (38)

Contrary to earlier reports, triphenylphosphine sulfide and phenyl isocyanate do not form phenyl isothiocyanate[140] but diphenylcarbodiimide[110].

The phosphine sulfide, like esters of thiophosphonic acids[141], is effective even in catalytic quantities. Since neither carbon oxysulfide nor triphenylphosphine oxide could be detected in the reaction products[110] the reaction appears to proceed by a course different from that followed by the formation of carbodiimide in the presence of phosphine oxide[142].

Triphenylphosphine sulfide is desulfurized by diphenylketene to form the phosphine oxide[140], and trimethyl thionophosphate is desulfurized to trimethyl phosphate by chloral[143]. Both reactions are formally similar to the Wittig olefination.

$$(C_6H_5)_3PS + (C_6H_5)_2C{=}C{=}O \rightarrow (C_6H_5)_3PO + {}^1/_n[(C_6H_5)_2C{=}C{=}S]_n$$

$$(CH_3O)_3PS + Cl_3CCHO \rightarrow (CH_3O)_3PO + {}^1/_n[Cl_3CCHS]_n$$

2. Reactions with Phosphoryl Compounds

Thiophosphoryl compounds exchange their sulfur for phosphoryl oxygen at 150–200 °C, the exchange taking place more readily as the sum of the electronegativities of the substituents on the thiophosphoryl group increases and as that of the substituents on the phosphoryl group decreases. The reaction rate is directly proportional to this electronegativity difference[144], and so corresponds to the substituent effects in the formation of pyrophosphate from triesters and diester chlorides of phosphoric acid[33].

Thiophosphoryl chloride is therefore the most suitable reagent for the conversion of phosphonyl[135,144] and phosphinyl chlorides[144,145] into their thio analogues. Under similar conditions, phosphine oxides are converted into phosphine sulfides by salts or *O*-alkyl esters of dimethylthiophosphinic acid[146]. *O*-Methyl dimethylthiophosphinate reacts with its *S*-methyl isomer to give esters of the dithiophosphinic acid, among other products[146], and small quantities of *O,O*-diphenyl *S*-methyl dithiophosphate are formed during the thermal isomerization of methyl diphenyl thiophosphate[147].

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[143] *H. Sohr* and *K.-H. Lohs*, Z. Chem. *7*, 153 (1967).

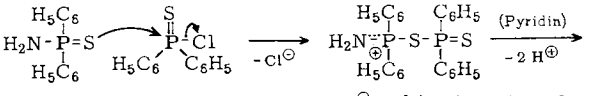
[144] *L. C. D. Groeneweghe* and *J. H. Payne*, J. Amer. chem. Soc. *83*, 1811 (1961).

[145] *L. C. D. Groeneweghe*, US-Pat. 3206442 (March 9th, 1962) Monsanto Chem. Co.; Chem. Abstr. *63*, 15007 (1965).

[146] *H. Teichmann*, *P. Gregorzewski*, and *G. Hilgetag*, unpublished.

[147] *H. Teichmann* and *G. Hilgetag*, unpublished.

The observed substituent effects require a strong positive charge at the phosphorus atom of the thiophosphoryl compound and a high electron density at the phosphoryl oxygen of the phosphoryl compound. It may therefore be concluded that the exchange reaction is initiated by a nucleophilic attack on the phosphorus atom of the thiophosphoryl compound by the phosphoryl oxygen (similar to the pyrophosphate synthesis mentioned above). However, the sulfurization of phosphine oxides by the thiophosphinate ion can hardly be understood in this way. Similarly, the formation of diphenyldithiophosphinate *(40)* from diphenylphosphinothioic amide *(39)* and chloride [148] can be explained only by the nucleophilic reactivity of the sulfur.



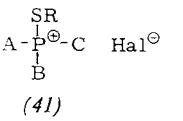
(39) *(40)*

V. Reactions with Alkylating Agents

The primary products of the action of alkylating agents on thiophosphoryl compounds are alkylthiophosphonium salts. However, these can be isolated unchanged only if they have no alkoxy groups attached to the phosphorus atom. Special conditions are required for the preparation of alkoxyalkylthiophosphonium salts [84,89]. Alkylations of compounds such as $(RO)_2P(S)OH$ [149], $(RO)_2P(S)NHSO_2Ar$ [150], or $(RO)_2P(S)NHCOAr$ [151], which undergo tautomeric changes, will not be dealt with here.

1. Thiophosphoric, Thiophosphonic, and Thiophosphinic Amides; Phosphine Sulfides

Triamides of thiophosphoric acid are alkylated to onium salts *(41a)* by alkyl halides, in some cases even at room temperature [152,153]; in contrast to *N*-alkylamides, *N*-arylamides do not react even under more rigorous conditions [152]. The compounds *(41b)–(41d)* are formed in a similar manner from thiophosphonic [153] and thiophosphinic amides [36,148] and from trialkylphosphine sulfides [35,154,155]. When the products are heated under vacuum, alkyl halides are sometimes split off again [153]. The salts *(41d)* obtained from aromatic phosphine sulfides are difficult to prepare with alkyl halides [26,156]; they are best isolated as the fluoroborates or the like [36].



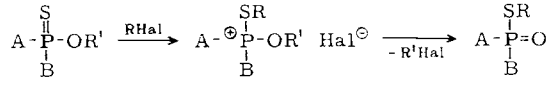
(41)

(a): A, B, C = R^1R^2N
(b): A, B = R^1R^2N; C = R^3
(c): A = R^1R^2N; B, C = R^3
(d): A, B, C = R^1

2. *O*-Alkyl Thiophosphates, Thiophosphonates, and Thiophosphinates

a) Reactions with Alkyl Halides

Since alkoxyalkylthiophosphonium salts *(42)* are cleaved at the *O*-alkyl bond by nucleophiles, the action of alkyl halides on alkyl esters of the thionophosphoric, thionophosphonic, and thionophosphinic acid series leads to thiol esters *(43)* (Pistschimuka reaction).



(42) *(43)*

Suitable starting materials are trialkyl thionophosphates [69,153,157–159], dialkyl aryl thionophosphates [158], trialkyl dithiophosphates [69,153,157], trialkyl trithiophosphates [69], dialkyl thiophosphoric amides and alkyl thiophosphoric diamides [153,157], and esters of thiophosphonic [153,157,158,160] and thiophosphinic acids [158,161].

The Pistschimuka reaction is analogous to the Michalski reaction (Section III, 2), but requires much more rigorous conditions (heating for many hours at 100–150 °C); its preparative value is frequently limited by poor yields and by side reactions such as the formation of trialkylsulfonium salts. However, these disadvantages can be overcome to a large extent by the use of strongly polar solvents, which considerably increase the reaction rate [153,157]. The substituents A and B favor the reaction in the order Cl < RS < RO < R < R_2N [153] by increasing the nucleophilic strength of the sulfur atom.

b) Reactions without the Addition of Alkylating Agents

The role of the alkyl halide in the Pistschimuka reaction can be taken over by the thiophosphoryl com-

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[161] *T. A. Mastrykova*, *T. A. Melentyeva*, and *M. I. Kabachnik*, Ž. obšč. Chim. *35*, 1196 (1965).

pound itself, since the esters mentioned all have alkylating properties. Trialkyl[70,153,162–164], dialkyl aryl[164,165–168], and alkyl diaryl thionophosphates[164,165,169,170], dialkyl thionophosphoryl halides[33,170], alkyl thionophosphoryl dihalides[170,171], *O,O,S*-trialkyl dithiophosphates[172], and alkyl esters of phosphonothionic[73] and phosphinothionic acids[173] can therefore be thermally isomerized into the thiol esters. However, the conditions are often even more severe than those of the Pistschimuka reaction, so that the formation of the thiol esters is frequently followed by secondary reactions (cf. the reviews[2,174]).

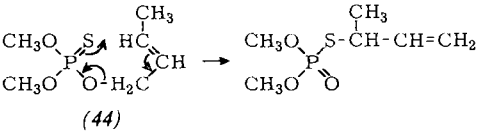
Solvents having a high dielectric constant again favor this reaction[153,163]. On the other hand, the substituent effect is opposite to that observed in the Pistschimuka reaction; the isomerization depends on the alkylating power of the ester, which is increased by electron-attracting substituents at the phosphorus atom[2,174]).

The thiophosphoryl sulfur is alkylated, not only by the thiono ester introduced, but also by the resulting thiol ester, provided that it still contains further P–O-alkyl groups; in this case the isomerization is autocatalytic[163]. Mixtures of thiono esters give mixed thiol esters[163].

$$(RO)_3PS + (R'O)_3PS \rightarrow (RO)_2P(O)(SR) + (R'O)_2P(O)(SR') + (RO)_2P(O)(SR') + (R'O)_2P(O)(SR).$$

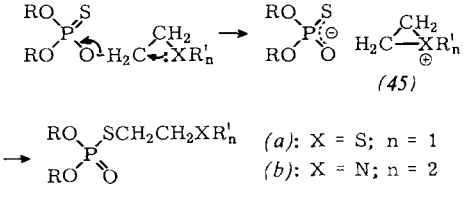
In contrast to the thermal isomerization, the isomerization induced by Lewis acids (cf. Section II, 4b) often proceeds almost quantitatively at or below room temperature. Since the thiol ester adducts formed can be broken down into their components, thiono esters that are unsuitable for thermal isomerization because of the instability of the thiol isomers can be converted in high yields into the thiol esters with the aid of Lewis acids[47,58,86]. The substituent effects are of the same nature as in the thermal isomerization. The rate of isomerization also depends on the acceptor strength of the Lewis acid, and decreases rapidly *e.g.* in the order $SnCl_4 > SnBr_4 > SnI_4$[58,86].

The thermal isomerization takes place more readily in allyl esters *(44)* than in alkyl esters; the reaction undoubtedly proceeds by a different mechanism in this case, since the products obtained are those of a Claisen rearrangement[175].



(44)

Finally, a further considerable increase in the rate of isomerization is observed in phosphorothionates containing a β-alkylthio[176–178] or dialkylamino group[179–182] in an ester residue. The same is true of β-alkylthioalkyl phosphoramidothionates[183] and phosphonothionates[178,184]. In these cases the reaction is no longer induced by the nucleophilicity of the thiophosphoryl sulfur; instead, the neighboring group effect of the nucleophilic center in the β position leads to the ready release of a cyclic sulfonium *(45a)* or ammonium cation *(45b)*, which *S*-alkylates the remaining thiophosphate ion in the usual manner.



(45)

(a): X = S; n = 1
(b): X = N; n = 2

The intermediate formation of the thiiranium[177] and aziridinium ions[179–181] has been demonstrated in various ways.

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[163] *H. Teichmann,* unpublished.

[164] *G. Hilgetag, G. Schramm,* and *H.Teichmann,* Angew. Chem. *69,* 205 (1957).

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[166] *Z. M. Bakanova, J. A. Mandelbaum,* and *N. N. Melnikov,* Ž. obšč. Chim. *26,* 2575 (1956); *H. L. Morrill,* US-Pat. 2601219 (July 17th, 1948) Monsanto Chem. Co.; Chem. Abstr. *46,* 8322 (1952); *V. Tichy,* Chem. Zvesti *9,* 3 (1955); Chem. Zbl. *1959,* 7747.

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Structure and Mechanism of Action of the Active Center of Yeast Pyruvate Decarboxylase

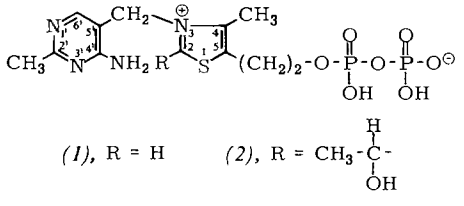
BY A. SCHELLENBERGER [*]

Dedicated to the memory of Prof. Dr. W. Langenbeck

Kinetic studies have shown that the two low molecular-weight components of yeast pyruvate decarboxylase (thiamine pyrophosphate and $Mg^{2\oplus}$ ions) first add rapidly and reversibly to the apoenzyme in binary equilibria. The resulting adduct then "cyclizes" in a rate-determining, practically irreversible reaction to form the thermodynamically stable holoenzyme. These results were supplemented and extended by the testing of numerous analogues of thiamine pyrophosphate in enzyme experiments and then used for the interpretation of the enzyme reaction.

Introduction

In 1961, *Holzer et al.* [1,2] showed that the enzymatic degradation of pyruvate by yeast pyruvate decarboxylase proceeds *via* a condensation product of thiamine pyrophosphate (TPP) *(1)*, which acts as the coenzyme, acetaldehyde. This relatively labile intermediate was called "active acetaldehyde" *(2)*.

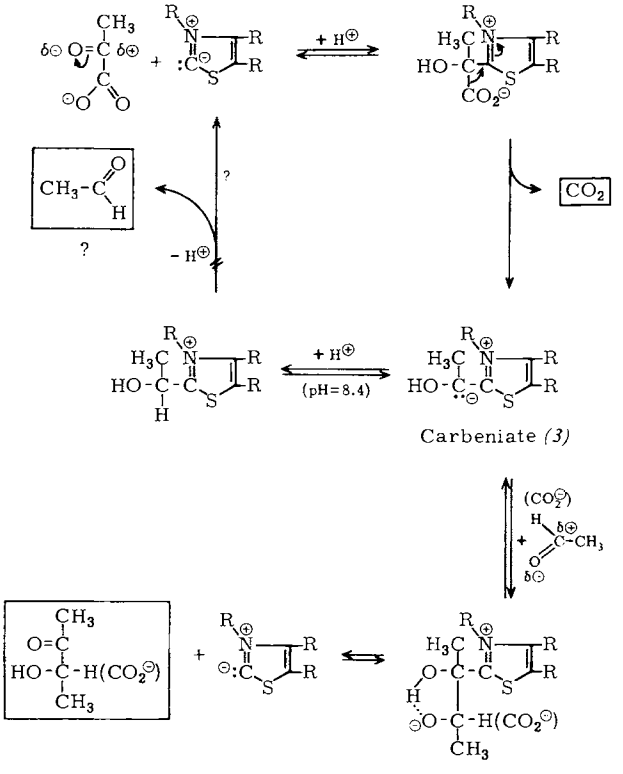


(1), R = H *(2)*, R = $CH_3-\underset{\underset{OH}{|}}{\overset{\overset{H}{|}}{C}}-$

It therefore seemed reasonable to apply the essential features of the catalytic decarboxylation of α-keto acids (Scheme 1), which was studied by *Ugai* [3], *Mizuhara* [4], *Breslow* [5], and *Sykes* [6] with thiazolium models, to the enzyme mechanism.

Though this seemed to solve the fundamental problem of the action of pyruvate decarboxylase (PDC), a number of questions still remained unanswered:

1. Why is the rate of reaction of "active acetaldehyde" four orders of magnitude lower than that of pyruvate under the action of the enzyme [2]?



Scheme 1. Decarboxylation of α-keto acids for thiazolium models at pH = 8.4.

2. Why is no acetaldehyde formed by the model mechanism shown in Scheme 1 [4]?

3. Has the pyrimidine portion of the thiamine pyrophosphate molecule any function, and if so, what is it?

4. Since the decarboxylation of the α-keto acids is thermodynamically practically irreversible, what is the mechanism of the inhibition of PDC by the reaction product?

A careful study of these questions has become possible only by the use of new methods.

The first essential was to find mathematical statements concerning the bonding mechanism of the holoenzyme complex on the basis of the kinetic parameters of the recombination (*i.e.* the resynthesis of the holoenzyme

[*] Prof. Dr. A. Schellenberger
Institut für Biochemie (Chemische Abteilung) der Universität Weinbergweg
DDR 402 Halle/S. (Germany)

[1] *H. Holzer* and *K. Beaucamp*, Angew. Chem. *71*, 776 (1959).

[2] *H. Holzer* and *K. Beaucamp*, Biochim. biophysica Acta *46*, 225 (1961); see also *H. Holzer*, Angew. Chem. *73*, 721 (1961); *H.-W. Goedde*, *B. Ulrich*, *C. Stahlmann*, and *H. Holzer*, Biochem. Z. *343*, 204 (1965).

[3] *T. Ugai*, *S. Tanaka*, and *S. Dokawa*, J. pharm. Soc. Japan *63*, 296 (1943).

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from its components, apo-PDC, metal ion, and thiamine pyrophosphate (TPP), in accordance with equation (1)).

$$\text{Apo-PDC} + \text{Mg}^{2\oplus} + \text{TPP} \underset{k_{back}}{\overset{k}{\rightleftharpoons}} \text{Holo-PDC} \qquad (1)$$

It was also desirable to study the function of the coenzyme with models whose structures substantially agreed with that of TPP. The experiments showed that the course of the enzyme reaction is much more complicated than was formerly thought.

I. Kinetics of the Recombination

In 1944, in a study of the cleavage and resynthesis of PDC, *Steyn-Parvé* and *Westenbrink* [7] pointed out a number of peculiarities, which we have been able to confirm and which are of general importance to the understanding of coenzyme-apoenzyme bonding.

Steyn-Parvé and *Westenbrink* demonstrated that resynthesized PDC is identical with the native enzyme, and found that the enzyme is cleaved into its components in accordance with equation (1) within a few minutes at pH = 8 without appreciable damage to the protein component. The resynthesis has a sharp optimum (stability optimum) at pH = 6.8, whereas the optimum of the pH-activity curve occurs at pH = 5.6.

An important observation in this work was the fact that when the quantity of TPP originally present in the yeast is brought together, under optimum conditions, with yeast that has been washed with alkali (*i.e.* freed from coenzyme), only a very small proportion recombines with the apoenzyme "... although carboxylase (PDC) is an undissociated enzyme...", and that the resynthesis does not proceed to completion even when a large excess of TPP is used. The authors concluded: "...so different end states are reached by dissociation and resynthesis..." (irreversible damage to the apoenzyme could be ruled out), and finally observed: "But why does potentially active apo-PDC not combine with sufficiently available TPP? This is the great riddle of the reconstitution that has not yet been solved".

This riddle, which we have called the "quasi-irreversibility" [8] of the bonding between the coenzyme and the apoenzyme, can be demonstrated very simply by the following experiment (cf. also [9]):

According to *Ullrich, Wittorf,* and *Gubler* [10], the molecular weight of highly purified PDC preparations is about 175000. Three to four TPP molecules and the same number of metal ions are incorporated into this protein molecule. A mixture of stoichiometric quantities of apo-PDC, TPP, and $Mg^{2\oplus}$ does not recombine within 3–4 hours even under optimum pH conditions. If, on the other hand, TPP and $Mg^{2\oplus}$ in considerable excess are allowed to act on purified apo-PDC, complete recombination takes place within 3–4 minutes, and, under favorable conditions, an enzyme having nearly the original activity can be obtained.

One should expect, therefore, that after separation of the excess of low molecular weight components (TPP and $Mg^{2\oplus}$), the holoenzyme would dissociate into its components again. The pure holoenzyme can be easily separated from the low molecular weight components (TPP and $Mg^{2\oplus}$) by filtration of the recombination reaction mixture through a molecular sieve (Sephadex G 25). It shows no decrease in activity due to dissociation [8] (Sephadex test).

1. Recombination and Stationary Phases

The quantity of holoenzyme formed by recombination of the components can be quickly and quantitatively determined from its catalytic activity by optical methods [11]. The acetaldehyde formed in the reaction is reduced to ethanol by reduced nicotinamide-adenine dinucleotide (DPNH) with alcohol dehydrogenase (ADH) as an auxiliary enzyme, and the consumption of DPNH is measured at 366 nm.

$$\text{Pyruvate} \xrightarrow{\text{PDC}} \text{Acetaldehyde} \underset{\text{DPNH}}{\overset{\text{ADH}}{\rightleftharpoons}} \text{Ethanol}$$

The use of a large excess of auxiliary enzyme and reducing agent (DPNH) shifts the rate-determining step into the PDC part of the enzyme chain and prevents feedback effects of the reaction product on the PDC.

The curves of extinction value against time (Fig. 1) show two characteristic phases [8]. In the first phase, the catalytic activity continuously increases (curved part of the graphs, recombination phase). In the second phase (linear part, recombination phase), the constant final rate has been reached and recombination to form the holoenzyme is practically ended.

The time occupied by the recombination phase depends on the nature of the metal ion built into the enzyme complex. The increase in the recombination rate in the order Mg < Co < Mn < Ca corresponds to the order of increasing complexing rates reported by *Eigen* and *Hammes* [12].

The stationary activity of the enzyme, on the other hand, is independent of the metal ion, as is shown by the fact that the linear parts of the curves $(dE/dt)_{max}$ are parallel. Thus the metal ion bound in the holoenzyme has no influence on the rate-determining step of the enzyme reaction.

The metal ion determines the stability of the holoenzyme complex. Though the Ca–PDC and Mg–PDC complexes have the same catalytic activity, the former dissociates completely into its components on filtration

[7] *E. Steyn-Parvé* and *H. G. K. Westenbrink*, Z. Naturforsch. *15*, 1 (1944).

[8] *A. Schellenberger, K. Winter, G. Hübner, R. Schwalberger, D. Helbig, S. Schumacher, R. Thieme, G. Bouillon,* and *K.-P. Rädler*, Hoppe-Seylers Z. physiol. Chem. *346*, 123 (1966).

[9] *A. V. Morey* and *E. Juni*, Bacteriolog. Proc. *1965*, 86 (P 78).

[10] *J. Ullrich, J. H. Wittorf,* and *C. J. Gubler*, Biochim. biophysica Acta *113*, 595 (1966).

[11] *E. Holzer, H.-D. Söling, H.-W. Goedde,* and *H. Holzer* in *H. U. Bergmeyer*: Methoden der enzymatischen Analyse. Verlag Chemie, Weinheim/Bergstr. 1962, p. 602ff.

[12] *M. Eigen* and *G. Hammes*, Advances in Enzymol. *25*, 1 (1963).

through Sephadex G25 [8], whereas the magnesium complex remains intact (Table 1). The rate of formation and the stability of the holoenzyme are thus independent of each other. They obey the laws of coordination chemistry, but do not affect the catalytic activity of the PDC.

Table 1. Influence of the metal ion and of structural changes in the coenzyme on the stability of the PDC complex. The recombination mixtures were separated on a Sephadex G 25 column after an incubation time of 5 minutes (for experimental details see [13]).

Coenzyme or analogue (Pyrophosphates)	Metal ion M^{2+}	% loading of apoenzyme with coenzyme or analogue after Sephadex filtration referred to TPP = 100 %	Ref.
Thiamine	Mg	100	[13]
Thiamine	Ca	0	[8]
Thiamine	—	0	
4'-Hydroxy-4'-deamino-T [a] (Hydroxy-T)	Mg	100	[13]
Hydroxy-T-	—	6	[13]
N-Methyl-T	Mg	1	[13]
2-Methyl-T	Mg	1	[8]
2-(1-Hydroxyethyl)-T	Mg	16 [b]	[8]
4-Nor-T	Mg	4	[14]
6'-Methyl-4-nor-T	Mg	100	[14]
6'-Methyl-T	Mg	44	[13]
6'-Methyl-4'-hydroxy-4'-deamino-T	Mg	26	[13]
N-1-Pyridine analogues	Mg	6	[15]
Pyrithiamine [c]	Mg	3	[13]
2'-Ethyl-2'-nor-T	Mg	> 90	[8]
4-Ethyl-4-nor-T	Mg	> 90	[8]

[a] T = thiamine.

[b] The activity still present is due to contamination with TPP.

[c] 2-Methyl-1-(4-amino-2-methyl-5-pyrimidinylmethyl)-3-(2-hydroxyethyl)pyridinium chloride.

2. Recombination Kinetics and the Rate-determining Step

We used $Mg^{2\oplus}$ ions in the following investigations, since these ions give an easily measurable recombination rate.

The amount of free apoenzyme (apo-PDC_f) at time t can be calculated from the slope of the extinction-time curve (Fig. 1). It can be seen in the case of the $Mg^{2\oplus}$ curve that for $dE/dt = 0$, the concentration of apo-PDC_f is equal to the initial concentration, whereas for $(dE/dt)_{max}$ (stationary rate) there is practically no free apoenzyme. The difference between the slope at time t and the maximum slope

$$(dE/dt)_{max} - (dE/dt)_t = C[\text{Apo-PDC}_f]_t$$

is proportional to the concentration of free apoenzyme at time t.

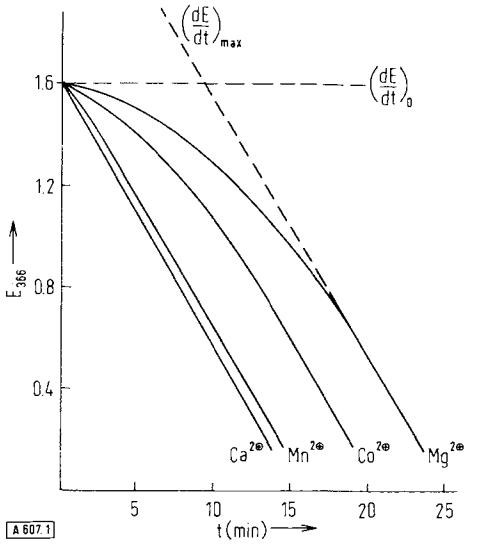


Fig. 1. Influence of metal ions on the recombination rate and the stationary rate for PDC at pH = 6.6 (for details see [8]).

When the concentrations of TPP, $Mg^{2\oplus}$, and pyruvate are constant, as is generally the case in view of the considerable excess of all three components over the apoenzyme, the recombination of the enzyme is a pseudo-first order reaction with respect to the apo-PDC_f [7, 16]. The rate equation for the recombination is then

$$v = -\frac{d[\text{Apo-PDC}_f]}{dt} = -\frac{d((dE/dt)_{max} - (dE/dt)_t)}{dt} = \bar{k}\,[\text{Apo-PDC}_f] \qquad (2)$$

where $\bar{k}$ is a function of the TPP, $Mg^{2\oplus}$, and pyruvate concentrations at constant pH and constant temperature:

$$\bar{k} = f([\text{TPP}],\ [Mg^{2+}],\ [\text{pyruvate}])$$

If the TPP concentration is varied while the $Mg^{2\oplus}$ and pyruvate concentrations are kept constant, the corresponding $\log((dE/dt)_{max} - (dE/dt))$/time curves give $\bar{k}$ as a function (k') of the TPP concentration

$$\bar{k}_{[Mg^{2\oplus}],\ [\text{pyruvate}]} = f([\text{TPP}]) = k'$$

A plot of k' against the TPP concentration gives curves such as are shown in Fig. 2 for two $Mg^{2\oplus}$ concentrations.

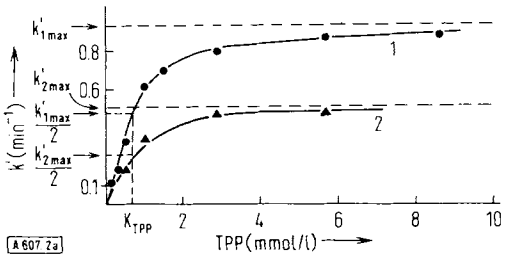
The rate of recombination increases with increasing TPP concentration up to a value at which all the TPP-binding sites on the apoenzyme are saturated. Provided that the rate constant for the formation of the apo-PDC–TPP binary complex is much greater than k', the TPP concentration at which the rate reaches half its maximum value is, according to the Michaelis-Menten relationship, equal to K_{TPP}, *i.e.* the decomposition constant of the apo-PDC–TPP binary complex. This value of K_{TPP} (0.65×10^{-3}) is independent of $Mg^{2\oplus}$ concentration (Fig. 2a).

[13] *A. Schellenberger, V. Müller, K. Winter*, and *G. Hübner*, Hoppe-Seylers Z. physiol. Chem. *344*, 244 (1966).

[14] *A. Schellenberger, I. Heinroth*, and *G. Hübner*, Hoppe-Seylers Z. physiol. Chem. *348*, 506 (1967).

[15] *A. Schellenberger, K. Wendler, P. Creutzburg*, and *G. Hübner*, Hoppe-Seylers Z. physiol. Chem. *348*, 501 (1967).

[16] *A. Schellenberger* and *G. Hübner*, Hoppe-Seylers Z. physiol. Chem. *348*, 491 (1967).



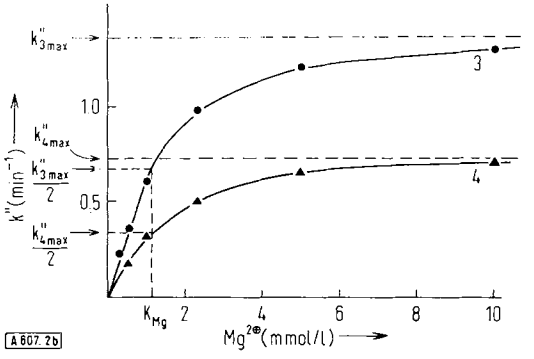


Fig. 2. Dependence of the recombination rate constant on the concentrations of TPP (k', Fig. 2a) and of Mg (k'', Fig. 2b) at pH 6.15. Concentrations: $Mg^{2\oplus}$ = 1 mM (curve 1), 0.5 mM (curve 2); TPP = 1 mM (curve 3); 0.5 mM (curve 4); pyruvate 34.3 mM.

In the same way, when the $Mg^{2\oplus}$ concentration is varied at constant TPP and pyruvate concentrations

$$\bar{k}_{[TPP],\ [pyruvate]} = f([Mg^{2\oplus}]) = k''$$

the dissocation constant of the apo-PDC–$Mg^{2\oplus}$ binary complex (K_{Mg} = 1.13×10^{-3}) is found as a quantity that is independent of the TPP concentration (Fig. 2b).

Thus the two primary steps in the recombination, *i.e.* the addition of TPP and $Mg^{2\oplus}$ to the active center of the apoenzyme, do not affect each other.

The dependence of the recombination rate constant $\bar{k}$ on the pyruvate concentration

$$\bar{k}_{[TPP],\ [Mg^{2\oplus}]} = f([pyruvate]) = k'''$$

is shown in Figure 3.

A recombination was started in the absence of substrate and the substrate was added after the times indicated in Fig. 3. From the parallel curves obtained after the introduction of pyruvate, extrapolation to the time at which the pyruvate

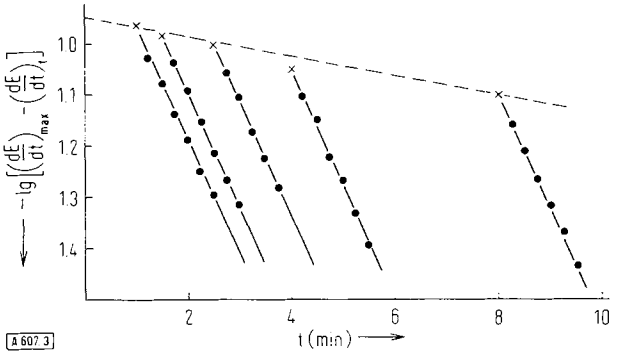


Fig. 3. $\mathrm{Log}((dE/dt)_{max}-(dE/dt)_t))$/time curves for the recombination of PDC after delayed addition of pyruvate. Temp. 25 °C, pH = 6.15 [16].

was added gave the values of $\log((dE/dt)_{max}-(dE/dt)_t)$ indicated by x. The resulting straight line corresponds to the rate of recombination of the enzyme in the absence of substrate. The recombination rate constant when pyruvate concentration is 0 can be calculated from the slope of this line, the value obtained being 4.36×10^{-2} min^{-1}.

The rate constant k''' = 5.25×10^{-1} min^{-1} obtained from the continuous lines (pyruvate concentration = 3.43×10^{-2} M) is one order of magnitude greater.

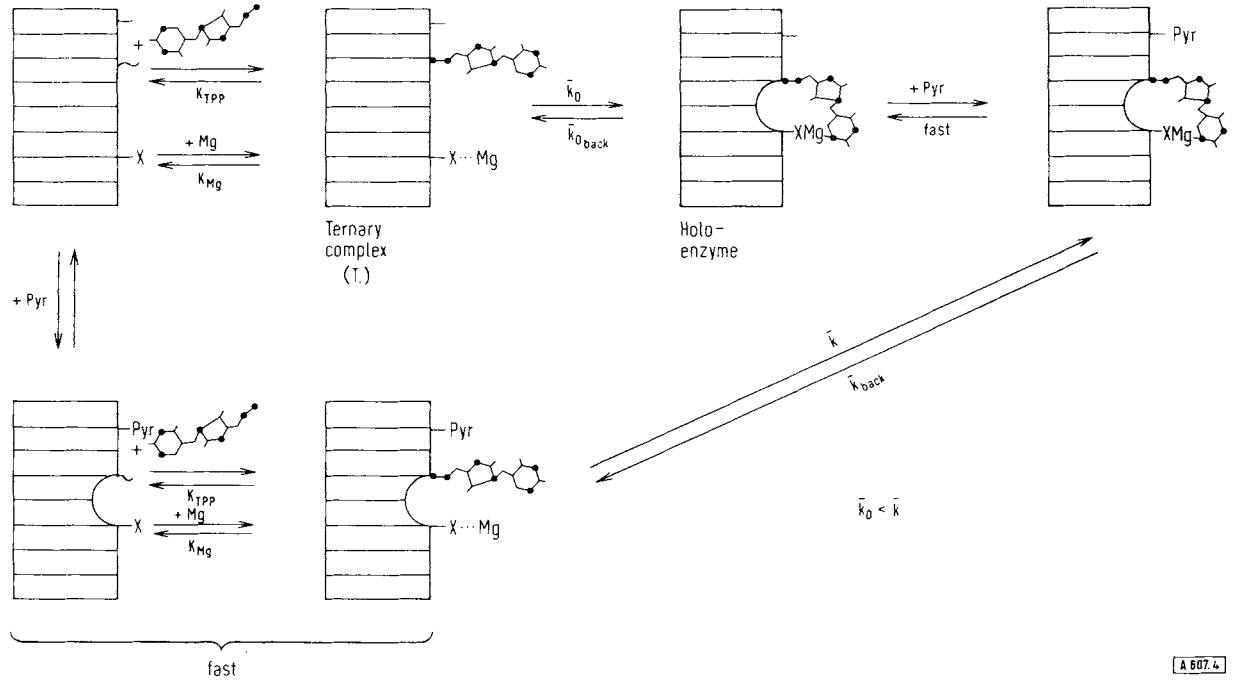


Fig. 4. Recombination scheme for PDC (active center) in the presence and absence of substrate. X: bonding site of the metal ion; ~: bonding center (basic) for the attachment of the pyrophosphate residue of TPP; —: position of substrate bonding (SH) $\bar{k}_0/\bar{k}_{0\ back}$: recombination in the absence of pyruvate (Pyr).

Variation of the pyruvate concentration at constant TPP and $Mg^{2\oplus}$ concentrations and comparison of the resulting curves with the pyruvate-dependence of the enzyme activity (stationary rate) showed the following[16]:

1. There is no preceding substrate-charging equilibrium controlling both the recombination and the stationary process.
2. The two primary equilibria between TPP and apo-PDC and between $Mg^{2\oplus}$ and apo-PDC are independent of the substrate concentration.

The mutually independent and relatively fast additions of TPP and of $Mg^{2\oplus}$ to the apoenzyme are followed by the formation of the thermodynamically stable ("quasi-irreversibility") holoenzyme complex, which is the rate-determining reaction ($\bar{k}$).

It could be shown by the Sephadex method described above, not only that $Mg^{2\oplus}$ ions are required for the stable bonding of apo-PDC to TPP (Table 1), but also that firm combination of $Mg^{2\oplus}$ ions with the apoenzyme takes place only in the presence of TPP[16]. Since no stable coordinate bonds could be detected between TPP and $Mg^{2\oplus}$, the thermodynamically stable holoenzyme complex[*] can only be formed by the simultaneous participation of all three components.

The "quasi-irreversibility" of the holoenzyme formation can thus be explained as a kinetically controlled equilibrium between the "cyclizable" ternary complex and the cyclized ("engaged") holoenzyme complex (Fig. 4). The concentration of the ternary complex is controlled *via* the two primary equilibria (K_{TPP} and K_{Mg}).

3. Formulae for the Recombination Kinetics[16]

The recombination rate, *i.e.* the rate of disappearance of apo-PDC$_f$ $\begin{pmatrix} A \\ \vdots \\ A' \end{pmatrix}$, is proportional to the concentration of "cyclizable" ternary product $\overset{A-TPP}{\underset{A'-Mg}{\vdots}}$ (T.):

$$v = -\frac{d\left[\begin{smallmatrix} A \\ \vdots \\ A' \end{smallmatrix}\right]}{dt} = \bar{k}\left[\begin{smallmatrix} A\text{-}TPP \\ \vdots \\ A'\text{-}Mg \end{smallmatrix}\right] \equiv \bar{k}\,[T.];\ \begin{smallmatrix} A \\ \vdots \\ A' \end{smallmatrix} \equiv \text{Apo-PDC}_f \quad (3)$$

The condition deduced from Fig. 2 that K_{Mg} and K_{TPP} do not affect each other can be introduced into the calculation *via* the following equilibria

$$\begin{smallmatrix} A \\ \vdots \\ A' \end{smallmatrix} + TPP \overset{K_{TPP}}{\rightleftharpoons} \begin{smallmatrix} A\text{-}TPP \\ \vdots \\ A' \end{smallmatrix}$$

$$\begin{smallmatrix} A \\ \vdots \\ A'\text{-}Mg \end{smallmatrix} + TPP \overset{K_{TPP}}{\rightleftharpoons} \begin{smallmatrix} A\text{-}TPP \\ \vdots \\ A'\text{-}Mg \end{smallmatrix}$$

$$\left(\begin{smallmatrix} A \\ \vdots \\ A' \end{smallmatrix} + \begin{smallmatrix} A \\ \vdots \\ A'\text{-}Mg \end{smallmatrix}\right) + TPP \overset{K_{TPP}}{\rightleftharpoons} \left(\begin{smallmatrix} A\text{-}TPP \\ \vdots \\ A' \end{smallmatrix} + \begin{smallmatrix} A\text{-}TPP \\ \vdots \\ A'\text{-}Mg \end{smallmatrix}\right)$$

Similar equilibria exist for K_{Mg}. Provided that [TPP] and [Mg] $\gg$ [apo-PDC$_f$], [T.] can be calculated from the resulting mass-action equations and correlated with the known quantity of apoenzyme used.

[*] We were able to confirm [16] the stability of the holoenzyme toward ethylenediaminetetracetic acid as described by *Juni* [9].

$$\left[\begin{smallmatrix} A \\ \vdots \\ A_0' \end{smallmatrix}\right] = \left[\begin{smallmatrix} A \\ \vdots \\ A' \end{smallmatrix}\right] + \left[\begin{smallmatrix} A\text{-}TPP \\ \vdots \\ A' \end{smallmatrix}\right] + \left[\begin{smallmatrix} A \\ \vdots \\ A'\text{-}Mg \end{smallmatrix}\right] + \left[\begin{smallmatrix} A\text{-}TPP \\ \vdots \\ A'\text{-}Mg \end{smallmatrix}\right]$$

One obtains

$$[T.] = \left[\begin{smallmatrix} A \\ \vdots \\ A_0 \end{smallmatrix}\right] \cdot \frac{[TPP]}{K_{TPP}+[TPP]} \cdot \frac{[Mg]}{K_{Mg}+[Mg]}$$

Insertion of [T.] in eq. 3 gives the desired rate equation for the recombination[*]

$$v = \bar{k}\left[\begin{smallmatrix} A \\ \vdots \\ A_0 \end{smallmatrix}\right] \frac{[TPP]}{K_{TPP}+[TPP]} \cdot \frac{[Mg]}{K_{Mg}+[Mg]} \quad (4)$$

Since the last two expressions in this equation must be $\leqslant 1$, the maximum recombination rate

$$v_{max} = \bar{k}\,[\text{Apo-PDC}_f] \cdot f;\ f = 1$$

is obtained when the TPP and $Mg^{2\oplus}$ concentrations are much greater than the order of magnitude of the two constants K_{TPP} and K_{Mg} ($\approx 10^{-3}$).

Though the $Mg^{2\oplus}$ concentration under physiological conditions is approximately of the same order of magnitude as K_{Mg}, the TPP concentration is much lower ($\approx 10^{-5}$ M), provided that there are no regions with greatly enriched TPP contents. Thus v_{max} decreases at least by a factor of $f \approx 10^{-3}$. It may therefore be assumed that TPP and $Mg^{2\oplus}$ are incorporated into the enzyme during the synthesis of the protein component on the ribosomes. Attempts to isolate the holoenzyme from the reaction mixture consisting of equivalent quantities of apo-PDC, metal ion, and TPP in accordance with eq. 1 must fail, despite the high thermodynamic stability of the holoenzyme, because of the order of magnitude of f ($\approx 10^{-8}$). Eq. 4 therefore provides the mathematical explanation of the "quasi-irreversibility riddle".

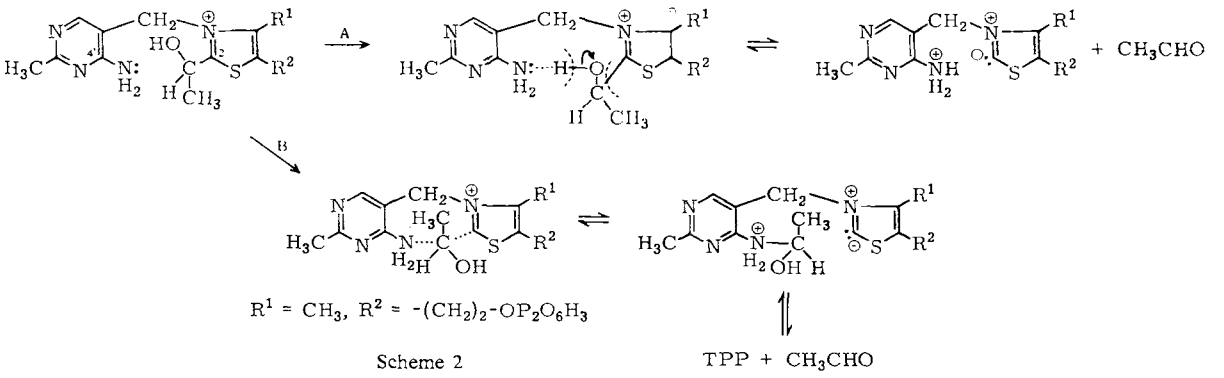
II. Mechanism of Action of the Enzyme

1. Model Experiments

In the investigation of enzyme mechanisms, model studies are still making important contributions to the determination of kinetic and thermodynamic parameters, owing to the fact that the nature of the protein component is unknown in most cases. In these studies it is possible to use very simple models, whose chemical characterization is easy, as was done by *Langenbeck* and his students. Models of this type led in 1933 to the fundamental discovery that the substrate and the catalyst can also react by way of covalent bonds[17].

[*] This equation is valid in principle for all reactions in which a macromolecule reacts with two different substrates at two positions that do not affect each other (inductively or sterically), the added residues then reacting with each other in the rate-determining reaction.

[17] *W. Langenbeck*, Ergebn. Enzymforsch. *2*, 314 (1933).



Scheme 2

Scheme 2. Extended model views of the decarboxylation of α-keto acids. Route A: general base catalysis, Route B: S_N2 reaction.

On the other hand, it is often difficult to decide whether observations made in model experiments are applicable to the enzyme process. For example, primary amines can bring about catalytic decarboxylation of α-keto acids, so that *Langenbeck* regarded these for a long time as decarboxylase models ("decarboxylators") [18]. However, it was finally found, partly by the work of *Langenbeck* and his students themselves, that neither the electronic situation of the amino group in thiamine [19] nor the chemical behavior of the α-imino acids detected as intermediates allowed any comparison to the enzyme process [20].

Ugai [3] recognized in 1951 that thiazolium salts can also decarboxylate α-keto acids. The mechanism proposed by *Breslow* [5] (Scheme 1) already contains essential elements of the enzyme process, but the results obtained in the model test and in the enzyme test differ, not only quantitatively, but also qualitatively (Table 2).

Table 2. Comparison of the catalytic activity of thiamine and thiamine analogues in the model test after *Mizuhara* (see Scheme 1) [4] with the coenzyme activity of the corresponding pyrophosphates [13,21].

Compound	Catalytic activity in model test. Acetoin formation in % from acetaldehyde	pyruvate	Coenzymatic activity of the pyrophosphate in %
Thiamine (T)	100	100	100
N-Methyl-T	165	96	0
N,*N*-Dimethyl-T	281	74	0
4′-Hydroxy-4′-deamino-T	65	15	0
6′-Methyl-T	–	18 [22]	0
2-Methyl-T	0	0	0

The only case in which the results are the same is that of 2-methylthiamine, which is blocked at the common reaction center.

A further approximation of the reactions of the model catalysts to the enzyme process was achieved by imitation of the pyrimidine part of the TPP molecule by the addition of organic bases such as alkoxide, imidazole, 2-aminopyridine, and 4-amino-2-methyl-5-hydroxymethylpyrimidine to the thiazolium catalysts [13]. These systems were the first enzyme models to produce acetaldehyde in detectable quantities. The experiments led us to assume that the elimination of aldehyde, which must be formulated for the model as a general base catalysis or as an S_N mechanism [13] (Scheme 2) takes place intramolecularly in the pyruvate decarboxylase under certain steric conditions, which will be discussed in Section II.4.

To support these views, the model catalysts had to be approximated still further to the TPP molecule. The compounds used differ from the natural prototype only in a few regions of the molecule. If the arrangement of the bonding groups of the analogue model corresponds to the specific situation in the apo-PDC component, the model can be tested enzymatically and under "physiological conditions" (pH, medium, concentration, temperature, *etc.*).

2. TPP Analogues as "Coenzyme Models"

The investigations on TPP analogues showed that some regions of the coenzyme can be changed without loss of the coenzyme activity, while other parts are highly constitution-specific. By systematic variation of the TPP molecule, it is possible in this way to study the bonding and function mechanism, provided that reliable and efficient methods are available for the characterization of the analogues.

Methods that have proved useful in the case of PDC are:

1. *The activity test*: The analogue is introduced during the recombination instead of TPP. If it is incorporated into the apoenzyme, one obtains information about the coenzyme activity of the analogue. Inactivity in this test can result from two causes: the analogue may not be functionally bound by the apoenzyme, or the course of the reaction on the analogue may be disturbed.

2. *The simultaneous test* [23]: An excess of TPP and analogue compete in a molar ratio of 1:1 for the bonding centers on the apoenzyme. Analogues that have no coenzyme activity, whose bonding to the apoenzyme in the presence of metal ions is irreversible and whose recombination proceeds as rapidly as the recombination with TPP, reduce the activity of the recombination mixture by half. If the analogue has no

[18] *W. Langenbeck* and *R. Hutschenreuter*, Z. anorg. Chem. *188*, 1 (1930).

[19] *A. Schellenberger*, Diploma Thesis, Universität Halle/Saale 1952; *K. G. Stern* and *J. L. Melnick*, J. biol. Chemistry *131*, 615 (1939).

[20] *A. Schellenberger*, *G. Osske*, and *W. Rödel*, Hoppe-Seylers Z. physiol. Chem. *329*, 149 (1962).

[21] *V. Müller*, Dissertation, Universität Halle/S. 1966.

[22] *J. Biggs* and *P. Sykes*, J. chem. Soc. (London) *1961*, 2595.

[23] *A. Schellenberger* and *K. Winter*, Hoppe-Seylers Z. physiol. Chem. *344*, 16 (1966); *322*, 164 (1960).

"affinity" for the active center, the apoenzyme would be fully charged with TPP, and full enzyme activity would be achieved.

3. *The Sephadex sieve test* [13]: Like the simultaneous test, this method (Table 1) provides information about the stability of the bonds in the holoenzyme. In contrast to the simultaneous test, however, the dissociation of the thermodynamically more or less stable holoenzyme-analogue complex is recorded. The values obtained by this method are more definite (they belong in principle to only one equilibrium (k'/k'_{back} [*])) than those obtained in the simultaneous test by competition of several equilibria (K_{TPP}, $K_{TPP'}$, k/k_{back}, and k'/k'_{back}).

4. *Investigations with [1-^{14}C]- and [2-^{14}C]-labeled pyruvate* [14]: The ability of the analogue to decarboxylate and to eliminate aldehyde can be determined separately by comparative short-term experiments with differently labeled substrate, by a method based on that described by *Holzer* [1] (*e.g.* Fig. 5).

The results obtained in the activity test and in the simultaneous test on the TPP analogues are shown in Table 3.

Table 3. Coenzyme activity and inhibitor action (simultaneous test) on TPP analogues (for experimental details see [23]).

Coenzyme or analogue	Coenzyme activity (steady state value) (%)	Reduction of enzyme activity in simultaneous test (%)	Ref.
Thiamine	100	—	
4'-Hydroxy-4'-deamino-T [a]	0	52 ± 7	[13]
N-Methyl-T	0	25 ± 3	[13,23]
N,*N*-Dimethyl-T	0	22 ± 3	[23]
Deamino-T	0	30 ± 5	[13,24]
2-Methyl-T	0	0	[8]
2-(1-Hydroxyethyl)-T	0	0	[8]
6'-Methyl-T	0	10 ± 3	[14]
6'-Methyl-4'-hydroxy-4'-deamino-T	0	2 ± 1	[13,14]
6'-Methyl-4-nor-T	22	—	[14]
4-Nor-T	24	25 ± 4	[14]
4-Ethyl-4-nor-T	32	4 ± 1	[8]
2-Methyl-4-ethyl-4-nor-T	0	18 ± 5	[8]
N-1-Pyridine analogue	13	11 ± 2	[15]
N-3-Pyridine analogue	0	0	[15]
Pyrithiamine [b]	0	0	[8]
2'-Ethyl-2'-nor-T	48	11 ± 2	[13]
5-(3-Hydroxypropyl)-5-nor-T	0	22 ± 3	[8]

[a] T = thiamine.

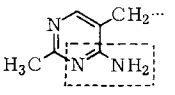
[b] See footnote [c] under Table 1.

3. Blockage of the Active Centers

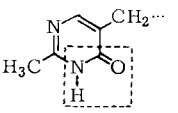
In the most favorable case, TPP analogues in which only the groups having catalytic function are blocked should still exhibit full binding capacity for apo-PDC. They should have no coenzyme activity, should give 50 % inhibition in the simultaneous test, and should not be separated from the holoenzyme complex on filtration through Sephadex molecular sieves. The only case in which this has been true so far is that of 4'-hydroxy-4'-deamino-TPP (hydroxy-TPP) *(4)* (cf. Tables 1 and 3).

[*] The primed constants belong to the coenzyme analogues.

[24] *A. Schellenberger, W. Rödel,* and *H. Rödel,* Hoppe-Seylers Z. physiol. Chem. *339*, 122 (1964).



TPP *(1)*



Hydroxy-TPP *(4)*

Since hydroxy-TPP, like TPP, forms stable bonds to apo-PDC only in the presence of metal ions (Table 1), the bonding between this analogue and apo-PDC may be assumed to be substantially the same as for the natural coenzyme. The amidine and amide regions surrounded by a dotted line are thus of no importance to the coenzyme-apoenzyme bonding.

According to the views outlined in Scheme 1, only C-2 of the thiazolium ring should be required for the decarboxylation of the substrate. However, the holoenzyme analogue prepared from hydroxy-TPP does not produce acetaldehyde (Table 3). This led to the assumption that the 4'-amino group is involved in the release of the aldehyde molecule (Scheme 2). Experiments with labeled pyruvate have confirmed the function of the 4'-amino group as a second reaction center (Fig. 5) [13]. After the addition to C-2, which can evidently take place without the operation of the apoenzyme (Fig. 5c), the pyruvate molecule is also decarboxylated by the hydroxy-TPP holoenzyme (Figs. 5b and 5d) (but as the optical test clearly shows, no acetaldehyde is eliminated).

In agreement with this result, no TPP analogue has so far been found in which the coenzyme activity is

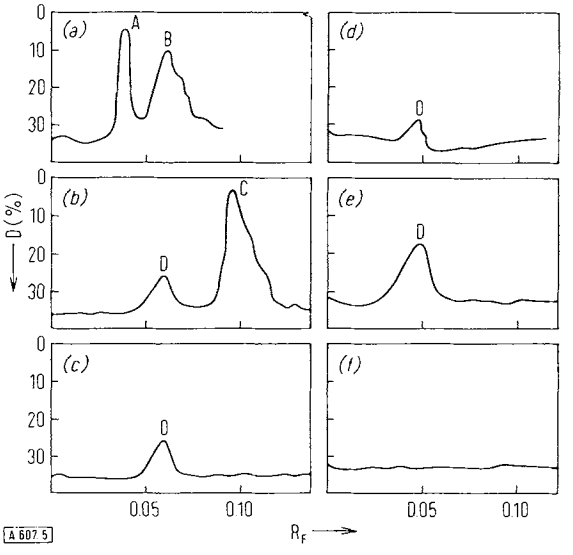


Fig. 5. Detection of the enzymatic formation of the "active acetaldehyde" analogues of hydroxy-TPP (autoradiogram of the reaction mixtures after separation by thin layer chromatography) [13].

A = active acetaldehyde; B = active pyruvate (after *Holzer*); C = 4'-hydroxy-4'-deamino-2-(1-hydroxyethyl)thiamine pyrophosphate; D = non-enzymatically formed condensation product of pyruvate and the 2-carbeniate atom of TPP.

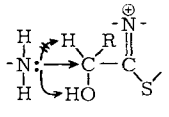
Mixture	Apoenzyme	Coenzyme	Pyruvate
(a)	+	TPP	[2-^{14}C]
(b)	+	Hydroxy-TPP	[2-^{14}C]
(c)	—	Hydroxy-TPP	[2-^{14}C]
(d)	+	Hydroxy-TPP	[1-^{14}C]
(e)	+	*N*-Methyl-TPP	[2-^{14}C]
(f)	+	2-Methyl-TPP	[2-^{14}C]

obtained when the amino group is modified [23]. However, of the compounds mentioned in Tables 1 and 3, only hydroxy-TPP has the full capacity for bonding to the apoenzyme. This is due to steric factors, which will be discussed in the following section.

As expected, the substitution of the decarboxylation center (2-methyl-TPP) also leads to an analogue having no coenzyme activity. However, the results of the simultaneous test and of the Sephadex test show that the 2-methyl group blocks the recombination process, so that in this case the activity test demonstrates not the disturbance of catalysis, but the hindrance of recombination [8]. The same is true of the intermediate product 2-hydroxyethyl-TPP [8]. When used instead of TPP, this acts as a TPP analogue for which recombination is hindered.

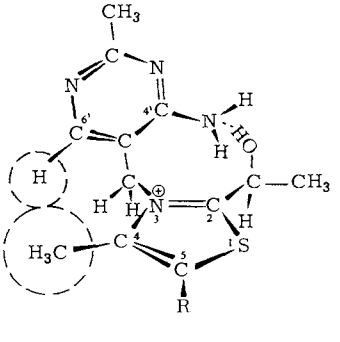
4. Stereochemistry of the Reaction Centers

The 4′-amino group can fulfil its catalytic function, *i.e.* the cleavage of the "active" aldehyde bond, only if it is in direct contact with the aldehyde portion to be released. Of the three possibilities shown in Scheme 3, the interaction of the free electron pair on the amino group with the very stable (almost no H–D exchange below pH = 8 [25]) α-C–H bond is unlikely so that only direct contact with the α-C atom (S_N mechanism), which carries a partial positive charge owing to the action of the hydroxyl group and the thiazolium ring, or with the hydroxyl proton (base catalysis) need be considered (Scheme 3).



Scheme 3. Three possibilities for the cleavage of the "active" aldehyde.

In both cases, the Stuart model shows that the methyl group in position 4 is almost in contact with the 6′-H atom (Fig. 6). The introduction of a methyl group into position 6′ (6′-methyl-TPP) leads to twisting of the molecule about the CH_2 bridge, which results primarily in separation of the two reaction centers, but also in a shift of the bonding groupings of the coenzyme [8, 14].



R = $-(CH_2)_2-O-P_2O_6H_3$

[A 607.6]

Fig. 6. Active acetaldehyde (redrawn Stuart model) in the position in which the two reaction centers are closest together (base catalysis mechanism A).

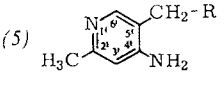
The intramolecular catalysis mechanism is accordingly much more sensitive to steric deformations than the bonding structure with the apoenzyme. The 6′-methylated TPP analogue has absolutely no enzyme activity, but still exhibits slight affinity for the apoenzyme (Table 3, simultaneous test). Hydroxy-TPP, on the other hand, completely loses its inhibiting action in the simultaneous test when methylated in position 6′. The twisting due to the 6′-methyl group is eliminated if the 4-methyl group is removed. 6′-Methyl-4′-nor-TPP exhibits coenzyme activity, and is not split off by Sephadex filtration [14]. 4-Demethyl-TPP (4-nor-TPP) is also active, but unlike the 4- and 6′-methyl analogues it is only loosely bound by the apoenzyme [14]. It follows that the methyl group in position 4 or 6′ takes part in the bonding between the coenzyme and the apoenzyme.

One might assume that, for steric reasons, the apoenzyme is capable of hydrophobic interaction with only one methyl group, whereas two methyl groups hinder each other in the bonding process. However, this is not so, since 4-ethyl-4-nor-TPP exhibits coenzyme activity, and is firmly bound by the apoenzyme (Tables 1 and 3 [8]). (A 4-ethyl group actually increases the affinity of 2-methyl-TPP (the recombination of which is hindered) for the apoenzyme to such an extent that it competes with TPP in the simultaneous test.)

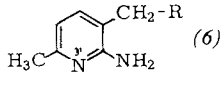
The equivalence of positions 4 and 6′ is one of the most important pieces of evidence in favor of the two-center mechanism based on intramolecular interaction. The corresponding conformation of the TPP molecule bound in the active center of the PDC is not identical with the structure found by *Pletcher* and *Sax* [26] in X-ray studies on TPP crystals.

5. The Function of the Pyrimidine N Atoms and the S Atom

The high affinity of hydroxy-TPP (which exists in the lactam form) for the apoenzyme can be deduced from the fact that the part of the molecule around N-3 is not directly involved in the bonding. This was confirmed by investigation of the two pyridine analogues *(5)* (*N*-1-pyridine analogue) and *(6)* (*N*-3-pyridine analogue).



(5)



(6)

The *N*-1-pyridine analogue exhibits distinct coenzyme activity as the pyrophosphate [15], whereas the pyrophosphate of the *N*-3-pyridine analogue has no coenzyme activity and is not bound by the apoenzyme,

[25] *J. Ullrich* and *A. Mannschreck*, European J. Biochem. *1*, 110 (1967); *J. J. Mieyal, R. G. Votaw, L. O. Krampitz*, and *H. Z. Sable*, Biochim. biophysica Acta *141*, 205 (1967).

[26] *J. Pletcher* and *M. Sax*, Science (Washington) *154*, 1331 (1966).

as is shown by the simultaneous test. It follows that the N-3 atom is neither catalytically active nor does it bind the apoenzyme. Mutual effects or tautomeric interaction between the 4′-amino group and the adjacent ring nitrogen atom are obviously also of no importance to the catalysis. However, the stability of the bonding between the coenzyme and the apoenzyme is reduced by the absence of the N-3 atom, as is particularly clear on filtration through Sephadex.

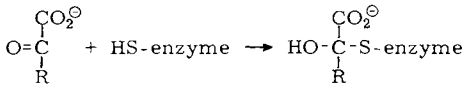
Since 4-aminopyrimidines are preferentially protonated in position 1 [27] it may be assumed that the bonding between N-1′ of the TPP molecule and the apoenzyme takes place through the intermediary of the metal ion, while the pyrophosphate residue, in agreement with the independence of K_{Mg} and K_{TPP}, is bound to the apoenzyme in the primary equilibrium without the assistance of the metal ion (acid-base interaction). This assumption is supported by the fact that unphosphorylated thiamine has no effect on the primary equilibrium TPP-apo-PDC and by the order of magnitude of K_{TPP} (the value 10^{-3} indicates salt-like bonding).

Replacement of the thiazole ring of thiamine by a pyridine ring gives pyrithiamine (2-methyl-1-(4-amino-2-methyl-5-pyrimidinylmethyl)-3-(2-hydroxyethyl)pyridinium halide [28]), whose pyrophosphate has no coenzyme activity and is not bound by the apoenzyme [8]. It thus behaves similarly to the *N*-3-pyridine analogue *(6)*. However, the conclusion that the sulfur also belongs to the binding group in the TPP molecule should be regarded with caution because of the large structural changes.

6. The Course of the Reaction

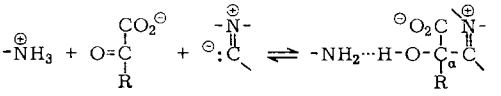
According to the experimental data available at present, the α-keto acids react on the enzyme in three stages: binding of the substrate, irreversible decarboxylation-, and cleavage of the active C–C bond.

Binding of the substrate: Experiments with Sephadex have shown that the pyruvate molecule is relatively strongly bound by the apoenzyme, even in the absence of metal ions. By inhibition experiments using SH reagents and by investigation of the n-π* transition of α-keto acids in the presence of cysteine we have recently been able to demonstrate [29] that this primary bonding of the substrate to the enzyme most probably proceeds *via* formation of a semimercaptal:



The following step is the attachment of the pyruvate molecule to C-2 of the thiazolium ring. According to NMR studies by *Ullrich* and *Mannschreck* [30] and MO calculations by *Pullman* [31], the TPP molecule very probably exists in the carbeniate form at the optimum pH value, a basic group of the active center or the carboxylate group of the substrate possibly favoring the cleavage of the (C-2)-H bond by accepting the proton. The results shown in Figure 5c suggest that the α-keto acid adds to the active form spontaneously, *i.e.* without the assistance of the apoenzyme.

Like the hydration of carbonyl compounds, the condensation is favored by protonation of the carbonyl oxygen. The adjacent 4′-NH_2 group in the protonated form may act as a donor. In this way, the hydrogen bonds required for the following steps would be formed during the binding process, and the new asymmetric α-C atom would be sterically oriented.



The substrate-specificity of yeast-PDC is not particularly pronounced. In addition to pyruvate, numerous β-monoalkylated and dialkylated α-keto acids (including cyclohexylglyoxylic acid) and phenylglyoxylic acid and their *m*- and *p*-substituted derivatives react [32]. According to the results obtained so far, the affinity and the rate of reaction are influenced in opposite directions by the inductive effect of the group in the β-position.

One of the few α-keto acids that are not made to react by the enzyme is glyoxylic acid. Recent investigations by *Hübner* with [^{14}C]-glyoxylic acid have shown that the acid is decarboxylated on the enzyme, but there is no cleavage of the "active" C–C bond, so that the coenzyme is blocked for the acceptance of further substrate molecules. The reason for the blockage of the elimination of aldehyde is described in connection with the models for the C–C cleavage.

Irreversible decarboxylation and stabilization of the α-carbanion (3): Since attempts to synthesize active pyruvate have so far been unsuccessful [33], it is not certain whether the apoenzyme participates in the decarboxylation by interaction with the thiazolium nitrogen or sulfur, or whether the active pyruvate is spontaneously decarboxylated to form active acetaldehyde.

The electron pair remaining after the elimination of CO_2 should (by analogy with the readily decarboxylated β-keto acids) lead to an increase in the bond order of the active bond, and so oppose the subsequent release of aldehyde.This resonance stabilization,which may be regarded as an important reason for the low aldehyde yields obtained with the thiazolium model catalysts, can occur only if the two residues (R,OH) remaining on the α-C atom lie in the same plane as the thiazolium ring.

[27] See, *e.g.*, *S. Mizukami* and *E. Hirai*, J. org. Chemistry *31*, 1199 (1966).

[28] *A. H. Tracy* and *R. D. Elderfield*, J. org. Chemistry *26*, 54 (1961).

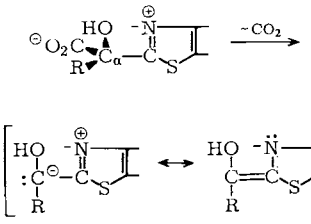
[29] *A. Schellenberger* and *G. Hübner*, Angew. Chem., in press.

[30] *J. Ullrich* and *A. Mannschreck*, Biochim. biophysica Acta *115*, 46 (1966).

[31] *R. L. Collin* and *B. Pullman*, Arch. Biochem. Biophysics *108*, 535 (1964).

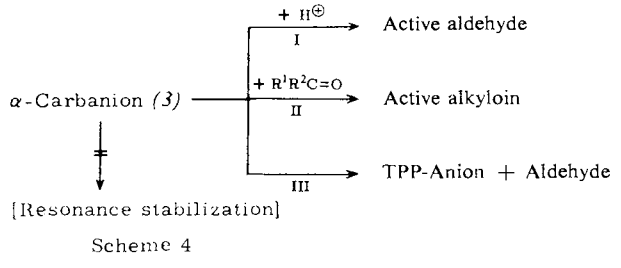
[32] *R. Henkel*, Diploma Thesis, Universität Halle/S. 1967.

[33] *T. Eyles*, *P. Sykes*, and *J. E. Downes*, J. chem. Soc. (London) *1965*, 4265.



Examination of the Stuart model shows that owing to the formation of a hydrogen bond between the amino and hydroxyl groups, the two residues on the α-C atom are practically perpendicular to the plane of the thiazolium ring. This greatly limits the interaction of the free electron pair with the π electrons of the ring and hence also the increase in the bond order of the active bond. Moreover, the stereospecificity and the high basicity of the α-C atom are retained.

Scheme 4 shows the possibilities for the stabilization of the carbanion *(3)*.



Scheme 4

Scheme 4. Possibilities for the stabilization of the carbanion *(3)*.

According to investigations by *Ullrich* and *Mannschreck*, and *Mieyal*, *Votaw*, *Krampitz*, and *Sable*, the α-C–H bond of active acetaldehyde exhibits only a very small H–D exchange below pH = 8 [25]. This suggests a high basicity of the α-carbanion *(3)*, from which one would expect the principal reaction to be immediate protonation [*], with formation of 2-(1-hydroxyethyl)-TPP *(2)* (route I), while the condensation with carbonyl compounds (supplied from the medium) to give the active alkyloin derivatives (route 2) should be an insignificant side reaction. The isotope effect observed in the formation of acetoin in D_2O [34] would thus be explained by a change in the contributions of the two reactions.

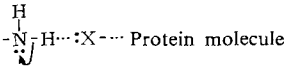
Direct cleavage of the α-carbanion *(3)* with formation of TPP anion and aldehyde (route 3) would be conceivable only if the protonation reaction I were retarded by a proton-free zone in the active center (which, in view of the high basicity of *(3)*, would also exclude the proximity of NH, OH, and related bonds). Even if this were so, it would not appear easy to explain the aldehyde inhibition (which requires an equilibrium that can be influenced *after* the irreversible decarboxylation) and the blockage of the release of aldehyde when hydroxy-TPP is used as the coenzyme or when glyoxylic acid is used as a substrate by means of mechanism III.

Cleavage of the active bond: In an earlier report [13], we formulated the cleavage of the active aldehyde bond as an intramolecular nucleophilic substitution on the α-C atom (Scheme 2, route B) on the basis of model experiments. However, the Stuart model showed that a collinear arrangement of the free orbital of the amino group with the active bond, as required for S_N2-reactions, is not possible. The angle with respect to the axis of the active bond is about 80 °.

On the other hand, sterically favorable conditions would exist for an intramolecular base catalysis (Scheme 2, route A). If the 6′-H atom in the atomic model is brought into contact with the 4-methyl group (cf. Section II.4), the 4′-amino group and the α-hydroxy proton approach each other sufficiently closely for easy formation of a hydrogen bond.

There were two objections to the intramolecular base-catalysis mechanism. Firstly, the basicity of the 4′-amino group is greatly reduced by the pyrimidine ring. Secondly, unless steric factors play a decisive part, *N*-methyl-TPP should have at least the same action as TPP, but this is not the case (Table 3). However, it is found in the Sephadex test, that *N*-methyl-TPP is only weakly bound by the apoenzyme. We regard this as evidence of the close contact of the amino group with the apoenzyme surface, which is evidently essential for the fulfilment of the base-catalytic function.

This presents a new point of view. A sterically and chemically suitable region in the binding center of the apoenzyme forms a hydrogen bond with one of the relatively acidic hydrogen atoms of the amino group, so turning this group out of its original resonance position and making contact with the hydroxyl proton possible.



The basicity of the 4′-amino N atom, and hence its catalytic activity, are increased by the interaction with the apoenzyme. At the same time it becomes clear why the bifunctional N atom becomes inactive as a result of methylation.

When the system is saturated with substrate, the product inhibition of PDC, which according to *Juni* [36] is noncompetitive, becomes active even at very low aldehyde concentrations. It must therefore be assumed that the release of the aldehyde following the irreversible decarboxylation determines the catalytic activity of the enzyme in the stationary state. At very low substrate concentrations, on the other hand, the loading of the enzyme with substrate or the decarboxylation is rate-determining, since in this case the inhibiting action appears only at higher aldehyde concentrations.

[*] The rate of protonation of carbeniate ions can be estimated from the position of the equilibrium and the rate of isotope exchange. For example, in the case of diethyl malonate, for which the exchange is still measurable, the value is of the order of 10^8 mole l^{-1} min^{-1} [35].

[34] *J. Ullrich*, Freiburg/Brsg., personal communication.

[35] *R. G. Pearson* and *R. L. Dillon*, J. Amer. chem. Soc. *75*, 2439 (1953).

[36] *E. Juni*, J. biol. Chemistry *236*, 2302 (1961).

The problems connected with the cleavage of the active bond can be studied on two models, whose function mechanisms have been investigated in detail and exhibit far-reaching analogies with the enzyme mechanism.

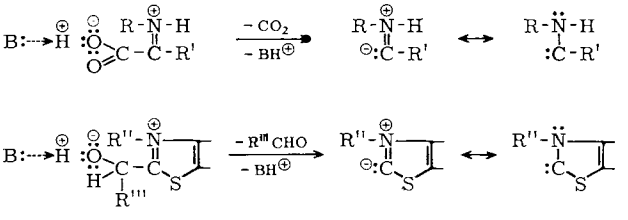
In the first model, the cleavage of the active C–C bond is compared with the decarboxylation of α-imino acids (Scheme 5). It is known that these compounds (unlike the α-keto acids) are readily decarboxylated, the immonium carboxylate form being regarded as the reactive species [37].

Our own work on the behavior of *N*-substituted α-imino acids [38] has shown that the (C-1)–(C-2) cleavage associated with the decarboxylation is mainly favored by the following effects:

1. The residue (CO_2) to be removed is pre-stablized by elimination of the acid proton, so that the release of the pair of bonding electrons, which is accompanied by resonance stabilization of the CO_2 molecule, is favored.

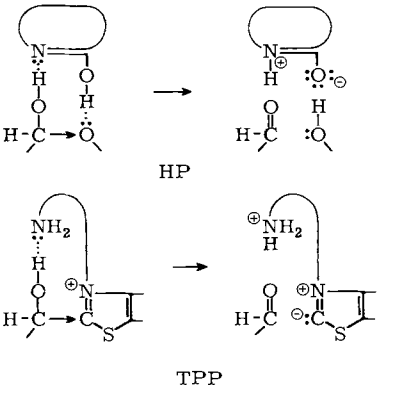
2. The decarboxylating action of the α-immonium group is increased by electron-attracting substituents on the N atom. Thus under identical conditions, the decarboxylation of the *N*-benzylated imino acid is approximately twice as fast as that of the *N*-ethylated imino acid.

Similar conditions are found for the cleavage of the C–C bond in the active aldehyde. The aldehyde molecule to be removed is pre-stablized by proton abstraction, a process that will be described more fully in the discussion of the second model. Moreover, the rate of cleavage is considerably increased by the strongly electron-attracting 4-aminopyrimidine ring on the nitrogen.



Scheme 5. Analogies between the decarboxylation of α-amino acids and the cleavage of the active aldehyde.

The second model is based on the relatively high acidity of the 2-C–H bond in the thiazolium ring, which has repeatedly been confirmed both experimentally [30] and theoretically [31]. There are thus analogies between the mechanism of the intramolecular base catalysis and the base-catalysed dehydration of geminal diols [39] and the base-catalysed cleavage of hemiacetals. This last reaction, which has been extensively studied for the mutarotation of glucose [40] is both acid-catalysed and base-catalysed; 2-hydroxypyridine, in which the acidic and basic groups are fixed in a favorable position for the reaction, has proved to be a particularly effective bifunctional catalyst. The cleavage of the C–O bond is formulated as the rate-determining step (again in analogy to the TPP mechanism) (Scheme 6).



Scheme 6. Comparison of the catalysis of mutarotation by 2-hydroxypyridine (HP) according to *Swain* with the TPP catalysis of the cleavage of active aldehyde. Both reactions are rate-determining.

For a quantitative consideration of the analogies between TPP catalysis and hydration-dehydration equilibria, the equilibrium constants (K_d) collected by *Greenzaid et al.* [41] are shown in Table 4.

Table 4. Equilibrium constants for the dehydration of carbonyl compounds (for investigation methods and errors, see [41]).

Carbonyl compound	K_d
CH_2O	5.0×10^{-4}
CH_3CHO	0.7
CH_3CH_2CHO	1.4
CH_3COCO_2H	0.42
$CH_3COCO_2^{\ominus}$	18.5

If one assumes that the addition of the carbonyl compound to the acidic 2-C–H bond corresponds to hydration and the elimination to dehydration, the following information can be obtained from the K_d values:

1. The reactivity of the undissociated α-keto acid toward anionoid components is higher than that of the corresponding anion, emphasizing the acid catalysis [42] in the addition process (4′-$^{\oplus}NH_3$-catalysis in the substrate addition and aldehyde inhibition).

2. Comparison of the pyruvate ion, which is only weakly hydrated [43] with acetaldehyde, which exists in the hydrate form to the extent of more than 50 %, suggests that the bond to be cleaved in the active acetaldehyde is much more stable than the C–C bond in active pyruvate. Consequently, no reaction on the enzyme is observed without the base-catalytic ac-

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celeration of the release of the aldehyde (hydroxy-TPP).

This observation should be of general importance to catalysis processes involving covalently bonded intermediates. If the original substrate-catalyst bond is strengthened in the course of any reaction on the catalyst or enzyme, a co-catalyst that promotes the cleavage of the reaction product will strongly influence the stationary rate.

3. An extreme position among the aldehydes is occupied by the almost completely hydrated formaldehyde, whose K_d value is lower by about three powers of ten. On the basis of our analogy, therefore, the stability of the bonding of active formaldehyde in the enzyme should be about three powers of ten greater than in the case of active acetaldehyde. This is the reason for the failure of the release of aldehyde to take place when glyoxylic acid is used as the substrate.

I am very grateful to my industrious and dedicated students, and in particular to Dr. K. Winter and Dipl.-Chem. G. Hübner. I am also grateful to Prof. Dr. H.-R. Schütte, who kindly provided laboratory facilities in the isotope laboratory of the Institut für Biochemie der Pflanzen der Deutschen Akademie der Wissenschaften in Halle/Saale.

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Mitochondrial Oxidative Phosphorylation [**]

BY G. SCHATZ [*]

Mitochondria can form ATP from ADP and inorganic phosphate, the required energy being supplied by respiration. This coupled process, which in sufficiently aerated normal animal cells furnishes the bulk of the cellular ATP, is termed oxidative phosphorylation. The overall reaction is intimately associated with the mitochondrial inner membrane and proceeds via a primary high-energy intermediate. This intermediate, in a manner as yet unknown, energizes the anhydride formation between ADP and inorganic phosphate. The coupling between respiration and ATP synthesis is mediated by proteins of the mitochondrial inner membrane which are known as "coupling factors". The mechanism of oxidative phosphorylation is at present being discussed in terms of three hypotheses which are generally referred to as "chemical", "chemiosmotic", and "conformational" hypotheses. None of these hypotheses has as yet been experimentally verified.

Introduction

Respiring cells can couple the energy generated during substrate oxidation to the synthesis of ATP *via* oxidative phosphorylation (reaction (1)).

$$ADP + P_i \xrightarrow{\text{respiration}} ATP \qquad (1)$$

Coupling between respiration and ATP formation has been detected in many microorganisms and higher forms of life and is always associated with, and dependent on, a membrane structure. In respiring bacteria, the enzymes of the respiratory chain and of oxidative phosphorylation are bound to the cell membrane. In nearly all other types of cells they occur, together with the enzymes of the tricarboxylic acid cycle, in characteristically shaped cytoplasmic organelles known as mitochondria. The number of mitochondria per cell is subject to considerable phylogenic variation. One rat-liver cell, for example, contains several thousand mitochondria, whereas certain unicellular algae may have only a single mitochondrion.

The mechanism of oxidative phosphorylation remains unknown although, over the past three and a half decades, it has been investigated in many laboratories [1, 2]. One reason for the failure of these attempts may be that it has not yet been possible to observe the process in a soluble system in the absence of a membrane structure. It thus appears that oxidative phosphorylation is inherently dependent on a membrane, and differs in this respect from most of the biochemical pathways that have so far been elucidated. Another reason has been the incomplete knowledge about the

[*] Dr. G. Schatz
Institut für Biochemie der Universität
Wasagasse 9
A-1090 Vienna (Austria)

[**] The following abbreviations are used: ADP and ATP: adenosine diphosphate and triphosphate; P_i: inorganic phosphate; $NAD(P)^+$ and NAD(P)H: oxidized and reduced nicotinamide-adenine dinucleotide (phosphate).

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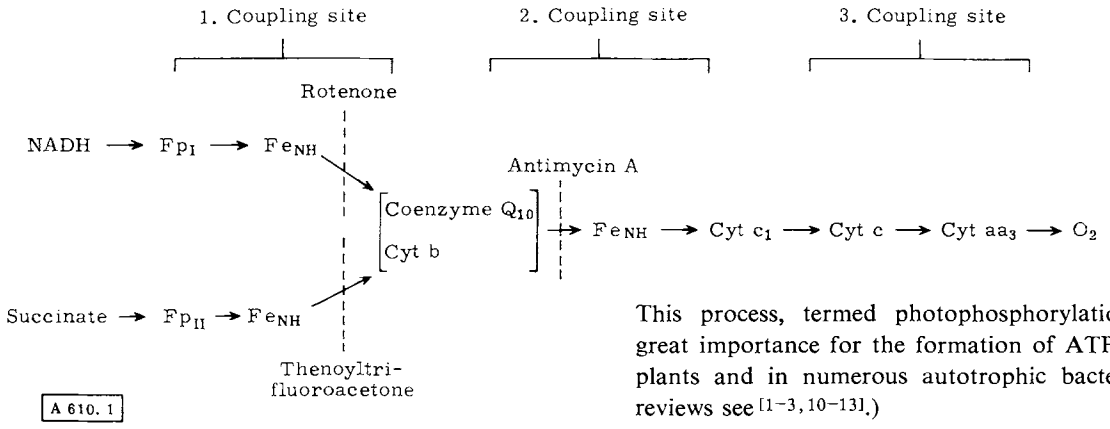


Fig. 1. The respiratory chain of mammalian mitochondria. Fp_I and Fp_{II}: flavoproteins of the NADH and succinate dehydrogenase, respectively; Fe_{NH}: nonheme iron; Cyt aa_3, b,c,c_1: cytochrome aa_3, b,c,c_1. The position of cytochrome b relative to coenzyme Q_{10} is not definitely known. It is also uncertain whether the components sensitive to rotenone [4], thenoyltrifluoroacetone [5], and antimycin A [6] are identical with known respiratory carriers or represent as yet unknown redox components. In mitochondria from *Saccharomyces cerevisiae*, the segment between NADH and cytochrome b appears to lack a coupling site [7, 8], a component sensitive to rotenone [7, 8], as well as nonheme iron involved in electron transport [9]. The broken lines symbolize an inhibition of electron transport.

mitochondrial respiratory chain. While the scheme given in Figure 1 is in agreement with most of the existing data, it has not been verified in all details and is probably incomplete [3].

It is generally assumed that in mammalian mitochondria the transport of one pair of electrons from NADH to oxygen generates a maximum of three molecules of ATP [1, 2]. However, the three "coupling sites" (cf. Fig. 1) cannot yet be assigned to definite redox reactions. This by itself makes it impossible to describe all steps of oxidative phosphorylation by chemical equations. Finally, progress has also been delayed by the fact that experiments dealing with oxidative phosphorylation often require elaborate preparative procedures or complex and costly equipment.

The present article is confined to a discussion of the results obtained with mitochondria. However, nearly all the main conclusions are also valid for bacteria, since in all the cases studied so far the coupling between respiration and the synthesis of ATP appears to obey a common principle. A similar principle probably also governs the light-coupled synthesis of ATP (reaction (1a)).

$$ADP + P_i \xrightarrow{\text{light}} ATP \qquad (1a)$$

This process, termed photophosphorylation, is of great importance for the formation of ATP in green plants and in numerous autotrophic bacteria. (For reviews see [1–3, 10–13].)

I. The Primary High-Energy Intermediate

Numerous observations suggest that the energy generated during respiration in the three segments of the electron-transport chain is not trapped directly as ATP, but first appears in a high-energy intermediate compound or in a high-energy "state" of the mitochondrial membrane. The energy of this still uncharacterized primary intermediate can be utilized either for anhydride formation between P_i and ADP *via* several unknown energy-transport reactions (Fig. 2, pathway 1), or for energizing directly (*i.e.* without passing through ATP) other endergonic reactions in mitochondria (Fig. 2, pathway 2).

Evidence that the actual synthesis of ATP is preceded by an intermediate of this type is provided *e.g.* by experiments with the antibiotic oligomycin, which blocks the synthesis of ATP in respiring mitochondria [6, 14] without affecting the active accumulation of inorganic cations [15–17] or the succinate-linked, energy-dependent reduction of acetylacetate [18] or α-ketoglutarate [19]. Still more conclusive evidence can be obtained with submitochondrial particles, which, in contrast to intact mitochondria, contain only extremely small amounts of endogenous adenine nucleotides and P_i. Even though these particles are thus unable to use the energy generated during res-

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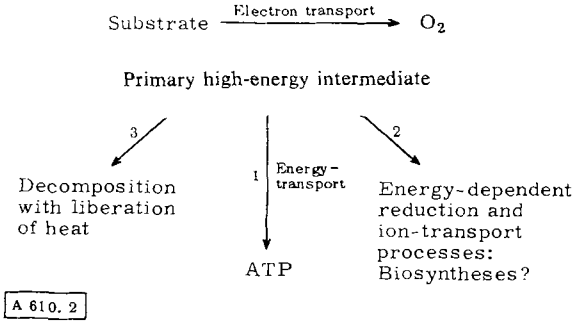


Fig. 2. Schematic diagram of possible reactions of the primary high-energy intermediate of oxidative phosphorylation.

piration for the synthesis of ATP unless both of these substances are added, they can still use this energy for endergonic reductions [20,21]. Thus P_i does not appear to be involved in the primary coupling reaction [20,21].

It might be argued that ATP synthesis and energy-dependent reduction and ion-transport processes could each proceed *via* a separate non-phosphorylated intermediate. Although this possibility cannot be entirely ruled out, it is unlikely since under suitable conditions energy-dependent mitochondrial reactions (*e.g.* the transport of ions [17,22,23], the rotenone-sensitive reduction of hexacyanoferrate(III) by succinate [24], and the transhydrogenase reaction [25]) can compete with ATP synthesis for the energy of respiration. This points to either a common intermediate or to different, but closely interacting intermediates.

Several authors have also discussed the participation of a non-phosphorylated intermediate of oxidative phosphorylation in mitochondrial protein synthesis [26,27] and in the activation of fatty acids [28,29,30]. However, the evidence that these processes are independent of ATP is not conclusive, since the rate of incorporation of amino acids by isolated mitochondria is at least four to five orders of magnitude lower, and the rate of fatty acid activation at least two orders of magnitude lower, than the maximum rate of oxidative phosphorylation [3,31,32].

Suppression of both ATP synthesis and reduction and ion-transport processes in intact respiring mitochondria causes an inhibition of substrate oxidation which is termed respiratory control [33]. While the exact mechanism of this inhibition has remained obscure, it is obviously the result of an accumulation of the primary high-energy intermediate of oxidative phosphorylation. This inhibition of electron transport represents a further possible reaction of the high-energy intermediate.

Finally, the intermediate may decompose spontaneously without providing useful chemical energy, the equivalent free energy probably being lost as heat (Fig. 2, pathway 3). In carefully isolated, intact mitochondria such a dissipative reaction is negligible. However, it can be greatly stimulated either by damage to the mitochondrial structure or by "uncouplers" such as 2,4-dinitrophenol [34], arsenate [35], or 2-(*m*-chlorophenyl)hydrazonomalonodinitrile [36]. ATP synthesis and other energy-coupled reactions are thereby inhibited and ultimately totally blocked while respiration remains unchanged or is even intensified.

It has been argued that ATP synthesis at each of the three coupling sites could involve several non-phosphorylated intermediates [11]. This view is not shared by the present author, since there appears to be no compelling reason for such a postulate.

While the existence of a primary high-energy intermediate of oxidative phosphorylation is virtually certain, its structure and reaction characteristics cannot yet be defined in chemical terms. Since the question as to the nature and mode of formation of the primary intermediate amounts to a question about the mechanism of oxidative phosphorylation, the definition of this intermediate constitutes the salient, and distinguishing, feature of each of the hypotheses discussed below.

II. Hypotheses on the Mechanism of the Reaction

The present discussion on the mechanism of oxidative phosphorylation centers around three hypotheses, *i.e.* the "chemical", the "chemiosmotic", and the "conformational" hypothesis. The following discussion considers how well each hypothesis satisfies the observed facts and whether it is amenable to experimental verification.

As mentioned earlier, the mechanism of oxidative phosphorylation resembles that of photophosphorylation which has also remained unknown [1,37,37a]. This similarity has proved important for testing the various hypotheses experimentally, since many experiments can be carried out more easily and more conclusively with isolated chloroplasts than with isolated mitochondria. In the present article, however, experiments with chloroplasts are mentioned only when they contribute to the discussion, as in the case of the "chemiosmotic" hypothesis.

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1. The "Chemical" Hypothesis

According to the "chemical" hypothesis, which was first formulated by *Slater* [38], an exergonic redox reaction between two adjacent respiratory carriers AH_2 and B leads to a high-energy chemical bond (symbol ~) between A and a substance X (reaction (2)). The non-phosphorylated compound A~X, which is common to electron transport and ATP synthesis, reacts with P_i to form a phosphorylated intermediate X~P, whose phosphoryl residue is finally transferred to ADP (reactions (3) and (4)):

$$AH_2 + B + X \rightleftharpoons A\sim X + BH_2 \quad (2)$$

$$A\sim X + P_i \rightleftharpoons X\sim P + A \quad (3)$$

$$X\sim P + ADP \rightleftharpoons ATP + X \quad (4)$$

These reactions represent one of the simplest formulations of the "chemical" hypothesis. The direct participation of P_i in the redox reaction (reaction (2a)) appears to be ruled out by the above-mentioned ex-

$$AH_2 + B + P_i \rightleftharpoons A\sim P + BH_2 \quad (2a)$$

periments with submitochondrial particles [20,21]. According to the "chemical" hypothesis, the term "high-energy intermediate" in Figure 2 stands for a chemical substance having a high-energy chemical bond. It is not specified whether the respiratory carrier present in the intermediate is in the oxidized (corresponding to reaction (2)) or in the reduced form.

The "chemical" hypothesis thus postulates a close analogy between oxidative phosphorylation and the ATP-forming steps of the triose phosphate dehydrogenase reaction, which was elucidated some time ago [39–41]. This is one of the strongest arguments in favor of the "chemical" hypothesis.

Respiratory control is rationalized by the assumption that in intact mitochondria the high-energy bonds of A~X and X~P are relatively stable. Without the addition of P_i and ADP, A would thus quickly be trapped as A~X and become unavailable for electron transport. Uncouplers are thought to react with the intermediate A~X, thereby breaking its high-energy bond and regenerating A.

There are several possible starting points for subjecting the "chemical" hypothesis to experimental scrutiny. Certain conditions, *e.g.* the state of respiratory control, should allow the accumulation, and detection, of high-energy forms of individual respiratory carriers (corresponding to A~X). Moreover, the high-energy intermediates formed at the three coupling sites should differ, since in each case X is bound to a different component of the respiratory chain. Finally, the isolation of a phosphorylated intermediate different from ATP (corresponding to X~P in reaction (3)) would support, if not prove, the "chemical" hypothesis. However, none of these predictions has so far been verified.

Despite considerable effort it is not known whether respiratory carriers are directly involved in the formation of the primary high-energy intermediate. Although several authors have suggested the participation of quinone phosphates [42,43] or NADH~P [44] in oxidative phosphorylation, these possibilities have not been proven and, indeed, seem unlikely. The data available for cytochrome b_{555}, which is interpreted by *Chance et al.* as a high-energy form of cytochrome b [45–47], are not sufficient to identify this interesting pigment as a high-energy intermediate in the sense of the "chemical" hypothesis. The existence of site-specific high-energy intermediates has also not been established. On the contrary, experiments with submitochondrial particles indicated [48] that the three coupling sites responded similarly toward inhibitors and uncouplers of oxidative phosphorylation as well as toward "coupling factors" (see below).

Finally, all attempts to identify a phosphorylated intermediate of oxidative phosphorylation have failed. The protein-bound phosphohistidine [49] discovered in mitochondria by *Boyer* and co-workers is not involved in oxidative phosphorylation [50]. The functions of the mitochondrial phosphoprotein isolated by *Beyer* [51] and of the unidentified phosphate fraction described by *Norman et al.* [52] have not yet been established. It is also still under dispute [53,54,54a] whether phosphomonoiodohistidine [55], suggested by *Perlgut* and *Wainio* as an intermediate of the oxidative phosphorylation, actually occurs in mitochondria. Protein-bound serine phosphate [56,57] or lipid phosphate [52,58] can probably also be ruled out as intermediates.

In spite of considerable effort, the "chemical" hypothesis has therefore not yet been confirmed. Most important of all, it is unable to explain one of the most fundamental characteristics of oxidative phosphorylation, *i.e.* the intimate association with a membrane structure. On the other hand, it is more amenable to

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experimental evaluation than the other hypotheses, and has therefore had a particularly stimulating effect on research.

2. The "Chemiosmotic" Hypothesis

According to the "chemiosmotic" hypothesis developed by *Mitchell*[37,59], respiration and ATP synthesis are coupled *via* a respiration-dependent proton transport through a "coupling membrane" rather than *via* formation of an energy-rich chemical compound. This proton transport is postulated to proceed synchronously with electron transfer from a reduced two-electron carrier AH_2 to an oxidized one-electron carrier B^{3+}, the active centers of which are arranged asymmetrically in the coupling membrane (cf. Fig. 3a and reaction (5)).

$$AH_2 + 2\,B^{3+} \rightarrow A + 2\,B^{2+} + 2\,H^+ \qquad (5)$$

The sum of one-electron and two-electron carriers participating in the transport of two protons is termed a "loop" (Fig. 3a); a "loop" formally corresponds to a coupling site of the "chemical" hypothesis.

The "chemiosmotic" hypothesis forbids passive diffusion of ions through the coupling membrane. The respiration-coupled proton pump thus generates not only a proton concentration gradient but also, by separating electric charges, an electric potential difference across the coupling membrane, *i.e.* a membrane potential. According to the "chemiosmotic" hypothesis, "primary high-energy intermediate" in Figure 2 stands for the free energy of an electrochemical potential.

Since there are obviously no membranes that are completely impermeable to ions, the relative contributions of the proton concentration gradient and of the membrane potential to the total energy of the electrochemical potential are difficult to predict. It is nevertheless clear that, contrary to the view of *Chance* and *Mela*[60], the "chemiosmotic" hypothesis does not necessarily invoke a considerable pH difference across the coupling membrane.

However, a coupling membrane impermeable to ions would also preclude the uptake of ionized substrates and cofactors into the interior of the mitochondria. The "chemiosmotic" hypothesis therefore assumes further that the coupling membrane contains ion-specific exchange-diffusion systems, which link the uptake of certain ions to the extrusion of similarly charged intramitochondrial ions.

The formation of ATP is explained in this hypothesis by the back-flow of protons through the coupling membrane, the free energy of the electrochemical potential driving the elimination of water between P_i and ADP *via* a membrane-bound vectorial ATPase system. The mechanism suggested for this ATP-forming step is not yet entirely satisfactory, and is one of the weakest points of the hypothesis.

Figure 3 schematically depicts the transport of two protons through the coupling membrane by a "loop" (and the simultaneous accumulation of OH^- on the other side) as well as the recombination of H^+ and OH^- by a vectorial ATPase system. The direction of the proton movements is not fixed by the "chemiosmotic" hypothesis; the direction shown in Figure 3 corresponds to empirical findings with isolated rat-liver mitochondria[61].

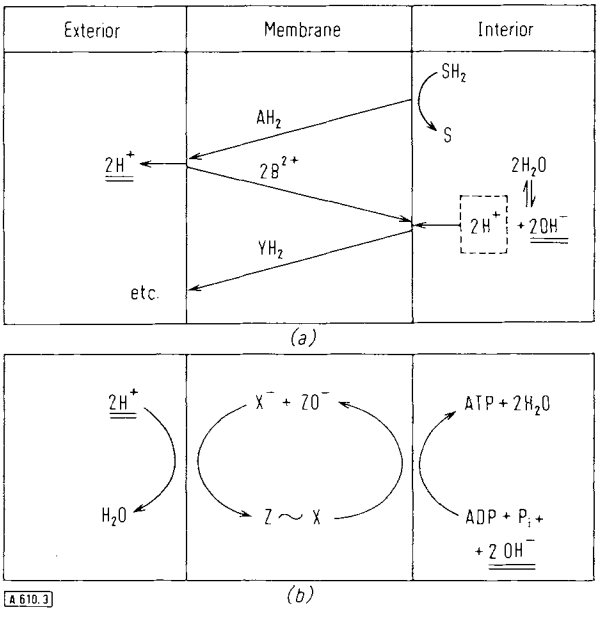


Fig. 3. Proton transport by a "loop" (a) and ATP synthesis (b) according to the "chemiosmotic" hypothesis. S and SH_2: oxidized and reduced substrate; AH_2 and YH_2: reduced two-electron (hydrogen) carriers; B^{2+}: reduced one-electron carrier; X^- and ZO^-: hypothetical functional groups involved in energy transport; Z~X: hypothetical high-energy intermediate involved in the energy transport, but not in electron transport.

Respiration in the absence of P_i and ADP would be expected to lead to an accumulation of H^+ and OH^- on opposite sides of the coupling membrane. This accumulation could inhibit electron transport by a back-reaction *via* the respiration-coupled "proton pump", thus inducing respiratory control.

According to the hypothesis, uncouplers increase the proton-permeability of the coupling membrane, and thereby collapse the electrochemical potential.

Mitchell[59] and *Mitchell* and *Moyle*[61,62] were able to show that, in agreement with the "chemiosmotic" hypothesis, both the oxidation of substrates and the hydrolysis of ATP led to proton movement in the same direction (*i.e.* an ejection of protons from the mitochondria). For each "loop" traversed by an electron pair and for each hydrolysed molecule of ATP, two protons were pumped from the mitochondria into the suspension medium. The required impermeability to ions of the mitochondrial inner membrane (as the actual "coupling membrane", see below) was also confirmed[37,63].

[59] *P. Mitchell*, Nature (London) *191*, 144 (1961).
[60] *B. Chance* and *L. Mela*, Nature (London) *212*, 372 (1966).
[61] *P. Mitchell* and *J. Moyle*, Nature (London) *208*, 147 (1965).
[62] *P. Mitchell* and *J. Moyle*, Nature (London) *208*, 1205 (1965).
[63] *J. B. Chappell* and *K. Haarhoff* in: The Biochemistry of Mitochondria, Proc. Third Meeting Fed. European Biochem. Societies, Warsaw 1966, in press.

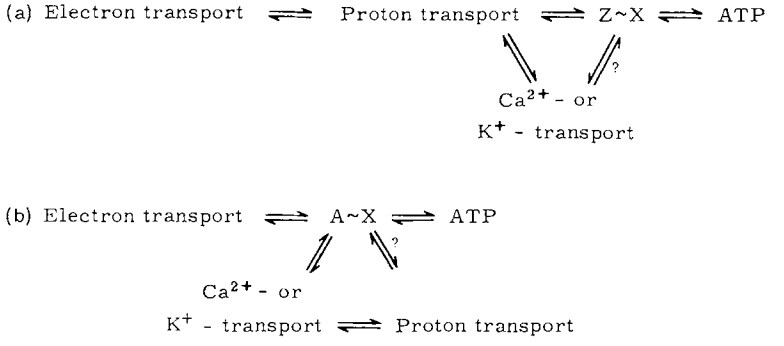
It should be emphasized that the term "impermeability to ions" simply implies a barrier to passive diffusion. Ions such as Ca^{2+}, P_i, or anions of certain dicarboxylic acids can in fact be taken up into the interior of the mitochondria; however, this uptake does not involve passive diffusion, but probably specific enzyme-controlled transport processes, which couple the uptake of cations or anions to the ejection of H^+ or OH^- [63]. Though little is known about these transport systems, they seem to correspond to the exchange-diffusion systems required by the "chemiosmotic" hypothesis.

This hypothesis received particularly strong support from investigations on the action of uncouplers, since such chemically unrelated uncouplers as 2,4-dinitrophenol, 2-(*m*-chlorophenyl)hydrazonomalonodinitrile, and dicoumarol all greatly increased the permeability of the mitochondrial membrane to protons [37,64,64a]. *Bielawski et al.* also showed that 2,4-dinitrophenol increases the electrical conductivity of synthetic lipid membranes by more than two orders of magnitude [65]. Both of these observations are difficult to explain in terms of the "chemical" or the "conformational" hypothesis (see below).

Assuming comparable reaction mechanisms, the experimental results obtained with chloroplasts may also be regarded as an argument for the "chemiosmotic" hypothesis. By suddenly raising the pH of the suspension medium, *Jagendorf et al.* [66,66a] were able to obtain ATP synthesis in non-illuminated chloroplasts that was blocked by uncouplers of photophosphorylation. Control experiments indicated that this ATP synthesis was due to the induction of an electrochemical potential across the grana membranes in the sense of the "chemiosmotic" hypothesis, and not to a pH-induced electron transport or unknown intermediates of photophosphorylation that were already preformed in the chloroplasts.

Attempts to detect an analagous pH-induced ATP synthesis in isolated mitochondria were at first unsuccessful [37,67,68]. *Reid et al.* [69] subsequently reported that rat-liver mitochondria incorporated $^{32}P_i$ into ATP if the pH of the suspension medium was suddenly lowered. However, the extent of this incorporation was too small to rule out formation of $AT^{32}P$ *via* any preformed intermediates of oxidative phosphorylation or *via* residual exchange and electron-transport reactions.

While these experimental data are no doubt impressive, they do not prove the "chemiosmotic" hypothesis. Indeed, according to more recent investigations, the proton movements observed in isolated mitochondria [61,62] appear to be secondary reactions of a respiration-coupled transport of Ca^{2+} or K^+ from the suspension medium into the mitochondria [63,70,71], and not reactions of "loops" and vectorial ATPase systems as envisioned by the "chemiosmotic" hypothesis (Fig. 4a).



A 610. 4

Fig. 4. Interrelationships between electron transport, ATP synthesis, and ion transport according to the "chemiosmotic" (a) and "chemical" (b) hypotheses.

As indicated in Figure 4b, the respiration- and ATP-coupled proton transport observed by *Mitchell* and *Moyle* can thus be relatively easily explained in terms of the "chemical" hypothesis.

According to Figure 4b, the "chemical" hypothesis could even account for the pH-induced ATP-synthesis in chloroplasts [66a], since a sudden change in the proton activity of the suspending medium could induce a back-reaction leading to the formation of A ~ X and, hence, of ATP. Moreover, the concept of the "loop" is difficult to reconcile with the structure of the respiratory chain, since the segment between cytochrome c and cytochrome aa_3 contains a coupling site, but no two-electron carriers. According to *Slater* [71a], the "chemiosmotic" hypothesis is also doubtful on thermodynamic grounds, since the free energy required for ATP synthesis appears to exceed the

[64] *J. B. Chappell* and *A. R. Crofts*, Biochem. J. *95*, 393 (1965).

[64a] *P. Mitchell* and *J. Moyle*, Biochem. J. *104*, 588 (1967).

[65] *J. Bielawski, T. E. Thompson*, and *A. L. Lehninger*, Biochem. biophysic. Res. Commun. *24*, 948 (1966).

[66] *G. Hind* and *A. T. Jagendorf*, J. biol. Chemistry *240*, 3195 (1965).

[66a] *A. T. Jagendorf* and *E. Uribe*, Proc. nat. Acad. Sci. USA *55*, 170 (1966).

[67] *E. C. Slater*, personal communication.

[68] *R. E. McCarty* and *G. Schatz*, unpublished.

[69] *R. A. Reid, J. Moyle*, and *P. Mitchell*, Nature (London) *212*, 257 (1966).

[70] *B. Chance* and *L. Mela*, Nature (London) *212*, 369 (1966).

[71] *R. S. Cockrell, E. J. Harris*, and *B. C. Pressman*, Biochemistry *5*, 2326 (1966).

[71a] *E. C. Slater*, Europ. J. Biochemistry *1*, 317 (1967).

energy content of the ion gradients proposed by *Mitchell*[37]. However, this objection is not necessarily valid, since the energy-requirement of ATP formation in mitochondrial membranes and the thermodynamic characteristics of extremely small volumes, such as those of submitochondrial particles, are still under dispute[71b–71e].

The experiments and arguments published thus far can neither prove nor refute the "chemiosmotic" hypothesis. It would be clearly disproved *e.g.* by the identification of an intermediate common to electron- and energy-transport or by the demonstration that oxidative phosphorylation can also take place in a soluble system. Nevertheless, the action of uncouplers, the tight linkage of oxidative phosphorylation to a membrane structure, and the pH-induced ATP synthesis can be more readily explained by the "chemiosmotic" than by either the "chemical" or "conformational" hypothesis.

3. The "Conformational" Hypothesis

The parallels between the ATPase reaction catalysed by mitochondria and by myosin led *Boyer* to assume that the energy liberated during the electron transport could be "captured" as a high-energy conformation of a protein and thus in principle be coupled to the ATP synthesis[13,72]. As a possible intermediate reaction *Boyer* discussed the formation of an intramolecular high-energy S~acyl bond (Fig. 5).

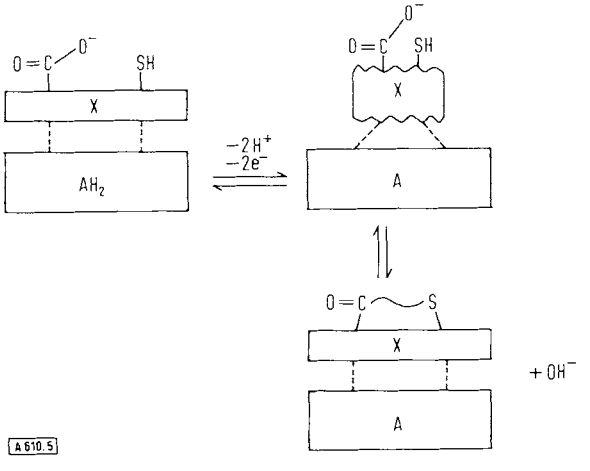


Fig. 5. The primary coupling reaction according to the "conformational" hypothesis. A and AH_2: oxidized and reduced respiratory carrier X: hypothetical coupling protein, which is either identical with or in close interaction with A.

This formulation resembles the "chemical" hypothesis in that it invokes an analogy with ATP synthesis catalysed by triose phosphate dehydrogenase, for which the intermediate formation of an S ~ acyl bond is well established[39–41]. The uncoupling action of 2,4 - dinitrophenol is interpreted as a cleavage of the S ~ acyl bond to form a grouping $2,4\text{-}(NO_2)_2\text{-}C_6H_3\text{-}O$ Acyl, which hydrolyses spontaneously.

It is left open whether the coupling process involves a conformational change of a respiratory carrier or of a protein not directly involved in electron transport. In the first case the "conformational" hypothesis would simply be a detailed variant of the "chemical" hypothesis. In the second case the "conformational" hypothesis would not call for an intermediate common to electron- and energy-transport, and would thus differ from the "chemical" hypothesis. According to this latter alternative it would even be conceivable that each respiratory chain contains only a single coupling site and that the energy generated in the three segments of the respiratory chain is always used for deforming the same protein (*e.g.* a "contractile protein" of the mitochondrial inner membrane). However, this presupposes interactions between the various membrane proteins that are still hypothetical[72].

The "conformational" hypothesis can plausibly account for the close linkage between oxidative phosphorylation and a membrane structure and is compatible with the great similarity of the three coupling sites as well as with the well-documented dependence of mitochondrial structure on the reactions of energy-coupling[2,73]. On the other hand, it shares with the "chemical" hypothesis the inability to explain the chemical diversity of uncoupler substances. At present this hypothesis offers few starting points for experimental investigations.

III. Coupling Factors

A coupling factor is a mitochondrial protein, which, when added to suitable mitochondrial particles, increases their ability to carry out oxidative phosphorylation. The most obvious interpretation of this stimulation is an acceleration of the energy-transport chain (Fig. 2, pathway 1), the coupling factor thus being regarded as an enzyme specifically involved in energy transport. While investigations on coupling factor 1 (F_1) do indeed suggest such a mode of action, there exists as yet no conclusive proof that this assumption is valid for any of the known coupling factors. In most cases it is merely possible to rule out, more or less, any trivial effect, such as binding of naturally occurring uncouplers[74].

Since the first coupling factors were isolated from beef heart mitochondria [75,76], numerous reports on the isolation and characterization of such factors have appeared which present a rather confusing pic-

[71b] *H. Baum*, Nature (London) *214*, 1326 (1967).

[71c] *P. Mitchell*, Nature (London) *214*, 1327 (1967).

[71d] *B. Chance*, Nature (London) *214*, 399 (1967).

[71e] *P. Mitchell*, Nature (London) *214*, 400 (1967).

[72] *P. D. Boyer* in *T. E. King*, *H. S. Mason*, and *M. Morrison*: Oxidases and Related Redox Systems. Wiley, New York 1965, p. 994.

[73] *A. L. Lehninger* in *M. Kasha* and *B. Pullman*: Horizons in Biochemistry. Academic Press, New York 1962, p. 421.

[74] *M. E. Pullman* and *E. Racker*, Science (Washington) *123*, 1105 (1956).

[75] *M. E. Pullman*, *H. S. Penefsky*, and *E. Racker*, Arch. Biochem. Biophysics *76*, 227 (1958).

[76] *A. W. Linnane*, Biochim. biophysica Acta *30*, 221 (1958).

ture[3,10,11]. The test particles and the purities of the coupling proteins differ so widely that the results obtained by different research groups can only occasionally be compared.

Investigations by *Racker* and co-workers have led to the identification and at least partial purification of three coupling factors which are designated as F_1, F_2, and F_3[77–80]. According to recent studies[80], the action of a fourth factor F_4[82], which is similar to the structural protein described by *Richardson et al.*[81] is at least partly due to F_2 and F_3 bound to structural protein. *Andreoli et al.*[83] and *Lam et al.*[84,84a] isolated two further coupling factors (FA and FB). Though these have not yet been carefully compared with F_1, F_2, or F_3, the published data suggest that at least part of the action of FA is due to F_1, which could be present in FA either as a modification product (see below) or complexed to the naturally occurring F_1 inhibitor[85]. On the other hand, the coupling factor described by *Beyer*[86] (termed ATP synthetase II) is not identical with F_1[87]; its relationship to the other coupling factors is still unclear.

All the coupling factors mentioned so far were isolated from bovine heart mitochondria. *Wadkins* and *Lehninger* described a coupling factor from rat-liver mitochondria, which differed from F_1 in that it catalysed an ADP–ATP exchange reaction[88]. However, *Groot* and *Van den Bergh*[88a] were unable to confirm the coupling factor activity of this protein. The coupling factors described by *Linnane*[76] and *Hommes*[89] have not yet been characterized in detail.

The existence of site-specific coupling factors, which was claimed only a few years ago[90–92], must now be seriously doubted. Reports of such factors were probably mainly due to inadequate methods for measuring the individual coupling sites. Until recently, only the third coupling site (cf. Fig. 1) could be assayed independently of the others[93]. However, a new method for the selective measurement of the first coupling site in submitochondrial particles[48] now permits the determination of the effect of each factor on two different coupling sites. It is now clear that F_1, F_2, and F_3 influence all three coupling sites[48,79,80]. Claims of a coupling factor specific for the first coupling site[91] could not be confirmed[95]. Moreover, reports on the existence of a specific factor for the third coupling site[90,92] have proved to be completely unfounded[94].

Most of the coupling factors isolated from mitochondria are quite inhomogeneous protein fractions whose mode of action is unknown. Detailed information only exists for coupling factor F_1, which will now be briefly discussed.

In 1958, *Pullman et al.*[75] solubilized F_1 from bovine heart mitochondria by shaking with glass beads, characterized it as mitochondrial ATPase[77], and purified it to homogeneity in the ultracentrifuge[77]. According to *Penefsky* and *Warner*[96], F_1 is a compact, symmetrical molecule of molecular weight 284000 which consists of about ten subunits each having a molecular weight of 26000. Recent studies indicate that the ATPase activity of isolated mitochondria is inactivated by irradiation with high-energy electrons; since an analysis according to the target theory gave a molecular weight of between 260000 and 290000, F_1 appears to exist in the mitochondrial membrane as the undissociated molecule[96a]. After negative staining with phosphotungstate, individual F_1 molecules appear in the electron microscope as approximately spherical structures having a diameter of 80 to 85 Å[97]. Addition of the purified protein to suitable submitochondrial particles of low phosphorylating capacity strongly stimulates ATP formation without significantly affecting the rate of respiration[78]. Solubilized F_1 catalyses an ATPase reaction that is not inhibited by oligomycin, and is rapidly denatured at 0 °C, but not at room temperature[77,96].

On the other hand, since the ATPase activity of membrane-bound F_1 is strongly inhibited by oligomycin[14,15] and is stable at low temperatures, the separation of the enzyme from mitochondrial membranes is accompanied by remarkable changes in its properties. This phenomenon, termed "allotopy"[97a], prompted *Racker* and associates to isolate a particulate

[77] *M. E. Pullman, H. S. Penefsky,* and *E. Racker,* J. biol. Chemistry *235,* 3322 (1960).

[78] *H. S. Penefsky, M. E. Pullman, A. Datta,* and *E. Racker,* J. biol. Chemistry *235,* 3330 (1960).

[79] *J. M. Fessenden* and *E. Racker,* J. biol. Chemistry *241,* 2483 (1966).

[80] *J. M. Fessenden, M. A. Dannenberg,* and *E. Racker,* Biochem. biophysic. Res. Commun. *25,* 54 (1966).

[81] *S. H. Richardson, H. O. Hultin,* and *S. Fleischer,* Arch. Biochem. Biophysics *105,* 254 (1964).

[82] *T. E. Conover, R. L. Prairie,* and *E. Racker,* J. biol. Chemistry *238,* 2831 (1963).

[83] *T. E. Andreoli, K.-W. Lam,* and *D. R. Sanadi,* J. biol. Chemistry *240,* 2644 (1965).

[84] *K.-W. Lam, J. B. Warshaw,* and *D. R. Sanadi,* Federat. Proc. *25,* 529 (1966).

[84a] *K.-W. Lam, J. B. Warshaw,* and *D. R. Sanadi,* Arch. Biochem. Biophysics *119,* 477 (1967).

[85] *M. E. Pullman* and *G. C. Monroy,* J. biol. Chemistry *238,* 3762 (1963).

[86] *R. E. Beyer,* Biochem. biophysic. Res. Commun. *16,* 460 (1964).

[87] *R. E. Beyer* and *G. Schatz,* unpublished.

[88] *C. L. Wadkins* and *A. L. Lehninger,* Federat. Proc. *22,* 1092 (1962).

[88a] *G. S. P. Groot* and *S. G. Van den Bergh,* Biochim. biophysica Acta, in press.

[89] *F. A. Hommes,* Biochim. biophysica Acta *71,* 595 (1963).

[90] *D. E. Green, R. E. Beyer, M. Hansen, A. L. Smith,* and *G. Webster,* Federat. Proc. *22,* 1460 (1963).

[91] *A. L. Smith* and *M. Hansen,* Biochem. biophysic. Res. Commun. *8,* 136 (1962).

[92] *G. Webster,* J. biol. Chemistry *240,* 1365 (1965).

[93] *E. E. Jacobs,* Biochem. biophysic. Res. Commun. *3,* 536 (1960).

[94] *D. E. Green,* personal communication.

[95] *G. Schatz* and *E. Racker,* unpublished.

[96] *H. S. Penefsky* and *R. C. Warner,* J. biol. Chemistry *240,* 4694 (1965).

[96a] *Y. Kagawa,* Biochim. biophysica Acta *131,* 586 (1967).

[97] *Y. Kagawa* and *E. Racker,* J. biol. Chemistry *241,* 2475 (1966).

[97a] *E. Racker,* Federat. Proc., in press.

mitochondrial component (F_0) which could specifically bind soluble F_1 and thereby rendered it again cold-stable and sensitive to oligomycin [98,99]. F_0 was found to be a relatively crude membrane fraction devoid of F_1, but still containing phospholipids and the entire respiratory chain [98,99]. Further purification gave a product (CF_0) which contained only traces of cytochromes and phospholipid, yet had retained the characteristic ability of binding, and modifying, soluble F_1 [100].

The action of F_0 on soluble F_1 appears to be more than simple adsorption of F_1 on a structured matrix, since unpublished investigations [101] have shown that F_1 associated with mitochondria of the "petite" mutant of *Saccharomyces cerevisiae* is not inhibited by oligomycin and is rapidly inactivated in the cold. The F_1 bound to these respiration-deficient and largely non-functional mitochondria thus resembles in some respects the soluble enzyme, and differs from F_1 bound to the respiring mitochondria of the wild type [102]. Purified F_1 from the mutant has the same enzymic and immunological properties and the same molecular weight as purified wild-type F_1. Like the latter, it becomes cold-stable and sensitive to oligomycin on complex formation with beef heart F_0. This suggests that the "petite" mutation [103] in *S. cerevisiae* modifies an F_0-like mitochondrial component, rather than F_1 itself. The F_0-deficiency of the mutant mitochondria is evidently not a simple consequence of their respiratory deficiency; anaerobically grown wild-type yeast cells contain undifferentiated promitochondria which also lack a functional respiratory chain, yet contain membrane-bound F_1 that is cold-stable and inhibited by oligomycin [101, 103a].

Since F_1 catalyses an ATPase reaction [77] and forms complexes with ADP [104], it was assumed that F_1 in mitochondria catalyses the terminal, ATP-forming step of the energy-transport chain [1, 77]. However, *Lee* and *Ernster* reopened the question of the mode of action of F_1, and of coupling factors in general, with their observation that oxidative phosphorylation in submitochondrial particles of low phosphorylating capacity could be considerably increased by the addition of small quantities of oligomycin (< 0.4 µg per mg of mitochondrial protein). Larger amounts of oligomycin (> 0.4 µg per mg), on the other hand, inhibited oxidative phosphorylation. Since the stimulating action of oligomycin (which does not occur in mammals) evidently could not be explained by a direct participation in energy-transport, *Lee* and *Ernster* assumed that the stimulation of ATP synthesis by oligomycin was indirect, and resulted from inhibition of the "dissipative reaction" (Fig. 2, pathway 3), which in submitochondrial particles successfully competes with energy-transport for the primary high-energy intermediate. This interpretation of the stimulating effect of oligomycin was confirmed by *Fessenden* and *Racker* [79] and by *Lam et al.* [104a].

Lee and *Ernster* also tried to explain the stimulating action of the various coupling factors by an indirect effect of this type [105]. However, since they used submitochondrial particles that still contained considerable quantities of endogenous F_1 [79], their line of reasoning seemed doubtful, at least with regard to F_1. Indeed, their tacit assumption that oligomycin would stimulate oxidative phosphorylation even in particles completely devoid of F_1 was conclusively shown to be incorrect. *Racker* and *Horstmann* [106] obtained non-phosphorylating particles of extremely low F_1 content. While addition of F_1 and F_3 to these particles induced a significant respiration-coupled ATP synthesis, oligomycin alone was without effect. Stimulation by oligomycin was only observed in the presence of suboptimal amounts of F_1 (and an excess of F_3). Similar experiments by *Lam et al.* on FA-deficient beef heart particles indicated that the stimulation of oxidative phosphorylation by oligomycin also required FA [104a]. Furthermore, *Fessenden* and *Racker* [79] found that the effect of small quantities of oligomycin on beef-heart particles containing F_1 was completely blocked by a specific antiserum against beef-heart F_1. This clearly demonstrates that the stimulating effects of F_1 and of oligomycin are fundamentally different; it also suggests that the promotion of ATP synthesis by F_1 is at least partly due to an enzymic acceleration of a step in the energy-transport chain.

However, other experiments indicate that the action of F_1 as a coupling factor cannot be fully explained by an enzymic function [102]. F_1 isolated from normal yeast mitochondria stimulates oxidative phosphorylation in F_1-deficient bovine heart particles deficient in, but not completely devoid of F_1. This stimulation by the yeast enzyme requires the presence of enzymically active bovine heart F_1 in the test particles, but is not affected when the enzymic activity of the yeast enzyme bound to the bovine particles is almost completely inhibited by a specific antiserum. Thus yeast F_1 probably stimulates oxidative phosphorylation in bovine heart particles not by direct, *i.e.* enzymic, participation in the energy-transport chain, but (analogous to oligomycin) indirectly by inhibition of the competing dissipative reaction.

These experiments suggested, moreover, that a similar non-enzymic effect also contributes to the coupling action of bovine heart F_1, since the enzymic and physical properties of yeast F_1 and bovine F_1 are

[98] *E. Racker*, Biochem. biophysic. Res. Commun. *10*, 435 (1963).
[99] *Y. Kagawa* and *E. Racker*, J. biol. Chemistry *241*, 2461 (1966).
[100] *Y. Kagawa* and *E. Racker*, J. biol. Chemistry *241*, 2467 (1966).
[101] *G. Schatz*, J. biol. Chemistry, in press.
[102] *G. Schatz, H. S. Penefsky*, and *E. Racker*, J. biol. Chemistry *242*, 2552 (1967).
[103] *B. Ephrussi* and *H. Hottingeur*, Cold Spring Harbor Sympos. quant. Biol. *16*, 75 (1951).
[103a] *G. Schatz*, Biochim. biophysica Acta *96*, 342 (1965).
[104] *H. Zalkin, M. E. Pullman*, and *E. Racker*, J. biol. Chemistry *240*, 4011 (1965).
[104a] *K.-W. Lam, J. B. Warshaw*, and *D. R. Sanadi*, Arch. Biochem. Biophysics *117*, 594 (1966).
[105] *C.-P. Lee* and *L. Ernster*, Biochem. biophysic. Res. Commun. *18*, 523 (1965).
[106] *E. Racker* and *L. Horstman*, J. biol. Chemistry *242*, 2547 (1967).

virtually identical [102]. This non-enzymic effect of F_1 could be interpreted as a change in the structure of the mitochondrial membrane induced by F_1. F_1 would then act not as a catalyst, but as a membrane component, which in some unknown way prevents the spontaneous dissipation of the primary high-energy intermediate. However, while enzymic and "structural" effects are superimposed on each other in the binding of bovine heart F_1 to bovine heart particles, the interaction between yeast F_1 and bovine heart particles appears to involve only the "structural" effect.

A structural function of this nature could also explain why, according to ATPase measurements, F_1 accounts for at least 10 % of the protein of bovine heart particles [106]. It had previously been difficult to explain why a purely catalytic component of the energy-transport chain should be present in such large quantities.

A non-catalytic function is also indicated by the fact that F_1 stimulates the respiration-coupled, energy-dependent transhydrogenase reaction (Fig. 2, pathway 2). This effect of F_1, unlike its stimulating action on the respiration-coupled ATP synthesis, is not decreased by an antiserum against F_1 [107].

Treatment of bovine heart F_1 with dicyclohexylcarbodiimide represents an especially elegant means of differentiating the two F_1-effects. The chemically modified protein is enzymically inactive, yet as effective as a coupling factor as the enzyme from yeast [108].

While the existence of a "structural" effect of F_1 is thus very likely, it has not yet been directly documented experimentally. According to the "chemiosmotic" hypothesis, however, addition of F_1 to F_1-deficient beef heart particles should decrease their permeability to protons.

The foregoing sections show that a knowledge of the structure of the mitochondrial membrane is apparently essential to an understanding of oxidative phosphorylation. The last section of this survey is thus devoted to a brief discussion of some current questions relating to mitochondrial structure.

IV. The Structure of the Inner Mitochondrial Membrane

Mitochondria are composed of two membrane systems, an inner and an outer mitochondrial membrane. It is now firmly established that the two membranes differ in their ultrastructure [109–111], their chemical composition [112, 113], and their enzyme content [112–116].

The respiratory chain and oxidative phosphorylation are associated entirely with the inner mitochondrial membrane [112, 117].

Electron-microscopic studies on isolated, negatively stained mitochondria have shown that the inner mitochondrial membrane, unlike the outer one, is lined with densely and regularly spaced "knobs" about 80–90 Å in diameter, which are joined to the membrane continuum by cylindrical "stalks" [109–111, 118, 119]. Electron micrographs by *Smith* [118] and *Fernández-Morán et al.* [119] indicate, moreover, that this continuum itself consists of approximately globular "base pieces" about 90 Å in diameter (cf. Fig. 6).

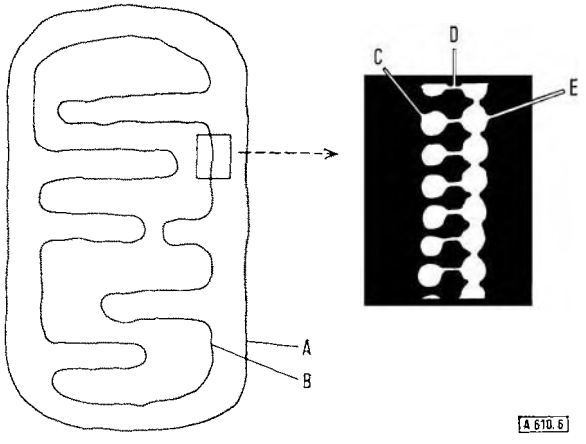


Fig. 6. Schematic representation of a positively stained miochondrion (left) and of the ultrastructure of the negatively stained inner mitochondrial membrane (right). A: outer membrane; B: inner membrane; C: "knob"; D: "stalk"; E: base piece.

The hypothesis that each "knob" represents a complete electron-transport chain [120, 121] proved to be untenable [2, 109, 118, 122]. The minimum molecular weight of an electron transport chain (1.2×10^6, cf. [123]) requires a sphere at least 170 Å in diameter, and is thus incompatible with the size of the membrane-bound "knobs". *Fernández-Morán et al.* [119] then suggested that each "knob" contains only a part of the respiratory chain, *i.e.* cytochrome oxidase. This possibility was also refuted, since treatment of mitochondrial particles with ultrasound [124, 125] or with trypsin and urea [117] led to

[107] *J. M. Fessenden* and *E. Racker*, unpublished experiments, cited in [102].

[108] *H. S. Penefsky*, unpublished experiments, cited in [102].

[109] *D. F. Parsons*, J. Cell Biol. *16*, 620 (1963).

[110] *W. Stoeckenius*, J. Cell Biol. *17*, 443 (1963).

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a loss of "knobs", without significant decrease in cytochrome content or electron-transport activity.

Racker et al. finally identified the "knobs" as the coupling factor F_1 (*i.e.* mitochondrial ATPase). Stepwise treatment of submitochondrial particles with trypsin and urea led to preferential degradation of the "knobs" and simultaneous loss of ATPase activity [97, 117]. Moreover, the individual molecules of highly purified, negatively stained F_1 preparations from bovine heart [97] and yeast [102] were indistinguishable from "knobs". Finally, it was possible to bind purified bovine heart F_1 to F_1-free mitochondrial membranes (F_0), thus restoring to the particles both ATPase activity and membrane-bound "knobs" [117, 97].

While a participation of the "knobs" in electron transport can now be definitely ruled out, the question of where and how the respiratory chain is anchored in the inner mitochondrial membrane cannot yet be answered. *Green* and *Tzagoloff* [126] speculate that each "base piece" represents one segment of the electron-transport chain, and that the electron transfer between the "base pieces" is effected by "mobile" redox components such as cytochrome c or coenzyme Q. This assumption is not supported by experimental observations of *Kagawa* and *Racker* [97], who obtained vesicle formation on addition of phospholipid to a complex of F_1 with CF_0 (see above). These vesicles were covered with numerous membrane-bound "knobs", and were morphologically indistinguishable from respiring submitochondrial bovine heart particles, although they were practically free from cytochromes and flavin.

The chemical and enzymic properties of the "stalk" are completely unknown. The localization and function of the "structural protein", first isolated by *Criddle et al.* [127] from bovine heart mitochondria, also remain to be established. This protein fraction, which is insoluble at pH values near 7, lacks prosthetic groups, but forms water-soluble complexes with myoglobin, cytochrome b, cytochrome aa_3, and phospholipids [127, 128, 81]. *Criddle et al.* [127] therefore assumed that the protein functions as the basic skeleton of the mitochondrial respiratory chain, ensuring the correct alignment of the individual carriers. Evidence from other laboratories suggested, moreover, that "structural protein" also functions in oxidative phosphorylation [99], the control of the tricarboxylic acid cycle [128a], and the extrachromosomal control of mitochondrial function [129].

Quantitative studies on complex formation with myoglobin and cytochrome c and end-group determinations suggest that "structural protein" is homogeneous [130–130b]. On the other hand, electrophoresis in acrylamide gels reveals numerous bands [131–133a]. The considerable discrepancies between the results of amino-acid analyses carried out on bovine heart "structural protein" in various laboratories [127, 129, 134] also argue against homogeneity. According to *Kopaczyk et al.* [135] the protein does not even seem to be the basic skeleton of the mitochondrial respiratory chain, as originally assumed; for example, it could be separated from individual segments ("complexes") of the respiratory chain (cf. [136]) without loss of electron-transport activity. However, these experiments are by no means conclusive, since it was not proved that "structural protein" had been completely removed. *Woodward* and *Munkres* [137], on the other hand, doubt the existence of a specific "structural protein" of the inner mitochondrial membrane, since they were able to isolate "structural protein", not only from mitochondria, but also from nuclei, from microsomes, and even from a high-speed supernatant. On the other hand, experiments with yeast cells showed that "structural protein" of mitochondria differs from that of other cell fractions in forming complexes with ATP, which are dissociated by the glycoside atractyloside [137a].

Existence, specificity, and function of a "structural protein" of the inner mitochondrial membrane thus remain an open question. Since electrophoretic investigations on "structural protein" fractions are subject to some uncertainty because of their low solubility and their tendency toward complex formation, the author feels that also the question of homogeneity is still unsettled.

Reports on the isolation of an actomyosin-like "contractile protein" from mitochondria [136, 138, 139], on the other hand, have definitely been shown to be incorrect. The published results could not be reproduced [140], and in one case appear to be explained by the isolation of an impurity in the mitochondrial fraction under

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investigation[141]. However, the participation of an unknown "contractile protein" in energy-coupled mitochondrial volume-changes[73] or in oxidative phosphorylation (*e.g.* in the sense of the "conformational" hypothesis) is thereby by no means excluded.

Outlook

The problem of oxidative phosphorylation appears to be adequately defined from the phenomenologic point of view, *i.e.* most of the possible reactions of the primary highenergy intermediate are probably known or can be predicted.

Research on oxidative phosphorylation is being concentrated increasingly on structural aspects, a strong incentive being provided by the steady improvement of electron-optical methods and by the restatement of the "chemiosmotic" hypothesis. Promising developments can be expected from experiments with artificial lipid bilayers, whose properties strikingly resemble those of biological membranes. If individual purified coupling factors could be bound to such artificial membranes, it might be possible to study the influence of this binding on the catalytic properties of the proteins and on the electrical conductivity of the membrane or a membrane potential. This experimental system could also furnish direct proof for a "structural" function of coupling factors. The long-range objective of such experiments would be the reconstruction of the energy-transport chain and the mitochondrial inner membrane.

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Hexamethylphosphoramide

BY H. NORMANT[*]

Growing interest is being shown in the role of the solvent (particularly polar solvents) in chemical reactions[1–4]. The most remarkable polar aprotic solvent appears to us to be the hexamethylated triamide of orthophosphoric acid, $OP(N(CH_3)_2)_3$, which is known as hexamethylphosphoramide or tris(dimethylamino)phosphine oxide. Hexamethylphosphoramide[5–7] has recently been studied with respect to its solvent properties for gases[5], for many organic and inorganic salts[7], and for polymers[5], as well as its use as a polymerization co-catalyst. However, these aspects are not considered in the present paper, which deals with the physical and chemical properties of hexamethylphosphoramide, and in particular with its use as a reaction medium. Our own work on hexamethylphosphoramide began in 1961, and until then very little work had been done on this compound. Even in a paper published by Parker[1b] in 1965, very little reference is made to hexamethylphosphoramide.

I. Physical and Chemical Properties of Hexamethylphosphoramide (HMPT)

A. Preparation

Michaelis[8] prepared triamides of orthophosphoric acid by treatment of phosphorus oxide trichloride with an excess of secondary amine. The reaction with dimethylamine leads in accordance with eq. (a) to hexamethylphosphoramide (HMPT):

$$OPCl_3 + 6\ HN(CH_3)_2 \rightarrow OP(N(CH_3)_2)_3 + 3\ H_2N(CH_3)_2^{\oplus}Cl^{\ominus} \qquad (a)$$

The chlorine atoms can be replaced one at a time. The first replacement is strongly exothermic, whereas the other steps proceed less readily, and only on heating. The reaction is

[*] Prof. Dr. H. Normant
Faculté des Sciences, Laboratoire de Synthèse Organique,
1, Rue Victor-Cousin
Paris (Ve) (France)

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generally carried out in an inert organic solvent[7]. The quantity of $HN(CH_3)_2$ required can be reduced by the addition of Na_2CO_3 or NH_3. After removal of the precipitated chlorides, the filtrate is rectified.

HMPT is a colorless mobile liquid, which is miscible with water in all proportions. It is also miscible with many polar and nonpolar organic solvents, but not with saturated hydrocarbons. It can be extracted from aqueous solution by chlorinated solvents, with which it forms complexes[9]. This property makes it superior to amides of carboxylic acids (cf. Table 1). The toxicity of HMPT is low: LD ≈ 6 g/kg[7] for oral administration to rats.

Table 1. Partition coefficients of a few acid amides between water and chlorinated hydrocarbons.

	Dimethyl-formamide	*N*-Methyl-acetamide	HMPT
$CHCl_3/H_2O$	0.77	0.099	5.53
CH_2Cl_2/H_2O	0.57	0.088	2.07
$ClCH_2-CH_2Cl/H_2O$	0.29	0.039	0.58

B. Structure

The HMPT molecule is pyramidal, as can be seen from the Stuart-Briegleb model (see Fig. 1). The polar or double-bond character of the P–O bond varies

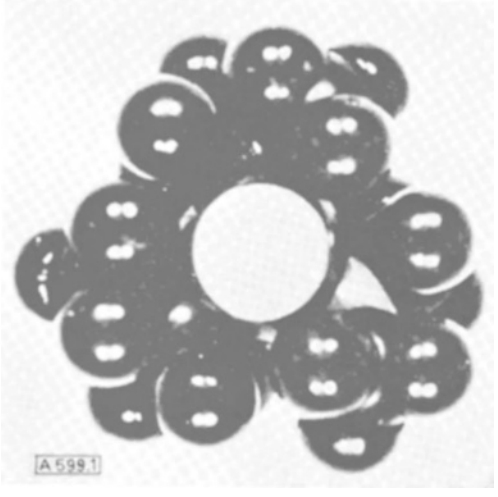


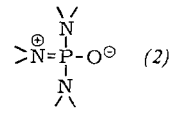
Fig. 1. Stuart model of $OP(N(CH_3)_2)_3$ (HMPT). The phosphorus atom is concealed by the oxygen atom.

according to the other substituents[10,11]; 50% ionic character must be assumed in HMPT (see formula *(1)*).

$$F_3P{=}O \quad ((CH_3)_2N)_3\overset{\delta\oplus}{P}{-}\overset{\delta\ominus}{O} \quad (CH_3)_3\overset{\oplus}{P}{-}\overset{\ominus}{O}$$

(1)

Formula *(2)* has also been proposed[12].



(2)

The symmetrical distribution of the positive charge over the  grouping and the high electron density on the oxygen give rise to a large dipole moment and an unusually high basicity.

C. Physical Constants

Table 2. Physical constants of HMPT.

Physical quantity	Numerical value
M.p. (°C)	7.20
Cryoscopic const.	6.93 ± 0.07 [13]
B.p. (°C/mm)	235/760
	115/15
	68–70/1
Dielectric const.	ε = 30/20 °C
ε = f(t)	[21]
Dipole moment μ (fluid)	5.37 D/25 °C [21]
	4.31 D/25 °C [12]
(in benzene)	5.54 D/25 °C [21]
Vapor pressure	0.07 mm/30 °C [16]
Vapor pressure curve	[17]
Density d_4^{20}	1.0253 [18]
n_D^{20}	1.4582 [18]
n_4^{25}	1.4570 [19]
Refractive index in IR region	[20]
Dynamic viscosity	3.5 cS/60 °C [14]
NMR: $\delta^{21}P$	23.4 ppm [25] (against 85% H_3PO_4)
Enthalpy of formation from $O{=}PCl_3$ and $HN(CH_3)_2$	H_f° (gas) ≈ −114.1 kcal/mol [24]

Table 3. IR absorption bands of HMPT.

Band position	Assignment
7.1–9.8 μm	C–N (stretching vibration)
7.5–8.5 μm	P–O (stretching vibration) [*]
13.9 μm	P–N (stretching vibration)

[*] In chlorinated hydrocarbons (CCl_4, $CHCl_3$, $CHCl_2-CCl_3$, $Cl_2CH-CHCl_2$, CH_2Cl_2) this band appears at 8.26–8.32 μm; it also varies a little in other solvents [22, 23].

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D. Basicity

A particularly suitable method for the determination of the ability of a solvent to contribute part of a pair of electrons to a compound AH (*e.g.* $CHCl_3$), *i.e.* the basicity of the solvent, is NMR spectroscopy [26]. For each solvent there is a value $\Delta\delta_\infty$ ($CHCl_3$) = $\delta_\infty - \delta$ (cf. Table 4) [3, 27, 28], where δ_∞ and δ respectively are the chemical shifts at infinite dilution of a solution of chloroform in the solvent in question and in an inert solvent such as cyclohexane.

Table 4. Comparison of the $\Delta\delta_\infty$ values [3, 27, 28] of various solvents.

Solvent	$\Delta\delta_\infty$	Solvent	$\Delta\delta_\infty$
Cyclohexane	0	Cyclohexanone	1.06
Dioxane	0.64	$OP(OC_4H_9)_3$	1.28
$P(N(CH_3)_2)_3$	0.68	DMF	1.30
Ether	0.70	DMSO	1.34
THF	0.80	Tetramethylurea	1.37
Acetone	0.94	HMPT	2.03

A similar basicity scale was obtained from the C–Br vibrations in the IR spectra of alkyl or vinyl bromides. These C–Br vibrations are strongly dependent on the basicity of the solvent. It could be shown [28, 29] that the solvent-bromide interaction varies in the same manner as the solvent-proton interaction.

Table 5 [4] shows a comparison of the polar aprotic solvents in current use. HMPT has the lowest dielectric constant and the highest basicity of all the solvents listed.

Table 5. Physical properties of solvents.

Solvent	DC	μ (Debye)	Δδ (ppm)
Dimethylformamide	36.7	3.90	0.78
Dimethylsulfoxide	49	4.03	1.05
Ethylene glycol carbonate	95	4.86	0.41
Tetramethylenesulfone	44	4.7	0.78
HMPT	30	4.3–5.3	1.89

E. Hexamethylphosphoramide as an Electron Donor in Complexes

1. Complexes with Organic Compounds

The donor properties of some OP compounds in relation to compounds containing active hydrogen vary in the following order [31]:

$$((CH_3)_2N)_3PO > (C_2H_5O)_3PO > (C_2H_5S)_3PO > (C_6H_5S)_3PO > ((C_2H_5)_2N)_3PO$$

(It is interesting to note that HMPT and its hexaethyl analogue are situated at opposite ends of this series.)

The acceptor properties of the chlorinated hydrocarbons studied [23, 30] vary in the order:

$$CHCl_3 > Cl_2CH-CCl_3 > Cl_2CH-CHCl_2 > CH_2Cl_2$$

Mono- and dicarboxylic acids (*e.g.* nicotinic and isonicotinic acids, *o*- and *m*-methylbenzoic acids), phenols and diphenols (α- and β-naphthols, chlorophenols [33]), alcohols and aromatic amines, glycols, *etc.* react with HMPT to form stable crystalline stoichiometric complexes [32] (cf. Table 6). An H donor can be liberated from its complex by a stronger H donor (*i.e.* in this case a weaker acid). Thus water or methanol displace carboxylic acids. Terephthalic and isophthalic acids could be separated by fractional crystallization of the complexes followed by liberation of the acids [32].

IR studies on the stability of hydrogen halide-ketone and hydrogen halide-acid hydrazide complexes [173] confirm the conclusion that the association constants decrease in the order HBr > HCl > HF, corresponding to the decrease in acidity from HBr to HF.

Table 6. HMPT Complex formation.

HMPT-Complex with:		M.p. (°C)
o,- *m*-, *p*-$(HO_2C)C_6H_4$	2:1	70/52/128
p-$(OH)_2C_6H_4$	2:1	152
$HOCH_2-C_6H_5$	1:1	10
$H_2N-C_6H_5$	1:1	<0
p-$H_2N-C_6H_4-C_6H_4-NH_2$(*p*)	2:1	132
$HOCH_2-CH_2OH$	2:1	−20

HMPT also forms complexes with unsaturated hydrocarbons [32] (*e.g.* $HC\equiv CH$, $CH\equiv C-CH=CH_2$, $CH\equiv C-C_6H_5$, $CH_2=CH-CH=CH_2$, $CH_2=CH-C_6H_5$); however, the structure of these complexes is not yet known.

2. Complexes with Lewis Acids

Basic solvents form complexes with Lewis acids, the stability of the complex increasing with increasing basicity of the solvent; *e.g.* $(C_2H_5)_2O\cdot BF_3 < THF\cdot BF_3 < OP(N(CH_3)_2)_3\cdot BF_3$.

A number of crystalline complexes of HMPT are known: $OP(N(CH_3)_2)_3\cdot BF_3$ (m.p. 175 °C) [34]; $OP(N(CH_3)_2)_3\cdot BCl(C_6H_5)_2$ (m.p. 159–160 °C) [35]; $OP(N(CH_3)_2)_3\cdot OPCl_3$ (m.p. 170–180 °C); $OP(N(CH_3)_2)_3\cdot OPBr_3$ (m.p. 165–180 °C).

It is known from IR data [12] and dipole moment measurements [36] that metal salts also form complexes with HMPT by solvation of the cation (*via* the oxygen of the OP group) (see Table 7). Neutral molecules $MX_2\cdot 2\ OP(N(CH_3)_2)_3$ and ions $[M\cdot 4\ OP(N(CH_3)_2)_3]^{2\oplus}$ have a tetrahedral structure [12, 36].

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Table 7. Types of metal salt–HMPT Complexes.

M	Complex	Anion
Ag	$M(HMPT)X$	Halide
Co, Ni, Mn, Fe^{II}, Cu^{II}	$M(HMPT)_2X_2$	Halide
Pb^{II}	$M(HMPT)_3X_2$	Halide
Mg, Zn, Cd	$M(HMPT)_4X_2$	Halide
Co, Ni, Mn, Fe^{II}	$M(HMPT)_4X_2$	$ClO_4^{\ominus}$
Cr^{III}, Fe^{III}	$M(HMPT)_6X_3$	Halide
Ti, Sn	$M(HMPT)_2X_4$	Halide

HMPT-complexes of the tetrachlorides and tetrabromides of thorium and uranium have recently been detected, and their stabilities were compared with those of the corresponding dimethyl sulfoxide complexes [37].

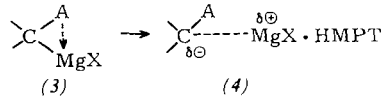
The tendency of a polar solvent to form complexes with a Lewis acid generally increases with increasing basicity of the solvent, *i.e.* the tendency increases in the order DMSO < DMF < HMPT.

3. Complexes with Organometallic Compounds

The stability of solvated Grignard compounds increases with increasing stability of the solvent [34]: $2(C_2H_5)_2O{\cdot}RMgX < 2THF{\cdot}RMgX < 2OP(N(CH_3)_2)_3{\cdot}RMgX$.

Thus less basic solvents can be displaced from the complex by more basic solvents [37]. Magnesium compounds of the type MgR_2 dissolve in HMPT [38], while compounds of the type RMgBr precipitate out as $MgBr_2{\cdot}2\,OP(N(CH_3)_2)_3$; $MgBr_2$ forms the stable adduct $MgBr_2{\cdot}4\,OP(N(CH_3)_2)_3$ [39]. This generally strong solvation has the following consequences:

Organomagnesium compounds of the type *(3)* (A = OR [40], halogen [41]) exhibit autosolvation. Their stability and reactivity is increased by the addition of $OP(N(CH_3)_2)_3$, since this leads to disappearance of the "carbenoid" form *(3)* in favor of an ionic structure *(4)*.



(3) *(4)*

It has also been found that the rate of the exchange reaction

$$(CH_3{-}CH{=}CH{-}CH_2)_2Zn + CdCl_2 \rightleftarrows (CH_3{-}CH{=}CH{-}CH_2)_2Cd + ZnCl_2 \qquad (b)$$

decreases (THF > DMSO > HMPT) with increasing basicity of the solvent, *i.e.* with increasing solvation of the cadmium ion [42]. The solvation in HMPT even makes possible the direct synthesis of organometallic compounds from RX and magnesium or cadmium [43]. Unsaturated bromine compounds react at 0 °C; only the iodides react in the saturated series.

The isolable, acetone-soluble complex $CdBr_2{\cdot}4OP(N(CH_3)_2)_3$ (m.p. 112 °C [43]) is formed in this way, but can also be obtained directly from $CdBr_2$ and HMPT.

F. Hexamethylphosphoramide in Electrochemistry

Until recently very little use had been made of HMPT as a solvent for electrochemical processes. For example, no mention has been made of its use in polarography. A stable $Ag^{\oplus}/Ag$ reference electrode can be used for voltametry [44] in HMPT. Solutions of $NaClO_4$ and $LiClO_4$ and their mixtures have been specially studied in relation to their water content. The results indicate that the behavior of HMPT differs from that of other solvents [45].

HMPT can also be used as a solvent for electrolysis [46]. Metal salts dissolve to give ion pairs and in some cases even form free ions. Anions are practically unsolvated (steric hindrance around the $P^{\delta\oplus}$), whereas cations are strongly solvated (owing to the sterically easy accessibility of the $O^{\delta\ominus}$ atom). Thus $(C_6H_5)_3CM$, $(C_6H_5)_2CHM$, and $C_6H_5CH_2M$ (M = alkali metal or MgX) dissolve to give intensely red solutions (see Section IV). $C_6H_5CH_2MgCl$ prepared in ether solution is colorless; on addition of HMPT, however, the solutions assumes the characteristic red color of the benzyl anion [45a].

Though to our knowledge no organometallic compounds have so far been electrolysed in HMPT, metal salts such as $MgBr_2{\cdot}2(C_2H_5)_2O$ and CaI_2 have been electrolysed with the aid of a consumable Mg or Cd anode and a Pt cathode. In both cases 2,3,4,5-tetrahydrobenzophenone present in the solution could be reduced in a yield of more than 80% to 1,2,3,4,5,6-hexahydrobenzophenone.

G. Polarity of the Solvent

Polar solvents can give rise to various molecular interactions. These polarity effects are related to a first approximation to the dipole moments μ, the dielectric constants ε, and $\Delta\delta$ the chemical shift of the $CHCl_3$ proton in the ^1H-NMR spectrum. For example, a nucleophilic substitution in accordance with eq. (c) may be carried out and compared in various solvents. The rate constants k and activation energies $E^{\neq}$ obtained are shown in Table 8. The special position of

Table 8. Data for the reaction (c) in various solvents.

Solvent	$k_{25\,°C}$ ($l{\cdot}mole^{-1}\,sec^{-1}$)	$E^{\neq}$ ($kcal{\cdot}mole^{-1}$)
Acetonitrile	4.31×10^{-2}	17.12
DMF	2.37×10^{-2}	16.45
DMSO	1.14×10^{-2}	16.91
HMPT	1.75	13.40
Methanol	8.61×10^{-6}	21.18
Water	5.80×10^{-5}	21.41
Formamide	9.62×10^{-5}	20.08

[37] *K. W. Bagnall et. al.*, J. chem. Soc. (London) A *1966*, 737.

[38] *J. Fauvarque* and *J. F. Fauvarque*, C. R. hebd. Séances Acad. Sci. Sér. C *263*, 488 (1966).

[39] *F. Fauvarque*, Diplôme d'Etudes Superieures de Sciences Physiques, Paris 1964.

[40] *B. Castro*, Bull. Soc. chim. France *1967*, 1533.

[41] *J. Villiéras*, Bull. Soc. chim. France *1967*, 1511.

[42] *Cl. Agami* and *C. Prévost*, C. R. hebd. Séances Acad. Sci., Sér. C *263*, 304 (1966).

[43] *J. Chenault* and *F. Tatibouët*, C. R. hebd. Séances Acad. Sci., Sér. C *262*, 499 (1966).

[44] *J. E. Dubois*, *P. C. Lacaze*, and *A. Marie de Fiquelmont*, C. R. hebd. Séances Acad. Sci. Sér. C *262*, 181 (1966).

[45] *J. E. Dubois*, *P. C. Lacaze*, and *A. Marie de Fiquelmont*, C. R. hebd. Séances Acad. Sci., Sér. C *262*, 249 (1966).

[45a] *H. F. Ebel* and *R. Schneider*, Angew. Chem. *77*, 914 (1965); Angew. Chem. internat. Edit. *4*, 878 (1965).

[46] *P. Angibaud*, *H. Rivière*, and *B. Tchoubar*, unpublished.

HMPT is again obvious. Satisfactory correlations were given by the relationships $\log k = f(1/\varepsilon)$ and $\log k = f'(\Delta\nu)$ [3].

$$CH_3-(CH_2)_3Br + N_3^{\ominus} \rightarrow CH_3-(CH_2)_3N_3 + Br^{\ominus} \qquad (c)$$

Classification of solvents by the Z value [47]:

CH_3OH, C_2H_5OH, $(CH_3)_3COH$, CH_3CN, DMF, $CHCl_3$, HMPT, iso-octane

Classification of solvents by the F value [48]:

CH_3OH, C_2H_5OH, $(CH_3)_3COH$, CH_3CN, HMPT, DMF, $CHCl_3$, iso-octane

II. Chemical Reactions of Hexamethylphosphoramide

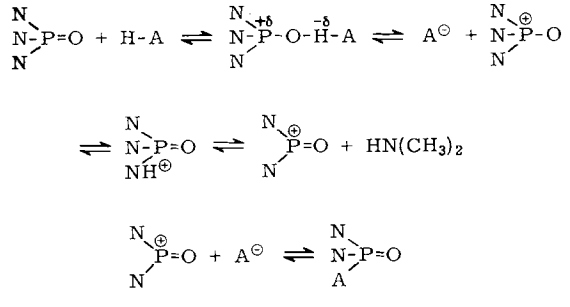
A. Reaction with Nucleophiles

HMPT is remarkably stable to nucleophiles (evidently because of steric screening of the $P^{\delta\oplus}$), and unlike the amides of carboxylic acids it is not hydrolysed in alkaline media (alkali metal hydroxides do not attack below 80 °C [127–132]; however, HMPT appears to react at 110–120 °C [151]). Thus HMPT is an ideal solvent for reactions with nucleophilic or basic reactants (cf. also Sections IV and V) [49].

B. Reaction with Electrophiles

HMPT is attacked by both Brönsted and Lewis acids. A reagent $H^{\oplus}A^{\ominus}$ brings about the replacement of one or more $N(CH_3)_2$ groups by A.

It is likely that a 1:1 complex is first formed by binding of the acid HA (*e.g.* HCl) *via* the oxygen of the OP group. This more or less stable complex gives a corresponding substitution product when heated. The reaction may be assumed to proceed by the following mechanism:



This reaction also takes place with the other $N(CH_3)_2$ groups though less readily. In aqueous acid solution the $N(CH_3)_2$ groups are replaced by OH (HA = H_2O).

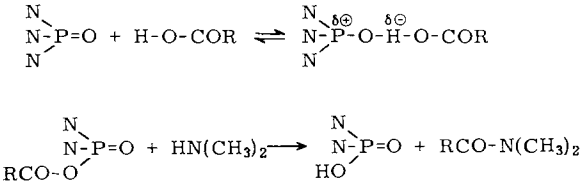
The rate of hydrolysis is of the same order of magnitude as that of a $-CO-N(CH_3)_2$ group [15].

The complex HMPT·$CHCl_3$ is also decomposed by heat. $HO-P(N(CH_3)_2)_2$ has been detected among the reaction products by NMR spectroscopy [174]. The reaction is assumed to proceed by the above mechanism, *i.e. via* a pentacoordinated intermediate, which seems rather unlikely to us (NMR investigations are in progress).

Carboxylic acids often give very stable 1:1 complexes with HMPT. At 180–200 °C, transamidation takes place [50]:

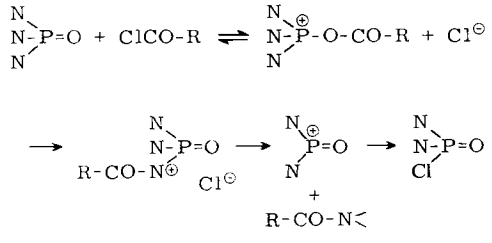
$$OP(N(CH_3)_2)_3 + 3\ RCO_2H \rightleftharpoons OP(OH)_3 + 3\ RCO-N(CH_3)_2.$$

A mechanism similar to that described would involve the formation of a mixed anhydride of the phosphorodiamidic acid and the carboxylic acid. The reaction



could also be extended to aromatic, unsaturated, and heterocyclic carboxylic acids (*e.g.* acetic, valeric, lauric, monochloroacetic, trichloroacetic, succinic, adipic, phthalic, benzoic, *p*-nitrobenzoic, *m*-toluic, and isonicotinic acids) and to sulfonic acids (yields = 50 to 95%). When the HMPT and the acid are present in a molar ratio of 1:3, H_3PO_4 and the amide of the acid are formed [51].

This substitution reaction does not appear to have been applied to alcohols as yet. Phenols give relatively stable 1:1 complexes (cf. Section I. E. 1) of unknown structure with HMPT. Acyl chlorides undergo nucleophilic attack by HMPT even in the cold; when the complex is heated, $N(CH_3)_2$ is replaced by Cl.



HMPT also reacts with chlorides of mineral acids (*e.g.* $SOCl_2$ and $POCl_3$). The monochloro derivative *(5)* could in principle be formed by a reaction [52] in accordance with eq. (d) or by a reaction [53] in accordance with equation (e).

$$2\ OP(N(CH_3)_2)_3 + OPCl_3 \rightleftharpoons 3\ \underset{(5)}{OP(Cl)(N(CH_3)_2)_2} \qquad (d)$$

$$OP(N(CH_3)_2)_3 + OP(N(CH_3)_2)Cl_2 \rightleftarrows 2\ \underset{(5)}{OP(Cl)(N(CH_3)_2)_2} \qquad (e)$$

[47] *E. M. Kosower*, J. Amer. chem. Soc. *80*, 3253 (1958); J. chem. Physics *61*, 230 (1964).

[48] *J. E. Dubois* and *A. Bienvenue*, Tetrahedron Letters *17*, 1809 (1966).

[49] *H. Normant*, unpublished.

[50] *R. L. Heider*, US.-Pat. 2603660 (July 15th, 1952); Chem. Abstr. *47*, 4900 (1953).

[51] *J. Kopecky* and *J. Smeikal*, Chem. and Ind. *36*, 1529 (1966).

[52] *P. Lester*, Chem. Abstr. *49*, 6300 (1954).

[53] *M. Pianka* and *B. D. Owen*, J. appl. Chem. *5*, 525 (1955); Chem. Abstr. *50*, 10642d (1956).

The alkali metal derivatives $OP(N(CH_3)_2)_2M$ (M = Li, Na, K) can be obtained in excellent yield from *(5)* [54, 18]. These in turn react with electrophilic reagents such as CH_3Br, C_2H_5Br, $C_7H_{15}Br$, $C_6H_5CH_2Cl$, CH_3OCH_2Cl, $C_4H_9OCH_2Cl$, and $C_4H_9SCH_2Cl$ to form phosphonic diamides.

C. Reaction with Alkali Metals

The reaction of HMPT with alkali metals leads *via* a radical-anion (see Section V) to two anions, the dimethylamine anion *(6)* and the diamidophosphite anion *(7)*.

$$OP(N(CH_3)_2)_3 + 2\ M \longrightarrow \begin{cases} (CH_3)_2N^{\ominus}\ M^{\oplus} & (6) \\ OP(N(CH_3)_2)_2\ M^{\oplus} & (7) \end{cases}$$

These react with alkyl bromides to give tertiary amines and phosphonic diamides. The reaction with benzyl chloride, on the other hand, does not lead to the expected phosphonic diamide *(9)*; on the contrary, the diamide *(8)* is formed by reaction with two molecules

$$((CH_3)_2N)_2PO\text{-}CH_2\text{-}C_6H_5 \underset{\ominus N<}{\rightleftharpoons} ((CH_3)_2N)_2PO\text{-}\overset{\ominus}{C}H\text{-}C_6H_5$$
(9)

$$\longrightarrow ((CH_3)_2N)_2PO\text{-}CH(C_6H_5)\text{-}CH_2\text{-}C_6H_5$$
(8)

of benzyl chloride. However, compound *(9)* could be obtained from $OP(N(CH_3)_2)_2M$ and benzyl chloride in an ether/benzene mixture. $NaNH_2$ can actually replace a methylene H atom in *(9)* by Na in HMPT as solvent; the compound *(8)* is obtained in good yield by the addition of benzyl chloride. Thus in the mixture *(6)*/*(7)*, the strong base *(6)* converts the compound *(9)* into a carbanion as it is formed; the carbanion is immediately benzylated to form *(8)*.

The presence of the base *(6)* also explains why a mixture *(6)*/*(7)* can metallate a hydrocarbon so weakly acidic as triphenylmethane (a blood-red solution is formed). In benzene [55], the radical-ion is not stabilized, but decomposed. The weak base *(7)* cannot be the metallating agent, since $OP(N(CH_3)_2)_2M$ does not react with triphenylmethane even at high temperatures; on the contrary, $OP(H)(N(CH_3)_2)_2$ [56] liberates triphenylmethane from triphenylmethylsodium.

The compound *(7)* can add to unsaturated compounds. With azobenzene, hydrolysis yields the adduct *(10)* [57], while with phenylacetylene (or α-bromostyrene) the adduct *(11)* is formed [58]. It is interesting to note that compound *(7)* can bring about the reductive dimerization of non-enolizable ketones with formation of epoxides *(12)* [59]. This new epoxidation method has also been applied to aldehydes ArCHO.

$$\begin{matrix} C_6H_5\text{-}N\text{-}NH\text{-}C_6H_5 \\ | \\ OP(N(CH_3)_2)_2 \end{matrix} \quad (10)$$

$$\begin{matrix} C_6H_5\text{-}CH\text{-}CH_2\text{-}P(N(CH_3)_2)_2 \\ | \qquad\qquad\quad \| \\ (N(CH_3)_2)_2PO \qquad O \end{matrix} \quad (11)$$

$$2\ Ar_2CO + \overset{\ominus}{O}P(N(CH_3)_2)_2M^{\oplus} \longrightarrow$$

$$Ar_2C\text{-}CAr_2 + O{=}P\text{-}N(CH_3)_2$$
$$\quad\ \diagdown O \diagup \qquad\quad |$$
$$\qquad O \qquad\quad O^{\ominus}\ M^{\oplus}$$
(12)

The reaction is also possible with $OP(OC_2H_5)_2M$ in place of $OP(N(CH_3)_2)_2M$ (M is preferably Na) [60].

D. Catalytic Action of Hexamethylphosphoramide

The reactions discussed in this section proceed more readily in the presence of HMPT, though this compound is not consumed in the reactions.

The formation of carbodiimides from isocyanates is accelerated by the addition of a small quantity of a polar solvent [61]. HMPT is much more effective than DMSO, as is shown by the data in Table 9 for the synthesis of diphenylcarbodiimide.

Table 9. Catalysis of the diphenylcarbodiimide synthesis.

Catalyst	C_6H_5–N=C=O	Temp. (°C)	Time (h)	Yield (%)
DMSO 0.006 mole	0.45 mole	162–164	2.5	13
HMPT 0.008 mole	0.45 mole	113–135	1.6	27

It has been assumed [6] that a cyclic imide *(13)* is formed as an intermediate:

$$\begin{matrix} N \\ N\text{-}\overset{\oplus}{P}\text{-}\overset{\ominus}{O} \\ N \end{matrix} + R\text{-}N{=}CO \rightleftharpoons \begin{matrix} \gtrdot P\text{-}O \\ | \quad | \\ R\text{-}N\text{-}C{=}O \end{matrix} \rightleftharpoons CO_2 + \gtrdot P{=}N\text{-}R$$

$$\gtrdot P{=}N\text{-}R + R\text{-}N{=}C{=}O \longrightarrow \begin{matrix} \gtrdot P\text{-}N\text{-}R \\ | \quad | \\ O\text{-}C{=}N\text{-}R \end{matrix}$$
(13)

$$\longrightarrow \gtrdot P{=}O + R\text{-}N{=}C{=}N\text{-}R$$

HMPT increases the rate of substituent exchange between trialkylboranes and 1-alkenes [62], *e.g.*:

$$B(C_4H_9)_3 + CH_2{=}CH\text{–}(CH_2)_7\text{–}CH_3 \rightarrow$$
$$(C_4H_9)_2B\text{–}(CH_2)_9\text{–}CH_3 + CH_2{=}CH\text{–}CH_2\text{–}CH_3$$

[54] *H. Normant* and *J. F. Brault*, unpublished.

[55] *H. Normant, T. Cuvigny, J. Normant*, and *B. Angelo*, Bull. Soc. chim. géol. géogr. France *1966*, 3442.

[56] *A. Szwierzak*, Bull. Acad. polon. Sci., Sér. Sci. chim., *13*, 609 (1965).

[57] *H. Normant* and *M. Larchevêque*, C. R. hebd. Séances Acad. Sci., Sér. C *260*, 5063 (1965).

[58] *H. Normant, T. Cuvigny, J. Normant*, and *B. Angelo*, Bull. Soc. chim. France *1966*, 3449. – The structure was confirmed by NMR spectroscopy.

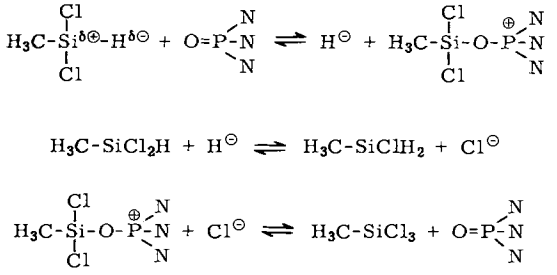
[59] *H. Normant, T. Cuvigny, J. Normant*, and *B. Angelo*, Bull. Soc. chim. France *1966*, 3443.

[60] *J. F. Normant*, Bull. Soc. chim. France *1966*, 3601.

[61] *J. J. Monagle* and *H. R. Nace*, US.-Pat. 3056835 (Oct. 2nd, 1962); Chem. Abstr. *58*, 3362 (1963); *J. J. Monagle*, J. org. Chemistry *27*, 3851 (1962).

[62] *A. J. Rutkowski, E. J. Inchalik*, and *A. Schriesheim*, US.-Pat. 3313225 (April 28th, 1964); Chem. Abstr. *61*, 4393d (1964).

In the presence of 0.5 to 15% of HMPT, dismutation of chlorosilanes takes place at fairly low temperatures[63], *e.g.* in accordance with eq. (f), probably in three steps: removal of a proton by the basic solvent, reduction by $H^{\ominus}$, and regeneration of the HMPT.



$$H_3C\text{-}SiCl_2H + H^{\ominus} \rightleftharpoons H_3C\text{-}SiClH_2 + Cl^{\ominus}$$

$$2\ H_3C\text{-}SiCl_2H \rightleftharpoons H_3C\text{-}SiCl_3 + H_3C\text{-}SiClH_2 \quad (f)$$

III. Hexamethylphosphoramide as a Reaction Medium with Electron Donor Properties

A. Anion Formation or Transmetallation

Hydrogen-metal exchange reactions lead to the formation of a salt or another organometallic compound:

$$AH + MR \rightleftharpoons RH + MA \text{ (or } M^{\oplus} + A^{\ominus})$$

The equilibrium lies to the right-hand side when AH is more strongly acidic than RH or when the base $R^{\ominus}$ is stronger than the base $A^{\ominus}$. (The acidities of various compounds AH are given in Table 10.)

Table 10. Acidity of various compounds.

AH	pK_a	AH	pK_a
CH_4	50	liq. NH_3	34
$C_6H_5CH(CH_3)_2$	37	$C_6H_5NH_2$	27
$(C_6H_5)_2C{=}CH{-}CH_3$	36	Acetone	19
$C_6H_5CH_3$	37	$(CH_3)_3COH$	19
$(C_6H_5)_2CH_2$	35	$CH_3{-}OH$	16
$(C_6H_5)_3CH$	33	H_2O	14
$HC{\equiv}CH$	26	$C_6H_5{-}OH$	9.9
Fluorene	25	Acetylacetone	9
Indene	21	C_6H_5SH	8
$C_6H_5C{\equiv}CH$	21	*p*-Nitrophenol	7.2
Cyclopentadiene	17	Pyrrole	5

The solvent plays an important part in exchange reactions of this type. Solvents possessing electron donor properties favor ionization, solvation (particularly of the cations $M^{\oplus}$), and dissociation of AH and MR. This is particularly true of HMPT, which is the best electron donor of all the common aprotic solvents, and also has excellent solvation properties. For example, it causes strong solvation of the alkali metal cations and formation of highly reactive free anions.

1. Alkoxide and Phenoxide Anions[64]

Alcohols and phenols, which are relatively strong acids, react readily with alkali metal hydrides and amides. The advantage of HMPT is that stoichiometric quantities of ROH or ArOH may be used, and since the $RO^{\ominus}$ and $ArO^{\ominus}$ anions are not solvated, the reactants are more reactive than in excess ROH or ArOH with autosolvated anions. It is even possible in HMPT to use such weakly acidic reactants as tert-butyl alcohol or allyl alcohol; diols give dianions under these conditions. Alkali metal carboxylates can be satisfactorily prepared in HMPT and converted into esters; this avoids the conventional preparation *via* silver carboxylates. Alkali metal salts have extremely high or even unlimited solubilities in HMPT[64].

2. Amide Anions[64]

Alkylamines are too weakly acidic to be converted into alkali metal amides by the action of alkali metal hydrides or amides (M = Na, K, Ca); the reaction takes place only with M = Li[65].

$$H_3C{-}NH_2 + MNH_2 \rightleftharpoons H_3C{-}NH{-}M + NH_3$$

In the case of higher alkylamines the more strongly basic organometallic compounds must be used.

On the other hand, arylamines ArNHR (R = H, alkyl, aryl), indole, carbazole, and phenothiazine react with NaH or $NaNH_2$ at room temperature in HMPT. The dianion $C_6H_5N^{2\ominus}$ can be formed from aniline. Amides of carboxylic acids and imides react readily even in the cold. The Na derivatives of indole, acetanilide, and phthalimide have unlimited solubility in HMPT.

3. Carbanions from Hydrocarbons

The rate of a hydrogen-metal exchange depends here on the acidity of the hydrocarbon and the basicity and polarity of the solvent.

a) Alkynes

Grignard compounds react in the cold with 1-alkynes in polar solvents as indicated in eq. (g)[66]; organozinc compounds react similarly in accordance with eq. (h)[67]. The accelerating effect of the solvent (HMPT is again the best) can be seen from Table 11[67].

$$R{-}C{\equiv}C{-}H + (CH_3)_2CH{-}MgCl \rightarrow R{-}C{\equiv}C{-}MgCl + C_3H_8 \quad (g)$$

$$2\ C_6H_5{-}C{\equiv}CH + Zn(C_2H_5)_2 \rightarrow (C_6H_5{-}C{\equiv}C)_2Zn + 2\ C_2H_6 \quad (h)$$

Table 11. Half-times of the reaction (h) at 50 °C in polar solvents [67].

THF	DMF	DMSO	HMPT
2.15 h	270 sec	200 sec	< 8 sec

[63] French Pat. 1444735 (March 19th, 1965), Rhône Poulenc.

[64] *H. Normant* and *T. Cuvigny*, Bull. Soc. chim. France *1965*, 1867.

[65] *E. Rengade*, Ann. Chim. Physique *11* (8), 348 (1907).

[66] *H. Normant* and *T. Cuvigny*, Bull. Soc. chim. France *1964*, 2004.

[67] *O. Okhlobystin* and *L. Zakharkin*, Ž. org. Chim. *3*, 257 (1965).

The behavior of 1-alkynes in HMPT depends on the base present as the other reactant [68]. Thus NaH does not react either with phenylacetylene or with acetylene. Higher 1-alkynes such as 1-heptyne isomerize to give a mixture of heptynes, in which the principal component is the 2-alkyne. The more strongly basic alkali metal amides, *e.g.* $NaNH_2$, on the other hand, react at room temperature to form 1-alkynides such as $R-C\equiv C-Na$. However, phenylacetylene and acetylene are not converted into the sodium derivatives in pure HMPT, since they form complexes with HMPT.

b) Triphenylmethane

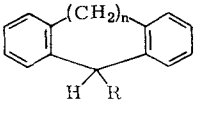
Triphenylmethylmagnesium halides cannot be prepared from triphenylmethane and Grignard compounds in weakly polar solvents such as ether or tetrahydrofuran; however, this reaction takes place with isopropylmagnesium chloride at 90 °C in HMPT [69], as is shown by the blood-red color of the solution.

Triphenylmethane cannot be metallated with alkali metal amides or hydrides (M = Li, Na, K) in tetrahydrofuran (stronger bases such as benzylsodium or allylsodium are required [70]), but is metallated even at room temperature in HMPT; the HMPT solutions are stable. Compounds $(C_6H_5)_3CM$ (M = Li, Na, K) have so far been prepared with alkali metal amides in liquid ammonia. Triphenylgermane can be metallated in a similar manner. Lithium aminoacetylides also react with triphenylmethane in HMPT as indicated in eq. (i) [71].

$$\text{N}-\text{C}\equiv\text{C}-\text{Li} + (C_6H_5)_3CH \rightarrow \text{N}-\text{C}\equiv\text{CH} + (C_6H_5)_3CLi \qquad \text{(i)}$$

c) Diphenylmethane

Diphenylmethane and the related hydrocarbons *(14a)* to *(14d)* can also be metallated in HMPT [72].



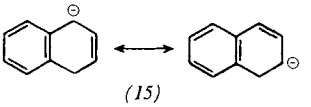
(14a), R = H, n = 0
(14b), R = C_2H_5, n = 0
(14c), R = H, n = 1
(14d), R = H, n = 2

Diphenylmethane is much less acidic than triphenylmethane, and reacts with isopropylmagnesium chloride only in HMPT and not below 100 °C (reaction recognized from the red color). However, it can be metallated with alkali metal amides and hydrides even at room temperature in HMPT. In less polar solvents, organosodium compounds must be used.

Fluorene *(14a)* can be converted into 9-fluorenylmagnesium chloride at 135–140 °C in xylene; this reaction proceeds at 40 °C in HMPT. Bis(9-fluorenyl)zinc can also be prepared in HMPT [67]. The acidic 9,10-dihydroanthracene *(14c)* can be metallated with isopropylmagnesium chloride or with sodium hydride even at room temperature. Dibenzocycloheptadiene *(14d)* reacts with $NaNH_2$ in HMPT, even in the cold, to give the deep orange 5-carbanion.

d) Hydrocarbons with Diene Structural Units [72]

Indene reacts with ethylmagnesium bromide at 100 °C in weakly polar solvents to form the mesomeric indenylmagnesium bromide, while the analogous reaction with isopropylmagnesium chloride in HMPT takes place at 30 °C. The strongly exothermic metallation of indene with sodium hydride in HMPT is best carried out at 0 °C; an orange-red anion is formed. 1-Alkylated indenes behave similarly. An H ↔ MgX exchange is possible at 35 °C in HMPT; the mesomeric anion is intensely red. The anions of the metallation products of 1,4-cyclohexadiene and 1,4-dihydronaphthalene exhibit a remarkable tendency toward aromatization [72],



(15)

$H_5C_6-CH=CH-\overset{\ominus}{C}H-C_6H_5$ *(16)*

The red anion *(15)* is formed in HMPT with isopropylmagnesium chloride at 90–95 °C; $NaNH_2$ leads to considerable polymerization of 1,4-dihydronaphthalene even in the cold.

1,3-Diphenylpropene also gives a red anion *(16)* on reaction with isopropylmagnesium chloride in HMPT at room temperature, while alkali metal compounds again cause polymerization.

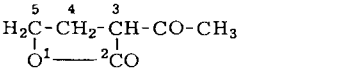
4. Carbanions from Heterosubstituted Hydrocarbons or from Hydrocarbons with Functional Groups [73]

a) Phenylacetic Acid and Malonic Acid Derivatives

The CH_2 protons of a benzyl residue are mobile if the benzyl residue is joined to an electron-attracting group. Thus phenylacetic acid reacts in the cold with isopropylmagnesium chloride or with sodamide in HMPT to form a dianion; the solubility of the disodium salt is infinite. Benzyl cyanide is metallated by NaH or $NaNH_2$ at 0 °C; the dianion is formed as well as the red-violet anion. The nitriles $C_6H_5-CHR-CN$ give the monoanion at 0 °C.

The following compounds can be monometallated with NaH or $NaNH_2$ in HMPT at 0 °C, the lactone in position 3:

$CH_2(CO_2C_2H_5)_2$, $CH_2(CN)CO_2C_2H_5$, $CH_2(CN)_2$,



$CH_2(CO_2CH_3)CO_2C_2H_5$, $CH_2(CO_2CH_3)_2$

[68] *T. Cuvigny* and *H. Normant*, Bull. Soc. chim. France *1965*, 1876.

[69] *T. Cuvigny* and *H. Normant*, Bull. Soc. chim. France *1964*, 2022.

[70] *T. Cuvigny* and *H. Normant*, Bull. Soc. chim. France *1965*, 1873.

[71] *J. Ficini* and *G. Barbara*, Bull. Soc. chim. France *1965*, 2787.

[72] *T. Cuvigny* and *H. Normant*, Bull. Soc. chim. France *1965*, 1874.

[73] *H. Normant* and *T. Cuvigny*, Bull. Soc. chim. France *1965*, 1881.

b) Methylated Aromatic Compounds

Toluene and 2-methylfuran cannot be metallated, while 2-methylthiophene reacts only with difficulty. β-Picoline does not react with $NaNH_2$ in HMPT; in the α- and γ-isomers, in which the anion is resonance-stabilized, the CH_3 group is acidic. α-Picoline reacts with $(CH_3)_2CH-MgCl$ in HMPT to give a red anion. α-Picoline and γ-picoline are also metalled by $NaNH_2$ at 0 °C; the reactions do not proceed so readily with NaH. 2,3-Dimethylquinoxaline is more acidic than α-picoline, and both methyl groups react with NaH even at room temperature to give a green-violet dianion.

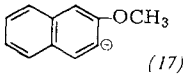
c) Other Compounds containing Replaceable Hydrogen

The haloforms react with the alkali metal compounds mentioned to give the anion $X_3C^{\ominus}$, which readily adds to the carbonyl group of a ketone in liquid ammonia [74]. This reaction does not proceed so smoothly in HMPT. On the other hand, the haloforms react readily with isopropylmagnesium chloride in HMPT. Trihalogenomethylmagnesium chlorides were obtained for the first time in a THF/hexamethylphosphoramide mixture (5:1 v/v) at −80 °C in accordance with eq. (k)[75]; the reaction does not take place with CF_3H.

$$X_3CH + (CH_3)_2CH\text{-}MgCl \rightarrow C_3H_8 + X_3C\text{-}MgCl \qquad (k)$$

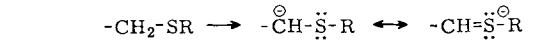
X = Cl, Br

The only methoxylated aromatic compound that has so far been made to react with $NaNH_2$ in HMPT is methyl β-naphthyl ether; the reaction presumably yields the red anion *(17)*.

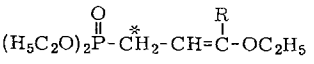


(17)

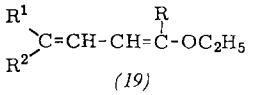
In the case of anions that contain the stronger acceptor group SR instead of OR, resonance stabilization is expected in accordance with:



The compounds $HC(SC_2H_5)_3$, $H_2C(SC_2H_5)_2$, $C_6H_5CH(SC_2H_5)_2$, and $C_6H_5CH(SC_6H_5)_2$, which had previously been converted into their anions [76] with alkali metal amides in liquid ammonia, were treated with $NaNH_2$ in HMPT. In the first two compounds the C–S bonds were cleaved; $C_6H_5CH(SC_2H_5)_2$ gives a black-green anion at 0 °C; the more acidic $C_6H_5CH(SC_6H_5)_2$ is metallated by NaH even at 0 °C. Acetophenone and acetonitrile react with sodium hydride in HMPT at 0 °C, with loss of one or two protons. Phosphonates of the type *(18)* can be readily deprotonated in the indicated position by NaH in HMPT to give carbanions. These add on to carbonyl compounds to give ethoxydienes *(19)*, which are otherwise difficult to obtain [77].



(18)



(19)

It may be assumed from these examples that the strong bases (*e.g.* organolithium compounds in THF) used so far in many other reactions can also be replaced by weaker bases if the reactions are carried out in HMPT, even at low temperatures.

B. Isomerization and Polymerization

Many isomerizations take place in alkaline media; such isomerizations depend on mesomeric carbanions and the possibility of prototropy. The reactions are strongly accelerated by polar solvents. An example of such a reaction is the allyl rearrangement of 2-phenylbut-1-ene [78].

The isomerization of 3-phenylpropene can be brought about in HMPT with NaH, even in the cold, the yield being about 70% [72]:

$$C_6H_5\text{-}CH_2\text{-}CH{=}CH_2 \rightarrow C_6H_5\text{-}CH{=}CH\text{-}CH_3$$

No appreciable polymerization takes place under these conditions. Anionic polymerization becomes more important when a stronger base (*e.g.* $NaNH_2$) is used or when the 3-phenylpropene is heated in the presence of a weak base (*e.g.* $(CH_3)_2CH-MgCl$) [79] The hydrocarbons listed in Table 12 react readily with $(CH_3)_2CH-MgCl$ in HMPT.

Table 12. Formation of anions from hydrocarbons and $(CH_3)_2CH-MgCl$ in HMPT.

Hydrocarbon	Color
$H_5C_6-CH_2-CH=CH-CH_3$	red
$(H_5C_6)_2C=CH-CH_3$	red
$H_5C_6-CH=CH-CH_2-CH=CH-CH_3$	faint pink
$H_5C_6-CH=CH-CH_2-C\equiv C-C_5H_{11}$	Prussian blue
$H_5C_6-C\equiv C-CH_2-CH=CH_2$	red
$H_5C_6-CH_2-C\equiv C-C_5H_{11}$	red

In the reaction with NaH or $NaNH_2$, the rapid disappearance of the color shows that polymerization has taken place. Similar polymerizations of olefins have been achieved even with organomagnesium compounds, but only in less polar solvents and only in the presence of halides of group IV B, V B, or VI B elements at low pressures.

[74] *H. G. Viehe* and *P. Valange*, Chem. Ber. *96*, 420 (1963).

[75] *H. Normant* and *J. Villiéras*, C. R. hebd. Séances Acad. Sci. *260*, 4525 (1965); *J. Villiéras*, *ibid. 261*, 4137 (1965).

[76] *H. Normant* and *T. Cuvigny*, Bull. Soc. chim. France *1965*, 1883.

[77] *G. Sturtz* and *G. Lavielle*, C. R. hebd. Séances Acad. Sci. *261*, 2679 (1965).

[78] *D. J. Cram et al.*, J. Amer. chem. Soc. *84*, 4358 (1962).

[79] *T. Cuvigny* and *H. Normant*, Bull. Soc. chim. France *1964*, 2003.

The mesomerism of the red anion formed from the thioether *(20)* (with $NaNH_2$ at room temperature in HMPT) is shown by the fact that it reacts mainly as the structure *(21)* [80].

$$(H_3C)_2C{=}CH\text{-}S\text{-}C_4H_9 \longrightarrow$$

(20)

$$H_2\overset{\ominus}{C}\text{-}C(CH_3){=}CH\text{-}S\text{-}C_4H_9 \longleftrightarrow H_2C{=}C(CH_3)\text{-}\overset{\ominus}{C}H\text{-}S\text{-}C_4H_9$$

(21a) *(21b)*

Alkyl cinnamyl ethers *(22)* are very readily rearranged into alkyl 3-phenylpropenyl ethers *(23)* by bases in HMPT [162]. The pure ethers are obtained in THF from cinnamyl bromide

$$H_5C_6\text{-}CH{=}CH\text{-}CH_2OR \rightleftharpoons H_5C_6\text{-}CH_2\text{-}CH{=}CH\text{-}OR$$

(22) *(23)*

$R = C_2H_5, C_7H_{15}$

and the corresponding alkoxide. However, if the reaction is carried out in HMPT, or if sodium cinnamylate is allowed to react with an alkyl halide RX in hexamethylphosphoramide, the main product is the ether *(23)*. The isomerization *(22)* → *(23)* is evidently caused by alkoxide; it proceeds very rapidly in a HMPT/benzene mixture (1:9) in the presence of anhydrous $NaOC(CH_3)_3$. The mesomeric carbanion is obtained in HMPT with bases such as alcoholates.

$$H_5C_6\text{-}CH{=}CH\text{-}\overset{\ominus}{C}H\text{-}OR \leftrightarrow H_5C_6\text{-}\overset{\ominus}{C}H\text{-}CH{=}CH\text{-}OR$$

Experience so far has shown that DMSO is the most suitable solvent for the isomerization of olefins. The solvent series found for the rearrangement 1-butene → 2-butene with $KOC(CH_3)_3$ was DMSO ≫ HMPT > TMU [172].

C. Anions in Hexamethylphosphoramide

As was mentioned earlier, anion reactivity is increased in polar aprotic solvents. Reactions involving anions, such as bimolecular elimination and bimolecular nucleophilic substitution, should therefore be accelerated by such solvents. Thus it has been shown [81] that the rate of alkylation of sodiomalonic acid derivatives in benzene is considerably increased by the addition of 10 to 20% of a polar aprotic solvent. The reactions with C_2H_5Br and with C_4H_9Br are accelerated by factors of 21 and 54 respectively by HMPT, and by factors of 6.3 and 15 respectively by DMSO.

1. Substitution

a) Carbon-Halogen Bond

The result of nucleophilic substitution in accordance with eq. (l) depends on the solvent (protonic or aprotic) [2].

$$MX + RX' \rightleftharpoons RX + MX' \qquad (l)$$

Halide anions are specifically solvated by protonic solvents *via* hydrogen bonds, smaller anions being more strongly solvated than larger anions. The variation of nucleophilic strength ($I^\ominus > Br^\ominus > Cl^\ominus > F^\ominus$) runs contrary to this basicity series. In polar aprotic solvents, on the other hand, the nucleophilicity and the basicity of the anions change in the same direction, in accordance with the electronegativity of the halogen atoms.

Elimination very often competes with substitution in HMPT (and in HMPT/THF mixtures) [82]. (The percentage of elimination product for RX′ = n-$H_{15}C_7Br$ with MX = LiF, LiCl, NaF, NaCl, KI, and Cu_2Cl_2 is zero to 62%; the transformations RBr → RCl and RBr → RI are unusual.) The $F^\ominus$ and $Cl^\ominus$ anions act as strong bases in HMPT; they therefore cause almost complete elimination of HBr from secondary alkyl bromides [82] (79% of elimination product from cyclohexyl bromide with LiCl + Li_2CO_3), and so provide a good method for the synthesis of olefins. A t-alkyl *p*-toluenesulfonate *(24)* exhibits substitution even in the cold; no olefins are formed [82].

$$p\text{-}CH_3\text{-}C_6H_4\text{-}SO_2\ OC(CH_3)_3 \xrightarrow{LiCl}$$

(24)

$$p\text{-}C_6H_4\text{-}SO_2\text{-}OLi + (CH_3)_3CCl$$

The result of the reaction is also influenced by the temperature, substitution being favored at about 60 °C and elimination at about 100–110 °C.

b) Carbon-Oxygen Bond

Alcohols (*e.g.* C_4H_9OH, t-C_4H_9OH, $CH_2{=}CH\text{-}CH_2OH$, $H_5C_2O\text{-}CH_2\text{-}CH_2\text{-}OH$, C_6H_5OH, $HO\text{-}(CH_2)_3\text{-}OH$) and carboxylic acids (*e.g.* propionic and hexanoic acids) can be alkylated in 40 to 100% yield with benzyl chloride, ethyl iodide, ethyl bromide, butyl chloride, or 1,4-dibromobutane in the presence of NaH or $NaNH_2$ [64]. The basic properties of the alkoxide anions $RO^\ominus$ lead to eliminations with formation of epoxides (*e.g.* 2,2-dimethyloxirane from $(CH_3)_2C(OH)CH_2Br$) and olefins (*e.g.* 1-octene from $C_8H_{17}Br$; butadiene from $Br\text{-}(CH_2)_4\text{-}Br$ with C_2H_5ONa and C_4H_9ONa).

c) Carbon-Nitrogen Bond

NH functional groups (*e.g.* in aniline, *N*-methylaniline, indole, carbazole, phenothiazine, saccharin, acetamide, phthalimide) can be alkylated with alkyl halides and alkyl sulfates (*e.g.* ethyl bromide, ethyl iodide, phenyl bromide, benzyl chloride, diethyl sulfate) in HMPT in the presence of NaH, $NaNH_2$ or K_2CO_3; the yields are excellent, and often quantitative [64].

The formation of alkyl azides from primary alkyl bromides and inorganic azides is greatly accelerated in HMPT; reaction (m) is 72 times as fast as in DMF and 150 times as fast as in DMSO. The activation

[80] *H. Normant* and *T. Cuvigny*, Bull. Soc. chim. France *1965*, 1884.

[81] *H. E. Zang et al.*, J. Amer. chem. Soc. *82*, 2895 (1960).

[82] *J. F. Normant* and *H. Deshayes*, Bull. Soc. chim. France *1967*, 2455.

energy, which is 15 to 17 kcal·mole^{-1} on average in polar aprotic solvents, is only 13.5 kcal·mole^{-1} in HMPT [3].

$$C_4H_9Br + N_3^{\ominus} \rightarrow C_4H_9{-}N_3 + Br^{\ominus} \qquad (m)$$

d) Carbon-Carbon Bond

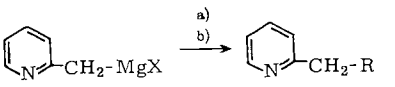
Carbanions occur in very diverse reactions. The reactions that have been most thoroughly studied with HMPT as the solvent are alkylations, which generally proceed in excellent yields; moderate yields are obtained on acylation and carboxylation in HMPT. A nitrile group can be introduced in accordance with a reaction such as (n) [83]; higher nitriles can be synthesized by alkylations, starting *e.g.* with C_6H_5-CH_2-CN or CH_3-CN [84]:

$$H_5C_2O{-}OC{-}(CH_2)_5{-}Cl + NaCN \rightarrow H_5C_2O{-}OC{-}(CH_2)_5{-}CN \quad (90\%) \qquad (n)$$

α) *C–C Linkages by Organomagnesium Compounds*

Hydrocarbon derivatives R'X' in which the halogen atom X' is very firmly bound cannot be induced to react with Grignard compounds RMgX in aliphatic ethers, even in THF. Such reactions take place only in HMPT [85] (cf. Table 13).

A selection of the derivatives that can be obtained *via* 1-indenyl-, 9-fluorenyl-, and α-pyridylmethyl organomagnesium compounds with alkyl halides, *p*-toluenesulfonates, and sulfates, as well as epoxides and CO_2 is shown in the following scheme [86].



a): + CH_2=CH-CH_2Br *(27a)*, R = CH_2-CH=CH_2

b): + H_5C_6-CHO *(27b)*, R = CHOH-C_6H_5

β) *C–C Linkages by Organometallic Compounds of the Alkali Metals*

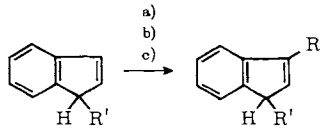
Alkyl bromides do not react with monosodium acetylide in THF. Reaction takes place only in polar aprotic solvents such as dimethylformamide [87]; higher yields (60 to 70%) are obtained in HMPT [88]. The reactions also proceed in THF with added HMPT (about 10%), and the elimination of HBr is suppressed in this medium. The yields are particularly high with primary alkyl bromides, chlorides, and *p*-toluenesulfonates, and higher than in liquid ammonia, in which the reactants are less soluble. The acetylide ion $HC{\equiv}C^{\ominus}$ behaves as a strong base in HMPT, and leads to considerable elimination from secondary and tertiary alkyl halides and *p*-toluenesulfonates.

Alkoxylated 1-alkynes can be obtained by the reaction of suitably substituted halides with monosodium acetylide in HMPT [88] (cf. Table 14).

Table 13. Results for the reaction RMgX + R'X' [a] → R–R' + MgXX' in HMPT.

RMgX	R'X'	R–R'	Yield (%) in THF	Yield (%) in HMPT
n-C_4H_9–MgBr	*n*-C_7H_{15}–Br	*n*-$C_{11}H_{24}$	8	42
n-C_5H_{11}–MgBr	C_6H_5–CH=CH–Br	C_6H_5–CH=CH–C_5H_{11}	30	29
n-C_5H_{11}–MgBr	C_6H_5–C≡C–Br	C_6H_5–C≡C–C_5H_{11}	10	55
CH_3–CH=CH–MgBr	*n*-C_7H_{15}–Br	CH_3–CH=CH–C_7H_{15}	71	43
C_6H_5–MgBr	C_6H_5–CH=CH–Br	C_6H_5–CH=CH–C_6H_5	20	20
C_6H_5–C≡C–MgBr	*n*-C_5H_{11}–Br	C_6H_5–C≡C–C_5H_{11}	0	43

[a] Vinyl bromides split off HBR to a great extent under these conditions; only in the case of aromatic Grignard compounds can this be avoided.



(25a), R = C_4H_9; R' = C_4H_9

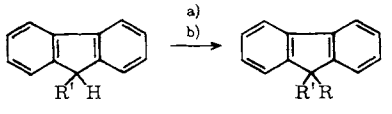
(25b), R = C_3H_5; R' = H

(25c), R = CH_2-CHOH-CH_3; R' = H

a): + $(C_2H_5)_2NMgCl$ + C_4H_9I

b): + i-C_3H_7MgCl + CH_2=CH-CH_2Br

c): + i-C_3H_7MgCl + Propene oxide



(26a), R = C_2H_5; R' = H

(26b), R = CO_2H; R' = C_2H_5

a): + $(C_2H_5)_2NMgCl$ + C_2H_5I

b): + i-C_3H_7MgCl + CO_2

[83] *B. T. Freure* and *H. J. Decker*, Chem. Abstr. *57*, 11032e (1962).

[84] *H. Normant* and *T. Cuvigny*, Bull. Soc. chim. France *1965*, 1882, 1887.

[85] *J. F. Normant*, Bull. Soc. chim. France *1963*, 1888.

[86] *T. Cuvigny* and *H. Normant*, Bull. Soc. chim. France *1964*, 2003.

[87] *T. F. Rutledge*, J. org. Chemistry *22*, 649 (1957).

[88] *J. F. Normant*, Bull. Soc. chim. France *1965*, 859.

Table 13a. Condensation of alkyl halides (and a tosylate) with $NaC{\equiv}CH$ [88].

RX	Solvent	Addition of $NaC{\equiv}CH$ (°C)	Reaction conditions (°C)	(h)	Product	Yield (%)
$n\text{-}C_7H_{15}Br$	DMF + THF	40	50	4	$C_7H_{15}C{\equiv}CH$	52
$n\text{-}C_5H_{11}Br$	DMF + THF	20	100	4	$C_5H_{11}C{\equiv}CH$	47
$n\text{-}C_7H_{15}Br$	HMPT	5	40	1.5	$C_7H_{15}C{\equiv}CH$	65.6
$n\text{-}C_7H_{15}Br$	HMPT [a]	20	40	3	$C_7H_{15}C{\equiv}CH$	72
$n\text{-}C_5H_{11}Br$	HMPT	20	[b]		$C_5H_{11}C{\equiv}CH$	57
$Br(CH_2)_6Br$	HMPT	20	40	3	$HC{\equiv}C(CH_2)_6C{\equiv}CH$	71
$C_6H_5CH{=}CHCH_2Cl$	HMPT	−50	0	2	$C_6H_5(CH{=}CH)_3C_6H_5$	8
C_4H_9OTos	HMPT	0	50	3	$C_4H_9C{\equiv}CH$	77
$n\text{-}C_7H_{15}Cl$	HMPT	20	[b]		$C_7H_{15}C{\equiv}CH$	60
$n\text{-}C_{12}H_{25}Br$	HMPT	10	70	3	$C_{12}H_{25}C{\equiv}CH$	72.6

[a] Reaction in 10 ml HMPT per 0.1 mole of alkyl halide.

[b] THF is evaporated off at 100 °C.

Table 14. Condensation of halogen derivatives with $NaC{\equiv}CH$ [88].

RX	Solvent	Temperature range (°C)	Duration (h)	Product	Yield (%)
$C_4H_9OCH_2Cl$	HMPT	5 → 40	2	$C_4H_9OCH_2C{\equiv}CH$	32
$C_4H_9OCH_2Cl$	HMPT	−40 → 5	8	$C_4H_9OCH_2C{\equiv}CH$	12.5
$C_4H_9OCH_2Cl$	THF	20 → 75	1	$C_4H_9OCH_2C{\equiv}CH$	18
2-Pyranyl-O−$(CH_2)_4Cl$	HMPT	20 → 50	2.5	2-Pyranyl-O−$(CH_2)_4C{\equiv}CH$	47
$(C_2H_5O)_2CH(CH_2)_3Cl$	HMPT	20 → 40–50	1	$(C_2H_5O)_2CH(CH_2)_3C{\equiv}CH$	47

ω-Alkyn-1-yl-trialkylgermanes, *e.g. (28)*, could be obtained by the same method in 60% yield [89].

$$(C_2H_5)_3Ge(CH_2)_4Br + NaC{\equiv}CH \rightarrow (C_2H_5)_3Ge{-}(CH_2)_4{-}C{\equiv}CH \quad (28)$$

In a process similar to that described above, alkynes with non-terminal triple bonds are obtained in yields of 50 to 80% from alkali metal 1-alkynides and halogenated compounds [90]. Metallation with NaH in THF (method A) is recommended when an acyl or carboxy residue is to be introduced in the next stage. In another method B, the metallation is carried out with $NaNH_2$ in HMPT and the product is alkylated in the same medium. Finally, in method C, the following scheme is used without isolation of the intermediates:

$$CH{\equiv}CH \xrightarrow[THF]{Na} CH{\equiv}C{-}Na \xrightarrow[HMPT]{RX} R{-}C{\equiv}C{-}H$$

$$\xrightarrow[HMPT]{NaNH_2} R{-}C{\equiv}C{-}Na \xrightarrow{R'X} R{-}C{\equiv}C{-}R'$$

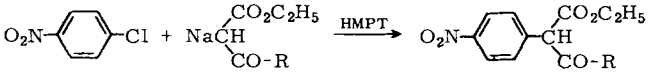
With the aid of these techniques it is possible to metallate dialkylethynylamines, *e.g.* to obtain the lithium derivative *(29)*, which can then be converted into ynamines having the general formula *(30)* by reaction with alkyl halides or *p*-toluenesulfonates [91].

$$RR'N{-}C{\equiv}C{-}Li \xrightarrow{RX} RR'N{-}C{\equiv}C{-}R$$
$$(29) \qquad (30)$$

Phenylacetic and malonic acid derivatives and 3-acetyl-2-oxotetrahydrofuran can be metallated with NaH or $NaNH_2$ and alkylated in good yields in HMPT or HMPT/THF [92].

γ) *Arylations*

Nucleophilic substitutions on aromatic compounds are always accelerated by polar aprotic solvents. It has so far been possible to use only the very reactive halogenobenzenes. Sodiomalonic acid and sodioacetoacetic ester can also be arylated in good yields with elimination of NaCl, by 2- or 4-nitrochlorobenzene (accelerating action of the solvents: HMPT > DMSO > DMF); while DMF gives partial $Cl \rightarrow N(CH_3)_2$ substitution in the aromatic compounds, HMPT is inert [93], *e.g.*:



$R = OC_2H_5, CH_3$

HMPT and copper salts have also been shown to accelerate reactions (o) and (p) [94–96].

$$p\text{-}O_2N{-}C_6H_4{-}Cl + HNAr \rightarrow p\text{-}O_2N{-}C_6H_4{-}NAr \quad (o)$$

$$p\text{-}Cl{-}C_6H_4{-}Cl + 2\ MS{-}C_6H_5 \rightarrow C_6H_5S{-}C_6H_4{-}SC_6H_5 \quad (p)$$

(M = K: 81% in *N*-methylbutyramide after 15 hours at 180 °C; M = Na: 26% in HMPT after 5 hours at 110 °C).

[89] *P. Mazerolles, M. Lesbre,* and *S. Marre,* C. R. hebd. Séances Acad. Sci. *261,* 4134 (1965).

[90] *T. Cuvigny* and *H. Normant,* Bull. Soc. chim. France *1965,* 1877.

[91] *J. Ficini* and *G. Barbara,* Bull. Soc. chim. France *1965,* 2787.

[92] *H. Normant* and *T. Cuvigny,* Bull. Soc. chim. France *1965,* 1882.

[93] *J. Bourdais* and *Cl. Mahieu,* C. R. hebd. Séances Acad. Sci., Sér. C *263,* 84 (1966.)

[94] U.S. Rubber Co. Brit. Pat. 839420 (June 29th, 1960); Chem. Abstr. *54,* 24549g (1960).

[95] *J. R. Campbelle,* J. org. Chemistry *29,* 1830 (1964).

[96] *H. Normant* and *T. Cuvigny,* Bull. Soc. chim. France *1965,* 1870.

Substitutions of bromo-, chloro-, and fluorobenzenes with mercaptans, secondary amines, and phenylacetylenes in HMPT have been achieved in good yields (generally about 50 to 80%), and under mild conditions [64,97]. These reactions must involve an elimination-addition mechanism, though no intermediate dehydrobenzene derivative has ever been found.

e) Alkylation of Ambident Ions

The relative reactivities of the various nucleophilic centers of an ambident anion depend on numerous factors, *e.g.* in alkylations on the cation, the alkylating agent, and the solvent.

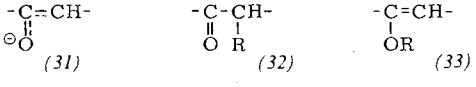
Table 15 illustrates the dependence of the course of the alkylation of sodium phenoxide and of sodium β-naphthoxide on the basicity of the solvent [98].

Table 15. Alkylation of sodium phenolate and β-naphtholate.

Solvent	Alkylation (%) at: C	O	Ref.
CH_3OH	35	65	[98]
CF_3-CH_2OH	93	7	[98]

In basic solvents, pyrroles are preferentially alkylated in the most strongly electronegative position *i.e.* on the nitrogen atom [99]. Thus the reaction of indolylsodium with benzyl chloride in HMPT leads to an 81% yield of *N*-benzylindole [64].

Enolates *(31)* in protonic solvents generally give *C*-alkylation to *(32)* [100]. In polar aprotic solvents, on the other hand, the principal reaction is found to be



(31) *(32)* *(33)*

O-alkylation with formation of the enol ether *(33)* [101]. This solvent-dependence was studied in the alkylation of metallated derivatives of the ketones cyclohexanone, acetophenone, acetylacetone, ethyl acetoacetate (alkylating agent: alkyl sulfates, $(C_2H_5)_3OBF_4$) [101], α,α-diphenylacetone (with ethyl bromide) [102], and 9-benzoylfluorene (with isopropyl bromide) [103]. The results obtained with 9-benzoylfluorene are shown in Table 16.

Table 16. Alkylation of 9-benzoylfluorene with isopropyl bromide.

Solvent	DC	Alkylation (%) at: C	O
t-Butanol	10–11	96	4
Ethanol	24–25	83	17
Methanol	32–33	82	18
Diglyme	7–7.5	61	39
THF	7–7.5	90	10
HMPT	29–30	44	56
DMSO	45–49	72	28

The more weakly basic organomagnesium compounds can react with enolizable ketones in HMPT to give very good yields of the enolized form [104]. The results for diisopropyl ketone are given in Table 17.

Table 17. Reaction of diisopropyl ketone in HMPT with organomagnesium compounds.

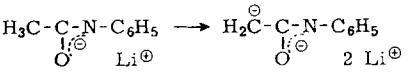
Organomagnesium compound	Enolization (%)	Reduction (%)	Addition (%)
H_3CMgBr	33	0	66
H_5C_2MgBr	100	Trace	Trace
$(H_5C_2)_2Mg$	40	Trace	60
H_9C_4MgBr	100	0	Trace
$(H_9C_4)_2Mg$	60	Trace	40
$i\text{-}H_7C_3MgBr$	100	0	0
$(i\text{-}H_7C_3)_2Mg$	100	0	0

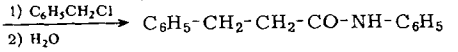
2-Butanone, 2,4-dimethylpentan-3-one, and cyclohexanone react with C_4H_9MgBr at 55 °C in HMPT to give 75, 95, and 90% respectively of the Mg enolates [104]. These Mg enolates could be alkylated with methyl iodide, methyl sulfate, and methyl *p*-toluenesulfonate in HMPT (this reaction does not take place in less polar solvents). As in the case of *N*-magnesium imino compounds [105], the reaction leads exclusively to *C*-alkylation:

$$XMg-O-C{=}CH \xrightarrow{RX} MgX_2 + O{=}C-CHR$$

If the cation of an imine can be strongly solvated as in its alkali metal derivative, alkylation can take place on the hetero atom. Thus sodium derivatives of enamines can be *N*-alkylated [106] (see Table 18).

The "ambident" anion can also give a dianion with strong bases. Thus acetanilide could be quantitatively *N*-alkylated by treatment with $NaNH_2$ in HMPT [64]. $NaNH_2$ in liquid ammonia gives only the same monoanion, whereas an excess of C_4H_9Li in ether or THF leads to a dianion *(34)*, which is then *C*-alkylated [107]. Methanesulfonamides behave in a similar manner [108].





f) Cyclopropane Derivatives and their Stereochemistry

Cyclopropane derivatives containing functional groups can be obtained by the reaction of compounds contain-

[97] *P. Caubère* and *H. Normant*, unpublished.

[98] *N. Kornblum et al.*, J. Amer. chem. Soc. *85*, 1141, 1148 (1963).

[99] *C. F. Hobbs et al.*, J. Amer. chem. Soc. *84*, 43 (1962).

[100] *J. M. Conia*, Record. chem. Progr. (Kreske-Hooker Sci. Lib.) *24*, 43 (1963).

[101] *G. J. Heiszwolf* and *H. Kloosterziel*, Chem. Commun. *1966*, 51.

[102] *H. D. Zook* and *W. L. Cumby*, J. Amer. chem. Soc. *82*, 1258, 1387 (1960).

[103] *J. P. Boisset, J. Boyer*, and *J. Rouzaud*, C. R. hebd. Séances Acad. Sci., Sér. C *263*, 1253 (1966).

[104] *J. Fauvarque* and *J. F. Fauvarque*, C. R. hebd. Séances Acad. Sci., Sér. C *263*, 488 (1966).

[105] *G. Stork* and *S. R. Dowd*, J. Amer. chem. Soc. *85*, 2178 (1966).

[106] *G. J. Heiszwolf* and *H. Klosterziel*, Chem. Commun. *1966*, 767.

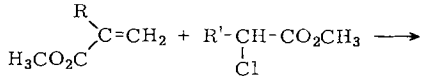
[107] *R. L. Gay, S. Boatman*, and *C. R. Hauser*, Chem. and Ind. *1965*, 1789 (1965).

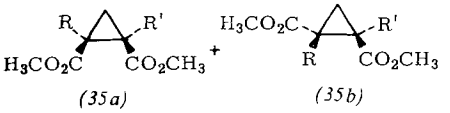
[108] *E. J. Corey* and *G. T. Kwiatkowski*, J. Amer. chem. Soc. *88*, 5652 (1966).

Table 18. Alkylation of imines.

Solvent	Diethylcellosolve		HMPT					
Base	NaH		$NaNH_2$					
Imine	*N*-Isopropylidene aniline		*N*-ethylcyclohexanone imine			*N*-ethyl iminodiethylketone		
Alkylation medium	$(H_5C_2)_3OBF_4$	$(H_5C_2)_2SO_4$	H_5C_2I	$(H_5C_2)_3OBF_4$	$(H_3C)_2SO_4$	H_5C_2I	$(H_5C_2)_3OBF_4$	$(H_3C)_2SO_4$
Products (%):	8	9	5	29	11	15	26	17
Enamine	88	49	5	53	75	17	29	57
C-alkylated	4	42	90	18	10	56	42	26
C-polyalkylated	—	—	—	—	4	12	3	0

ing activated double bonds *e.g.* (esters, nitriles, ketones, *etc.*) with carbanions of α-halogenated compounds (esters, nitriles, ketones, *etc.*). The base NaH gives much higher yields in HMPT than in nonpolar solvents [109]. The solvent influences, not only the rate of reaction but also the stereochemistry [2]. Whereas the reaction in benzene leads mainly to the *cis* isomer *(35a)*, the principal product in HMPT is the *trans* isomer *(35b)*. Some results are shown in Table 19.





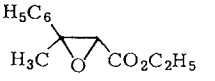
(35a) *(35b)*

Table 19. Yields and stereochemistry in the formation of the cyclopropane derivatives *(35a)* and *(35b)*.

	In Benzene		In Benzene + HMPT (50:50 v/v)	
	Yield (%)	*trans* : *cis* *(35b)* : *(35a)*	Yield (%)	*trans* : *cis* *(35b)* : *(35a)*
$R=R'=CH_3$	71	7 : 93	60	64 : 26
$R=H$, $R'=CH_3$	70	17 : 83	70	90 : 10
$R=R'=C_2H_5$	55	0 : 100	67	75 : 25
$R=H$, $R'=C_6H_5$	43	0 : 100	65	56 : 21
$R=CH_3$, $R'=C_6H_5$	38	0 : 100	46	43 : 25

If the same method is applied to α-halogenated ketones, the high reactivity of the carbanion in hexamethylphosphorane permits a) the competitive Favorsky reaction in the case of ketones with mobile α'-hydrogen, and b) the use of methyl vinyl ketone [110], which polymerizes when used in previous methods. *cis*- (25%) and *trans*-1,2-Diacetyl-1-phenylcyclopropane (75%) are obtained in a total yield of 70% from methyl vinyl ketone and α-chloro-α-phenyl acetone.

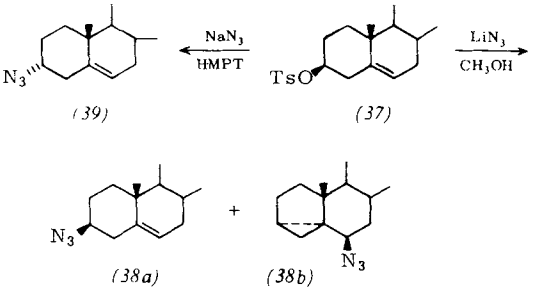
This group of reactions includes the Darzens reaction *e.g.* between acetophenone and ethyl chloroacetate [111], the yield of which can be increased in HMPT to 70% (50% in hexane, 57% in benzene), with preferential formation of the isomer *(36)* (59:41). Two stereoisomers of 3-methyl-3-phenyl-2-oxiranecarbonitrile are obtained from acetophenone and chloroacetonitrile; total yield and proportions of isomers depend upon the base and solvent used.



(36)

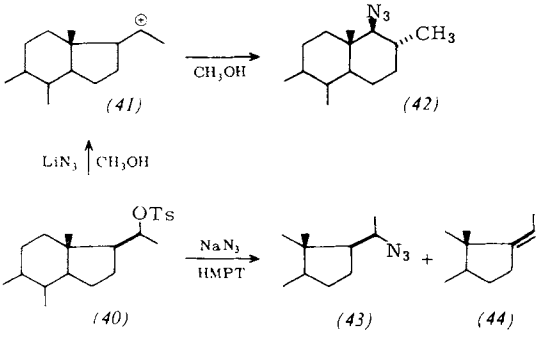
Relationships between the solvent and stereochemistry are also known in steroid chemistry. Both the 3β-Δ⁵-*p*-toluenesulfonate *(37)* [181] and the 20β-*p*-toluenesulfonate *(40)* [182] give different substitution products with alkali metal azides, depending on whether a protonic or aprotic solvent is used.

Thus in methanol *(37)* gives an i-steroid derivative *(38b)* by an S_N1 reaction *via* a carbenium ion. In polar aprotic media, on the other hand, an S_N2 reaction with inversion leads mainly to the 3α-azide *(39)*, the yield of which increases with increasing basicity of the solvent (DMSO: 30%; *N*-methylpyrrolidone: 71%; HMPT: 93%).



(39) *(37)* *(38a)* *(38b)*

The reaction of *(40)* in methanol leads mainly to a derivative of the D-homo series *(42)* by rearrangement of the carbenium ion *(41)*. In polar aprotic solvents, however, an azide *(43)* having an inverted configuration on C-18 is formed by an S_N2 reaction; the yield again depends on the basicity of the solvent (DMSO: 46%; *N*-methylpyrrolidone: 53%; HMPT: 65%). The elimination product *(44)* is also formed.



(41) *(42)* *(40)* *(43)* *(44)*

[109] *L. L. McCoy*, J. Amer. chem. Soc. *82*, 6416 (1960); *84*, 2246 (1962); *L. L. McCoy* and *C. W. Nachtigall*, J. org. Chemistry *27*, 4312 (1962).

[110] *M. Causse-Toller* and *R. Fraisse-Jullien*, Bull. Soc. chim. France *1966*, 430.

[111] *J. Seyden-Penne*, *Ch. Gibert*, and *B. Daurée*, C. R. hebd. Séances Acad. Sci., Sér. C *263*, 895 (1966).

Reduction of the azides with $LiAlH_4$ gives the corresponding amino steroids in very good yields.

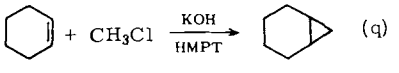
2. Eliminations

Halogenated compounds, sulfonated compounds, other compounds containing sulfur, and azides can enter into elimination reactions with formation of olefins, carbenes, alkynes, or amines. In the basic HMPT, nucleophilic substitutions (S_N2) compete with these E2 reactions. Table 20 shows the results obtained on elimination of hydrogen halide from halogenated vinyl compounds in HMPT with the aid of organomagnesium compounds [112–114].

Table 20. HX-elimination with Grignard compounds in HMPT.

RMgX	Halogenovinyl compound	Product	Yield (%)	Ref.
n-C_4H_9MgBr	n-$C_5H_{11}CCl{=}CHCl$(*cis*)	$C_5H_{11}-C{\equiv}C-Cl$ + $C_5H_{11}-C{\equiv}C-C_4H_9$	14 10	[112]
n-$C_7H_{15}MgBr$	$CHCl{=}CCl_2$	$C_7H_{15}-C{\equiv}C-Cl$	48	[113]
n-$C_5H_{11}MgBr$	$H_5C_6-CH{=}CHBr$	$H_5C_6-C{\equiv}C-H$	27	[114]
H_5C_6MgBr	$H_5C_6-CH{=}CHBr$	$H_5C_6-C{\equiv}C-H$	20	[114]

Similar results were obtained with stronger bases ($H^{\ominus}$, $NH_2^{\ominus}$, $HC{\equiv}C^{\ominus}$) in HMPT [115–117]. The formation of norcaradiene in accordance with eq. (q) [118] may involve a carbene mechanism.



(q)

Arylsulfonates such as *(45)* decompose to form olefins when heated in polar aprotic solvents [119].

$$Ar{-}SO_2{-}O{-}\underset{|}{CH}{-}CH_2{-} \rightarrow {-}CH{=}CH{-} + ArSO_3H$$

(45)

Cyclohexyl benzenesulfonate gives a 58% yield of cyclohexene at 40 °C in HMPT in the presence of $NaNH_2$ [116]. Similarly, the $CH{\equiv}C^{\ominus}$ anion in HMPT causes decomposition of β-ethoxyethyl methanesulfonate into ethyl vinyl ether [117].

The basic oxidation of mercaptans, disulfides, and sulfoxides often results in β-elimination in accordance with equations (s) to (u) to form olefins [120–123]. Aliphatic sulfones normally enter into this reaction only with difficulty (in KOH solution above 200 °C), but react readily in HMPT at 80 °C [121].

$$R{-}\overset{\ominus}{C}H{-}CH_2{-}S^{\ominus} \longrightarrow R{-}CH{=}CH_2 + S^{2\ominus}$$

$$R{-}\overset{\ominus}{C}H{-}CH_2{-}S{-}SR \longrightarrow R{-}CH{=}CH_2 + RS{-}S^{\ominus}$$

$$\overset{\ominus}{C}H_2{-}CH(CH_3){-}SO{-}C_3H_7 \longrightarrow CH_3{-}CH{=}CH_2 + C_3H_7{-}SO^{\ominus}$$

3. Autoxidation of Carbanions

Many compounds that form anions are autoxidized in appreciable yields in DMF or DMSO, even at room temperature; potassium t-butoxide has been used as the base in this reaction [124]. The accepted mechanism [125] is illustrated below for toluene:

$$C_6H_5{-}CH_2{-}H + B^{\ominus} \rightarrow BH + C_6H_5{-}CH_2^{\ominus}$$
$$C_6H_5{-}CH_2^{\ominus} + O_2 \rightarrow C_6H_5{-}CH_2{\bullet} + O_2{\bullet}$$
$$C_6H_5{-}CH_2{\bullet} + O_2 \rightarrow C_6H_5{-}CH_2{-}O{-}O{\bullet}$$
$$\rightarrow \ldots\ldots$$

The autoxidation should be accelerated as the formation of the carbanion is facilitated. HMPT, which was apparently first used as an autoxidation medium by *Wallace* [120–122, 127–132], is superior to other polar aprotic solvents for two reasons:

1) HMPT itself does not form carbanions, and so cannot autoxidize. Table 21 gives the data for 10% tritium exchange between toluene labeled in the CH_3 group and polar solvents [126]. DMSO exhibits considerable autoxidation, as do diglyme and dioxane [127].

2) HMPT is stable to bases, even to KOH at 80 °C, and is therefore superior to amides and lactams.

Table 21. Tritium exchange between $H_2TC{-}C_6H_5$ and polar solvents; time required for 10% exchange [126].

Solvent	Time (min)
DMSO	6
Dimethylsulfone	12
N-Methyl-2-pyrrolidone	48
Tetramethylene sulfoxide	420
HMPT	14000

When no β-elimination takes place, mercaptans and disulfides autoxidize in alkaline media to give sulfonic acids, often in yields of more than 90% (see Table 21a) [128]. The autoxidation of thioethers in 2 M K-t-butylate/HMPT leads to a carboxylic acid/sulfonic acid mixture [129]. With thioethers of the benzyl sulfide type, yields of 30 to 70% are obtained after 1 to 3 days; other thioesters give lower yields. Sulfoxides autoxidize in HMPT/$(CH_3)_3COK$ or HMPT/KOH at 80 °C, again with formation of carboxylic acid/

[112] *J. F. Normant*, Bull. Soc. chim. France *1963*, 1868.

[113] *J. F. Normant*, Bull. Soc. chim. France *1963*, 1876.

[114] *J. F. Normant*, Bull. Soc. chim. France *1963*, 1888.

[115] *T. Cuvigny, H. Normant*, and *J. F. Normant*, C. R. hebd. Séances Acad. Sci. *258*, 3502 (1964).

[116] *P. Caubere*, Bull. Soc. chim. France *1966*, 1293.

[117] *J. F. Normant*, Bull. Soc. chim. France *1965*, 859.

[118] *A. Schriesheim, C. A. Rowe jr.*, and *W. Bartok*, Chem. Abstr. *59*, 3772g (1963).

[119] *H. R. Nace*, J. Amer. chem. Soc. *81*, 5428 (1959).

[120] *T. J. Wallace et al.*, J. Amer. chem. Soc. *85*, 2739 (1963).

[121] *T. J. Wallace et al.*, Chem. and Ind. *1965*, 1268.

[122] *T. J. Wallace et al.*, Proc. chem. Soc. (London) *1963*, 137; J. chem. Soc. (London) *1965*, 1271.

[123] *H. Normant* and *T. Cuvigny*, Bull. Soc. chim. France *1965*, 1867.

[124] *G. A. Russel*, Preprints 17th Nat. Symposium, Bloomington, Ind. (USA) (25–29 June, 1961).

[125] *G. A. Russel et al.*, J. Amer. chem. Soc. *84*, 2652 (1962).

[126] *J. E. Hofmann et al.*, J. Amer. chem. Soc. *87*, 2523 (1965).

[127] *T. J. Wallace*, J. org. Chemistry *20*, 3770 (1965).

[128] *T. J. Wallace* and *A. Schriesheim*, Tetrahedron Letters *21*, 2271 (1965).

[129] *T. J. Wallace et al.*, J. org. Chemistry *30*, 3147 (1965).

Table 21a. Base-catalysed oxidation of Disultides (0.0125 mole R_2S_2); ratio, moles of base:moles R_2S_2 = 8:1.

R_2S_2	Solvent	Base	Temp. (°C)	R_2S_2 conversion (%)	Yield of RSO_3H (%)	Yield of RSH (%)	Time (h)
$(n\text{-}C_4H_9)_2S_2$	HMPT	KOH	23.5	98	92.3	3	41
$(n\text{-}C_4H_9)_2S_2$	HMPT	KOH	80	96	97	0	45
$(n\text{-}C_4H_9)_2S_2$	DMF	KOH	23.5	87.7	88.1	0	45
$(n\text{-}C_4H_9)_2S_2$	HMPT	NaOH	80	95	94.2	0.9	35
$(C_6H_5)_2S_2$	HMPT	KOH	23.5	97.7	88.1	—	22
$(C_6H_5)_2S_2$	HMPT	KOH	80	98	99	0	22.5
$(C_6H_5)_2S_2$	DMF	KOH	23.5	98.5	90	0.3	40
$(o\text{-}CH_3\text{—}C_6H_4)_2S_2$	HMPT	KOH	80	98	98	0	23

sulfonic acid mixtures[130]. Worthy of mention is the autoxidation of dimethylsulfone under these conditions.

Ketones autoxidize to give carboxylic acids, and diketones to give dicarboxylic acids; the rate of autoxidation in both cases increases with increasing ease of formation of carbanions[131]. The rate is highest in HMPT (HMPT > $(CH_3)_3COH \gg H_2O$); the yield of autoxidation product varies with the base in the order KOH ≈ NaOH ≫ LiOH.

Aromatic hydrocarbons that can form carbanions autoxidize in the presence of strong bases such as $KOC(CH_3)_3$ or KOH in HMPT to give carboxylic acids[126]. A number of examples are shown in Table 22. The methylthiophenes[132] and particularly the α-isomer, which has a resonance-stabilized carbanion, react in the same way.

Table 22. Autoxidation of aromatic hydrocarbons in $KOC(CH_3)_3$/HMPT or KOH/HMPT.

ArH	Ar—COOH	Yield (%)
Toluene	H_5C_6—COOH	25—30
o-Xylene	Phthalic acid	35—40
m-Xylene	Isophthalic acid	50
p-Xylene	Terephthalic acid	15
Tetralin	Phthalic acid	46

D. Comparison of Polar Aprotic Solvents

The ability to accelerate S_N2 and E2 reactions changes in the same direction as the electron-donating power: DMF < DMSO < TMU < HMPT. Differences in stability and in influence on chemical reactions are evidently also partly due to differences in the distances between the polar groups and the groups carrying hydrogen.

1. Reactivity of the Polar Group

In the polar group the oxygen is negatively polarized and the C, S, or P atom attached to it is positively polarized. Consequently, nucleophiles $B^{\ominus}$ introduced or formed during the reaction attack the positive C, S, or P atom. This can lead to the removal of amide ions from dimethylformamide and from tetramethylurea, and these ions then compete with the nucleophile $B^{\ominus}$ in substitution, addition, and autoxidation reactions. A substitution of this type is unlikely in the case of HMPT, since phosphoramides are much more stable than amides of carboxylic acids.

The strongly basic organometallic compounds of alkali metals and KOH attack DMF, DMSO, and tetramethylurea very effectively, whereas HMPT is not affected under the usual reaction conditions (even by KOH at 80 °C). Organomagnesium compounds do not attack even tetramethylurea[133,134]. Metallations are best carried out with strongly basic organometallic compounds in a mixture of HMPT with a nonpolar solvent such as benzene or toluene. On the other hand, organometallic compounds of cadmium, zinc, and tin can be prepared directly from the metals and alkyl halides in HMPT.

When sodium hydride is used the reaction may be carried out in DMF; however, part of the NaH reacts with the solvent even at room temperature[135]. Since DMSO is an oxidizing agent, the use of NaH in this solvent leads to an explosion hazard, even at temperatures only slightly above room temperature[136]. TMU and HMPT are inert to alkali metal amides and hydrides.

2. Ease of Removal of Hydrogen

Hydrogen atoms α to the polar group, *e.g.* in dimethylacetamide and even more so in DMSO, can be readily split off by bases[137] with formation of the anions $(CH_3)_2N\text{—}CO\text{—}CH_2^{\ominus}$ and $CH_3\text{—}SO\text{—}CH_2^{\ominus}$ respectively. Consequently, DMSO is an ideal reactant[137] rather than an ideal solvent in carbanion chemistry. Tetramethylurea and HMPT lose the hydrogen β to the polar group only under extreme conditions, if at all.

From all points of view, HMPT is the best polar aprotic solvent, and has great advantages even over liquid ammonia, in which most of the reactions discus-

[130] *T. J. Wallace*, J. org. Chemistry *30*, 4017 (1965).

[131] *T. J. Wallace et al.*, J. org. Chemistry *30*, 3768 (1965).

[132] *T. J. Wallace* and *F. A. Baron*, J. org. Chemistry *30*, 3520 (1965).

[133] *H. Normant*, Bull. Soc. chim. France *1963*, 1436.

[134] *A. Lüttringhaus* and *H. W. Dirksen*, Angew. Chem. *75*, 1059 (1963); Angew. Chem. internat. Edit. *3*, 260 (1964).

[135] *W. E. Truce* and *F. E. Roberts*, J. org. Chemistry *28*, 961 (1963).

[136] *D. B. Denney* and *L. Saferstein*, J. Amer. chem. Soc. *88*, 1839 (1966).

[137] *E. J. Corey* and *M. Chaykowsky*, J. Amer. chem. Soc. *84*, 866 (1962).

sed can be carried out. These advantages include ease of handling, absence of autoprotolysis (*e.g.* $(C_6H_5)_3CM$ can be synthesized), and greater solvent power for a large number of substances (*e.g.* for aliphatic bromine compounds).

IV. Hexamethylphosphoramide as an Electron Acceptor

A. Formation of Radical-Anions

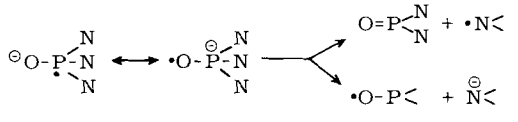
H. Normant et al. found that HMPT has the remarkable property of dissolving alkali metals (Li, Na, K) to form blue solutions (λ_{max} = 770 μ)[138]. It was shown[139–141] that these blue solutions contain radical-anions and are paramagnetic.

$$M + O{=}P(N(CH_3)_2)_3 \rightarrow [O^{\bullet}{-}P(N(CH_3)_2)_3]^{\ominus} + M^{\oplus}$$

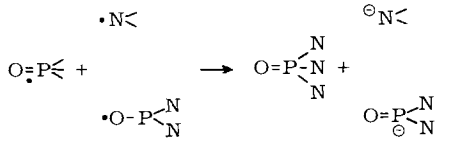
The EPR spectra are concentration-dependent, suggesting differences in the degree of solvation of the electron, *i.e.* of the radical-anion. The stability of the radical-anion accordingly depends on the alkali metal concentration and on the nature of the cation. In 1 M solutions, the blue color disappears after 10 to 15 min in the case of potassium and after 6 hours in the case of sodium or lithium. Mg[143], Ca, Sr, and Ba[144] also dissolve in HMPT to give blue solutions.

Mg solutions are more stable than Na solutions at the same concentration; solutions of alkaline earth metals, particularly Ba, are unstable. Decomposition gives a yellow color (λ_{max} = 390 μ). Our first suggestion[145] was that a mechanism involving two anions might be involved. However, the following mechanism is more probable.

The mesomeric radical-anion forms an anion and a free radical:



and the new radical is converted into another anion:



so that the overall reaction is:

$$2\ O{=}P\lessdot \rightarrow O{=}P\lessdot + O{=}\underset{\oplus}{P}\lessdot + {}_{\cup}N\lessdot$$

When polycyclic aromatic hydrocarbons are added to a solution of a metal in HMPT, they act as electron acceptors. The formation of hydrocarbon radical-anions depends mainly on three factors[146]:

a) The electron affinity, which is lower for all hydrocarbons than for the non-enolizable ketones[147]:

benzene < phenanthrene < biphenyl < naphthalene < anthracene < *o*- and *p*-terphenyl < benzophenone < fluorenone.

b) The reducing power of the metal, which decreases from the alkali metals, *via* magnesium, to the alkaline earth metals.

c) The solvating properties of the solvent (HMPT is greatly superior to dimethoxyethane and to THF in this respect).

The formation of radical-anions from biphenyl and naphthalene in THF solution with Li or Na has been used in syntheses[148]. A stable solution of anthracene radical-anions can also be prepared with sodium in HMPT[149]. Neither biphenyl nor naphthalene gives a radical-anion with magnesium in THF. Naphthalene reacts with Mg only in liquid ammonia[150] or in HMPT to give the radical-anion (detected by EPR spectroscopy)[144]. The green residue Mg(naphthalene)$(NH_3)_x$ that is left when the solvent is distilled off decomposes in DMSO and is insoluble in THF; it dissolves in HMPT to give a stable green solution, which can be used in exchange reactions for the preparation of aromatic radical anions $ArH^{\ominus}$ of anthracene, pyrene, and 1,1-diphenylethylene[143,179]. Biphenyl radical anions are obtained from biphenyl and solutions of Ca (or Sr or Ba) in HMPT. Electron exchange takes place on addition of naphthalene, which is a stronger electron acceptor:

$$H_5C_6{-}C_6H_5^{\ominus}{\bullet} + C_{10}H_8 \rightarrow H_5C_6{-}C_6H_5 + C_{10}H_8^{\ominus}{\bullet}$$

The electronic spectra of these radical anions in HMPT are only slightly influenced by the cation (Na^+, Mg^{2+}); the wavelengths at which the maxima occur are about 20 μ higher than in the spectra recorded in THF. Hexamethylphosphoramide is an excellent medium for the synthesis of metal ketyls[151].

The required alkali metal solutions (ammonia, lower amines) can be obtained, not only by dissolution of the metals, but also by electrolysis of suitable metal salt solutions. This second method can also be used when the solvent is HMPT (electrolysis of $MgBr_2$, CaI_2, and LiCl)[46,180]. Hydrogen is not liberated even in a HMPT/alcohol mixture, and a slight blue color, which rapidly disappears, is observed at the cathode; this color must be due to the HMPT anion-radical.

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[138] *T. Cuvigny, J. Normant,* and *H. Normant,* C. R. hebd. Séances Acad. Sci. *258,* 3503 (1964).

[139] *H. Normant, T. Cuvigny, J. Normant,* and *B. Angelo,* Bull. Soc. chim. France *1965,* 1561.

[140] *G. Fraenkel, S. H. Ellis,* and *Don T. Dix,* J. Amer. chem. Soc. *87,* 1406 (1965).

[141] *H. Normant, T. Cuvigny, J. Normant,* and *B. Angelo,* Bull. Soc. chim. France *1965,* 3441.

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[143] *M. Fontanille* and *P. Sigwalt,* C. R. hebd. Séances Acad. Sci., Sér. C *262,* 1208 (1966).

[144] *M. Fontanille* and *P. Sigwalt,* C. R. hebd. Séances Acad. Sci., Sér. C *263,* 316 (1966).

[145] *H. Normant, T. Cuvigny, J. Normant,* and *B. Angelo,* Bull. Soc. chim. France *1965,* 3442.

[146] *J. Vidal* and *Y. Chauvin,* Rev. Inst. Fr. Pétrole *19,* 1222 (1964).

[147] *B. J. McClelland,* Chem. Reviews *64,* 301 (1964).

[148] *H. Normant* and *B. Angelo,* Bull. Soc. chim. France *1960,* 354; *1961,* 1988; *1962,* 810.

[149] *S. Boileau* and *P. Sigwalt,* C. R. hebd. Séances Acad. Sci., Sér. C *262,* 1135 (1966).

[150] *C. Ivanoff* and *P. Markov,* Naturwissenschaften *50,* 688 (1963).

[151] *H. Normant,* unpublished.

B. Use of the Radical Anions in Syntheses

Solutions of alkali metals in HMPT can be used in the same way as solutions of alkali metals in liquid ammonia, *i.e.* for metallation, reduction, isomerization, polymerization, *etc.* [139].

1. Anion Formation and Metallation

Molecules ZH containing active hydrogen are metallated by solutions of alkali metals in HMPT, with formation of salt-like or covalent derivatives. However, no hydrogen is liberated, and a reaction in accordance with eq. (r) takes place instead. Solutions of K and of Li react more rapidly than Na solutions.

Table 23. Metallation in alkali metal-HMPT-solutions.

Compound metallated	Metal	Reaction partner	Product	Yield (%)
$n\text{-}C_4H_9OH$	Na	$Cl\text{-}CH_2\text{-}C_6H_5$	$C_4H_9\text{-}O\text{-}CH_2Ph$	77
$H_5C_6\text{-}NH\text{-}C_2H_5$	K	C_2H_5I	$Ph\text{-}N(C_2H_5)_2$	77
Phenthiazine	Na	CH_3I	*N*-Methylphenthiazine	85
CH_3CONH_2	K	$Cl\text{-}CH_2\text{-}C_6H_5$	$CH_3\text{-}CO\text{-}NH\text{-}CH_2\text{-}Ph$	[*]
$(C_6H_5)_3CH$	Na	CO_2	$(C_6H_5)_3C\text{-}CO_2H$	50
$(C_6H_5)_2CH_2$	K	$Br(CH_2)_4Br$	$[(C_6H_5)_2CH\text{-}(CH_2)_2\text{-}]_2$	87
Fluorene	Na	C_2H_5I	9-Ethylfluorene	73
$C_6H_5\text{-}CH_3$	Li	CO_2	$C_6H_5\text{-}CH_2\text{-}CO_2H$	little

[*] Low yields, also with $NaNH_2$.

$$2\ Z\text{-}H + 2\left[M^{\oplus}, O\overset{\ominus}{=}P\lesssim\right] \rightleftharpoons 2\ (Z^{\ominus}M^{\oplus}) + O{=}P\lesssim + \left[H_2, O{=}P\lesssim\right] \quad (r)$$

A mixture of HMPT and a nonpolar solvent such as ether, THF, or benzene may also be used. To avoid premature decomposition of the $HMPT^{\ominus}$ anion, the reactant ZH is added to the HMPT at the very beginning, and is added in the stoichiometric quantity.

All the reactions described in Section IV for alkali metal hydrides and amides can be carried out more economically with solutions of the alkali metal itself in HMPT. Table 23 shows the results of some reactions involving metallation on hetero atoms [152] or on "acidic carbon" [153].

Since HMPT is an aprotic solvent, it can be used for the metallation of acids as weak as toluene with alkali metal. With Li or K, the characteristic deep red solution of the benzyl anion is formed. Introduction of CO_2 into this solution gives phenylacetic acid (in small yields), together with $C_6H_5\text{-}(CH_2)_3\text{-}C_6H_5$, $C_6H_5\text{-}C_2H_5$, and other products.

It should also be possible to use this metallation method with high molecular weight compounds containing mobile hydrogen, *e.g.* with polyvinyldiphenylmethane, polyvinylfluorene, *etc.*

Alkali metals in pure HMPT surprisingly do not metallate the much more acidic 1-alkynes, even the relatively acidic phenylacetylene. In the case of phenylacetylene it was found that the diamidophosphite anion $OP(N(CH_3)_2)_2^{\ominus}$, which is formed by further reaction of the primary radical anion, adds to the triple bond. (Concerning complex formation and the entirely different behavior in liquid NH_3, see Section II.) 1-Alkynes must therefore be metallated in mixtures of HMPT with nonpolar solvents such as benzene or toluene (equilibrium between complexed and free 1-alkyne). The results are shown in Table 24 [154].

Table 24. Reactions of 1-alkynes in HMPT/benzene or HMPT/toluene mixtures [154].

Alkyne	M = Li	Product	Yield (%)
$(H_5C_2)_2N\text{-}CH_2\text{-}C{\equiv}CH$	$Br(CH_2)_4Br$	$[\text{-}(CH_2)_2\text{-}C{\equiv}C\text{-}CH_2\text{-}N(C_2H_5)_2]_2$	50
$H_5C_6\text{-}C{\equiv}CH$	CO_2	$H_5C_6\text{-}C{\equiv}C\text{-}CO_2H$	70
$HC{\equiv}CH$	$n\text{-}C_6H_{13}Br$	$CH_3(CH_2)_5\text{-}C{\equiv}CH$	14 [*]
$HC{\equiv}CH$	Cyclohexanone	1-Ethynylcyclohexanol	50
1,3-Dioxolan-2-yl-$(CH_2)_5\text{-}C{\equiv}CH$	$^{14}CH_3I$	$^{14}CH_3\text{-}(CH_2)_7\text{-}CHO$ [155]	80

[*] Low yields, since the strong base $HC{\equiv}C^{\ominus}$ causes cleavage of HBr from $C_6H_{13}Br$.

Compounds containing reactive hydrogen (carboxylic acids, esters, nitriles) as well as functional groups can be metallated and then allowed to react *e.g.* with halogen derivatives. In some cases (*e.g.* for $C_6H_5\text{-}CO\text{-}CH_3$, CH_3CN) the HMPT must be diluted with an inert solvent to avoid polymerization; this is always advisable for acylations and for the addition of CO_2.

2. Reduction of Unsaturated Compounds

A dianion of the monomer (see eq. (s)) or of the dimer (see eq. (t)) of an unsaturated compound can be formed by electron transfer from the $HMPT^{\ominus}$ anion. For example, the reduction of esters to vicinal diketones proceeds in accordance with eq. (t) [151]. We have paid special attention to reaction (s).

$$A{=}Z + 2\left[M^{\oplus}, O\overset{\ominus}{=}P\lesssim\right] \rightleftharpoons 2\ O{=}P\lesssim + M^{\oplus}\overset{\ominus}{A}\text{-}\overset{\ominus}{B}\ \overset{\oplus}{M} \quad (s)$$

$$2\ A{=}Z + 2\left[M^{\oplus}, O\overset{\ominus}{=}P\lesssim\right] \rightleftharpoons 2\ O{=}P\lesssim + 2\ \dot{A}\text{-}B^{\ominus}, 2\ M^{\oplus} \longrightarrow B^{\ominus}\text{-}A\text{-}A\text{-}B^{\ominus}, 2\ M^{\oplus} \quad (t)$$

In the aprotic HMPT, the reaction stops with the formation of the monomeric dianion $A^{\ominus}\text{-}B^{\ominus}$, whereas protonation takes place in primary amines or in liquid NH_3. However, the dianion can also be alkylated.

[152] *H. Normant, T. Cuvigny, J. Normant,* and *B. Angelo,* Bull. Soc. chim. France *1965*, 3447.

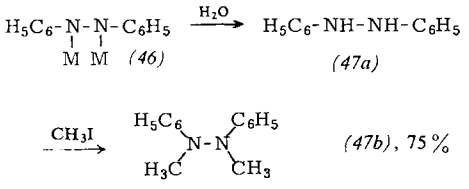
[153] *H. Normant, T. Cuvigny, J. Normant,* and *B. Angelo,* Bull. Soc. chim. France *1965*, 3448.

[154] *H. Normant, T. Cuvigny, J. Normant,* and *B. Angelo,* Bull. Soc. chim. France *1965*, 3449.

[155] *L. Pichat* and *J. P. Guermont,* personal communication.

a) Reduction of N=N or C=N Bonds

Metallation of *e.g.* azobenzene in a solution of an alkali metal in HMPT yields the compound *(46)*, from which *(47a)* is obtained by hydrolysis and *N,N'*-dimethyl-*N,N'*-diphenylhydrazine *(47b)* by methylation with CH_3I [156]. The analogous reductions of imines,



oximes, and hydrazones [156] leads to 30 to 70% yields of secondary amines, together with imines in the reactions of oximes and hydrazones.

b) Reduction of Aromatic Compounds

The products obtained by metallation of phenol ethers and arylamines with alkali metals can undergo an elimination, or the aromatic nucleus may be reduced. The (Birch) reduction proceeds as follows:

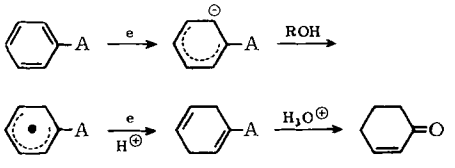


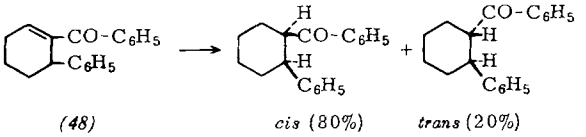
Table 25 shows the results obtained in a mixture of HMPT and $(CH_3)_3COH$ [156, 159].

Table 25. Reduction in HMPT/$(CH_3)_3COH$ (according to *Birch*).

	Products	Yield (%)
Anisole	Cyclohex-2-enone	50
Phenetole	Cyclohex-2-enone	25
N,N-Dimethyl- or *N,N*-Diethylaniline	Cyclohex-2-enone	20
Ethyl β-naphthyl ether	Tetralone	60
Methyl 2-naphthyl ether	1-Methoxytetralin + 1,2-Dihydronaphthalin + 1,4-Dihydronaphthalin	15 + 15 + 30

c) Reduction of α-Unsaturated Ketones

The reduction of α-unsaturated ketones with alkali metals in liquid ammonia or in lower amines leads to saturated ketones.

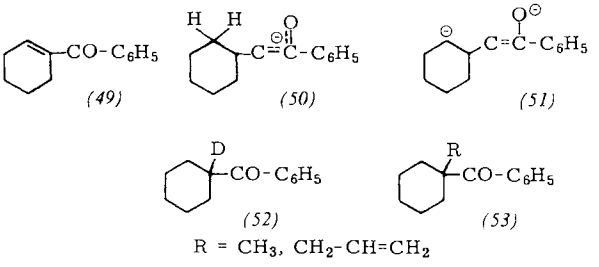


(48) *cis* (80%) *trans* (20%)

In the case of phenyl 6-phenylcyclohex-1-enyl ketone *(48)*, K or Li in liquid NH_3 or in HMPT gives the same overall yield (80%), and the isomer ratio of the reduced ketone is the same [46]. Isophorone, carvone, and pulegone, as well as ketones such as CH_3–CO–R (R = $CH{=}C(CH_3)_2$, $CH{=}CH{-}C_6H_5$, $CH{=}CH{-}C_2H_5$, $CH{=}CH{-}CH(CH_3)_2$, $CH{=}CH{-}C_5H_{11}$, $C(CH_3){=}CH{-}CH(CH_3)_2$) could be reduced to the saturated ketones in yields of 30 to 65% by this method [159].

In the electrochemical reduction of α-unsaturated ketones in HMPT, an electron is transferred from the $HMPT^{\ominus}$ radical-anion to the ketone molecule; the cathodic solution is colorless.

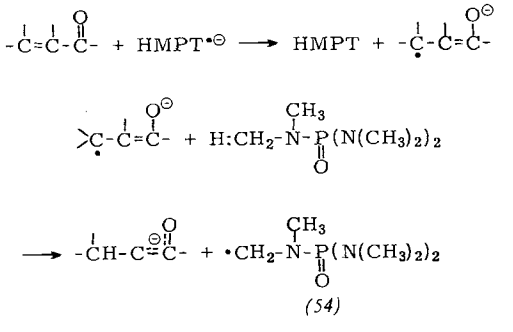
The ketone *(49)* can be reduced to the saturated ketone in a yield of more than 80%, irrespective of the electrolyte used (*e.g.* $MgBr_2$·Ether or CaI_2). A number of observations suggest that the reduction takes place *via* the enolate ion *(50)* rather than *via* the dianion *(51)*. Thus after storage of *(49)* in a solution of Li in HMPT, treatment with D_2O yields the deuterated ketone *(52)* [46]. The lithium derivative similarly gives α-alkylated ketones *(53)* [159]. It has been shown that



R = CH_3, CH_2–CH=CH_2

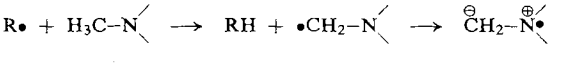
the reaction in liquid ammonia proceeds *via* the enolate ion *(50)* [157, 158].

The following mechanism is possible for the reduction of α-unsaturated ketones in HMPT:



(54)

It is in fact known that tertiary amines can act as H donors toward free radicals [142]:



The radical *(54)* may also be formed in solutions of alkali metals in HMPT in the presence of alkylated aromatic hydrocarbons, since CH_2 is inserted into the alkylated aromatic compound under these conditions. Thus toluene gives mainly ethylbenzene and 1,3-diphenylpropane, ethylbenzene gives cumene, and tetralin gives 1-methyl- and 1,4-dimethyltetralin and dimers [183]. Tetralin gives the same result on electrolytic reduction in HMPT (in the absence of protonic solvents) [180].

[156] *H. Normant* and *M. Larchevêque*, C. R. hebd. Séances Acad. Sci. *260*, 5062 (1965).

[157] *G. Stork* and *Y. Tsuji*, J. Amer. chem. Soc. *83*, 2783 (1961).

[158] *G. Stork* and *S. Darling*, J. Amer. chem. Soc. *82*, 1512 (1960).

[159] *M. Larchevêque*, unpublished.

d) Reduction of α-Unsaturated Carboxylic Acids

α-Unsaturated carboxylic acids can be reduced to saturated carboxylic acids with lithium as described in the previous Section[159]. The yields obtained in the reduction of $C_6H_5-CH=CH-CO_2H$ and $(CH_3)_2CH-CH=CH-CO_2H$ are 60 and 65% respectively.

e) Reduction of Alkynes containing Non-terminal Triple Bonds

3-Octyne and 3-hexyne are not reduced by solutions of Li in HMPT/ether or in HMPT/THF, but isomerize to form 1-alkynes[159]. 2-Methylhex-4-yn-3-ol isomerizes in the same way to give 2-methylhex-5-yn-3-ol. On the other hand, the reaction of alkynes (*e.g.* 2-nonyne, hex-1-ynylcyclohexane) with a solution of Li in HMPT/benzene (1:5 v/v) leads, on addition of water, to the corresponding *trans*-alkenes (55–60%).

3. Reductive Elimination

Electron transfer from an $HMPT^{\ominus}$ anion to a molecule A–Z can have the following consequences:

a) A–Z forms an anion and a new radical, which readily dimerizes;

b) A–Z forms two anions (this happens very readily where resonance stabilization is possible).

Table 26[160] shows the final products that can be obtained on addition of another reactant.

The cleavage of Ge-Ge bonds by solutions of potassium in HMPT[160] has recently been studied in the hexalkyldigermanes[161]. The trialkylgermylpotassium, which is stable in HMPT, reacts readily with trialkylgermyl, -silyl, and -stannyl halides to give mixed hexaalkyl-digermanes, -silylgermanes, and -germylstannanes, $R_3Ge-MR'_3$ (M = Ge, Si, Sn).

The cleavage ethers, R–O–R, by solutions of alkali metals in HMPT has been particularly intensively studied[162].

Dialkyl ethers are not cleaved, while diaryl ethers give phenols. The products obtained on cleavage of some alkyl aryl ethers, alkyl benzyl ethers, and α-unsaturated ethers are shown in Table 27. The reductions do not always proceed in the same manner. Thus with dibenzyl ether in liquid ammonia, an elimination brought about by the carbanion yields 1,2-diphenylethane[163] (just as in HMPT):

$$H_5C_6-\overset{\ominus}{C}H_2 + H_5C_6-CH_2-O-CH_2-C_6H_5 \rightarrow H_5C_6-CH_2O^{\ominus} + H_5C_6-CH_2-CH_2-C_6H_5$$

Ethers of the type $Ar-O-CH\diagup\diagdown$ can undergo Wittig rearrangement[164] to form alcohols. The reduction of aryl *p*-toluenesulfonates with potassium in HMPT leads mainly to phenols, while aryl phosphates (as in liquid ammonia[165]) give hydrocarbons[162].

$$(H_5C_2O)_2P(O)OAr \xrightarrow[2)\ H_2O]{1)\ K,\ HMPT} ArH$$

Compounds of the type Ar–O–Z ($Z \approx B\diagup\diagdown$, $Si\diagup\diagdown$, $Ge\diagup\diagdown$, $Sn\diagup\diagdown$) are broken down into two anions $ArO^{\ominus}$ and $Z^{\ominus}$ by solutions of potassium in HMPT. Protonation and alkylation give ZH and ZR respectively[166].

4. Polymerizations

Though HMPT has been used as a Lewis base with many other polymerization catalysts (*e.g.* organomagnesium and organoaluminum compounds as adducts with halides of elements of the Group IV, V, and VI triads)[167], it does not appear to have been used much for anionic polymerizations. Anionic polymerizations of reactive vinyl compounds[146,147,168] have frequently been initiated by solutions of alkali metals, which contain radical anions. Solutions of ($M^{\oplus}$ + $HMPT^{\ominus\bullet}$) or ($M^{\oplus}$ + $ArH^{\ominus\bullet}$), which can be readily prepared in HMPT, may become important in this application.

Table 26. Reaction of A–Z with another reaction partner and alkali-metal in HMPT.

Starting material A–Z	Alkali metal	Reaction partner	Product	Yield (%)
$H_5C_6-CH_2-Cl$	K	H_2O	$H_5C_6-CH_2-CH_2-H_5C_6$	75
$H_5C_6-O-CH_3$	K	H_2O	H_5C_6-OH	80
$H_5C_6-O-CH(H_5C_6)_2$	K	H_2O	$H_5C_6-OH + (H_5C_6)_2CH_2 + (H_5C_6)_3C-OH$	47 + 52 + 46
$(H_5C_6)_3P$	K	C_2H_5I	$(H_5C_6)_2P-C_2H_5$	58
$CH_3-S-S-CH_3$	K	$H_5C_6-CH_2Cl$	$CH_3-S-CH_2-H_5C_6$	81
$CH_3-S-S-CH_3$	K	$Cl-CH_2-CH_2-OH$	$CH_3-S-CH_2-CH_2-OH$	56
$H_5C_6-NH-NH-H_5C_6$	Li	H_2O	$H_5C_6-NH_2$	
$(H_5C_6)_3C-CH_2-H_5C_6$	K	CH_3I	$(H_5C_6)_3C-CH_3$	72
$(H_5C_6)_3Ge-Ge(H_5C_6)_3$	K	$H_5C_6-CH_2Cl$	$(H_5C_6)_3Ge-CH_2-H_5C_6$	56

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Table 27. Cleavage of alkylaryl ethers in alkali metal/HMPT solutions.

Ether	Product	Yield (%)
$C_6H_5-O-CH_3$	C_6H_5OH	76–80
$C_6H_5-O-C_2H_5$	$C_6H_5OH + C_6H_5OH \cdot HMPT$	20 + 65
β-$C_{10}H_7-O-CH_3$	$C_{10}H_8$ + β-Naphthol·HMPT	43 + 38
β-$C_{10}H_7-O-C_2H_5$	β-Naphthol·HMPT	51

Thus the reaction of *trans*-stilbene with solutions of sodium in HMPT followed by hydrolysis yields the dimeric *meso*-1,2,3,4-tetraphenylbutane[138] *(55)*:

$$H_5C_6-CH=CH-C_6H_5$$
$$\rightarrow \; H_5C_6-\overset{\ominus}{C}H-CH(C_6H_5)-CH(C_6H_5)-\overset{\ominus}{C}H-C_6H_5,\ 2\ Na^{\oplus}$$
$$\xrightarrow{H_2O} [H_5C_6-CH_2-CH(C_6H_5)]_2$$
(55)

Styrene and α-methylstyrene have been dimerized in a suspension of sodium in THF in the presence of *o*-terphenyl as an electron transfer agent[169]:

$$H_5C_6-CR=CH_2 \xrightarrow{2\ Na} H_5C_6-\overset{\ominus}{C}H-CH_2-\overset{\ominus}{C}H-C_6H_5,\ 2\ Na^{\oplus}$$
$R = H,\ CH_3$

The reaction continues a little further with potassium at −30 or −40 °C and in the presence of a small quantity of HMPT to act as the electron transfer agent. Only a little dimer is found on hydrolysis, the main products being low polymers.

Solutions of biphenylmagnesium in HMPT have been used to initiate the quantitative anionic polymerization of styrene, of α-methylstyrene, and of 2-vinylpyridine[170]. Solutions of magnesium in HMPT containing naphthalene polymerize styrene in a similar manner[179].

The results obtained so far[171], some of which have not yet been published, lead to the following conclusions: Even small quantities of alkali metal/HMPT increase the polymerization rate and permit the use of lower reaction temperatures. Many difficult copolymerizations can be satisfactorily carried out only in this system. The conventional polymerization promoters are active in HMPT.

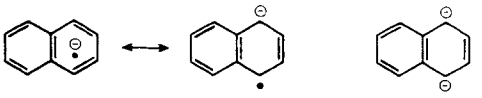
C. Comparison of Electron Acceptor Properties

An electron acceptor is taken here to be a system that is either completely regenerated (reducing action) or is reduced to the extent of 50% (anion-forming or metallation). These electron acceptors contain one or more double bonds; the most common are aryl ketones and polycyclic aromatic hydrocarbons.

Aryl ketones react with alkali metals to give metal ketyls; the radical-ions *(56)* are converted stepwise into alcohols *(57)* by protonation and reduction.

$$Ar_2C\overset{\ominus}{\cdot}O \longleftrightarrow Ar_2C\cdot-O^{\ominus} \qquad Ar_2CH-OH$$
(56) *(57)*

The polycyclic aromatic hydrocarbons form radical-ions and dianions under the action of reactive metals. Thus naphthalene forms the anion *(58)* and the dianion *(59)*. The dianion reacts with ZH to form dihydronaphthalene and the anion $Z^{\ominus}$ or the metallation product Z−M.

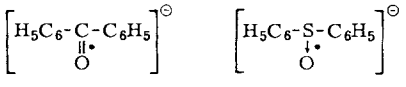


(58) *(59)*

These alkali metal/acceptor systems may be used for many metallation reactions in THF, *e.g.* when the metallation is followed by addition of CO_2 or when chemical separation of all the components of the solution is possible[148]. However, these cases are relatively rare. The difficulties are reduced if the reaction is carried out in alkali metal/HMPT, since the electron acceptor and its reduction product are soluble in water.

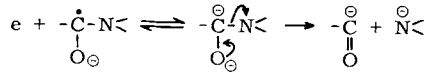
D. Comparison of Polar Aprotonic Solvents

The solvents DMF, TMU, and DMSO, whose electron donor character has already been discussed in Section IV, can also act as electron acceptors owing to their polar group, and can give generally unstable radical-anions.



(60) *(61)*

Aryl ketones form radical-ions such as *(60)*, which are stabilized by charge delocalization. The anions of the DMF and TMU molecules, which cannot be stabilized in this way, rapidly decompose into two ions[175,176].



Alkali metals actually give very unstable blue solutions in TMU; the color persists for only a few seconds at room temperature, and for a minute at −40 °C[175]. Triphenylmethane is the only substrate that can be metallated with an Na/K alloy in TMU. The decomposition follows the same course in HMPT, but the radical-anion is considerably more stable in this case (half-life of the blue color with potassium approx. 10–15 min, with Li and Na a few hours).

The aromatic sulfoxides should be similar to the diaryl ketones, since there is strong conjugation between the SO group and the aromatic nuclei; however, the radical-ion *(61)* is not very stable.

Diphenyl sulfone reacts with potassium in 1,2-dimethoxyethane to give blue solutions which are unstable even at −70 °C, but which give an EPR spectrum[177]. It may therefore be concluded that alkali metals react with DMSO to form the "dimsyl" anion *(62)*[178], and that the radical-ion *(63)* is extremely unstable.

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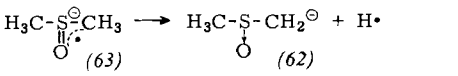
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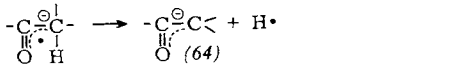
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(63) (62)

Similarly, amides of carboxylic acids with hydrogen atoms in the α position (*e.g.* dimethylacetamide and *N*-methylpyrrolidone) and enolizable ketones should give enolate ions *(64)* with alkali metals.



(64)

The stability of the radical-ions decreases in the order $HMPT^{\ominus\bullet} > TMU^{\ominus\bullet} > DMSO^{\ominus\bullet}$; this explains why HMPT is the only known polar aprotonic solvent that can be used for syntheses involving dissolved reactive metals.

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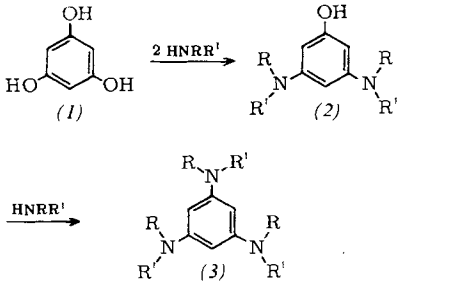
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COMMUNICATIONS

N-Persubstituted 3,5-Diaminophenols and 1,3,5-Benzenetriamines and their Protonation

By *F. Effenberger* and *R. Niess*[*]

N-Persubstituted 3,5-diaminophenols *(2)* and 1,3,5-benzenetriamines *(3)* have not been described previously. We have prepared aminobenzenes *(2)* and *(3)* by heating phloroglucinol *(1)* with secondary amines in an autoclave[1].



(1) (2) (3)

The reactions are carried out with an excess of amine (phloroglucinol : amine = 1:4), the molar ratio *(2)*:*(3)* obtained depending solely on the reaction temperature. The products can be purified by fractional distillation or recrystallization.

Amine used	Temp. (°C)	(2) Yield (%)	(2) M.p. (°C) (b.p., °C/mm)	(3) Yield (%)	(3) M.p. (°C) (b.p., °C/mm)
Pyrrolidine	20	100	174–185	–	
	180–200	–		95	179–181
Piperidine	180–200	98	154–156	–	
	280–300	–		40	184
Morpholine	180–200	91	185–187	–	
	280–300	–		37	308–312
Dimethylamine	130–150	68	(148/0.008)	22	
	220	14		69	(131/0.01)

With mineral acids the benzenetriamines *(3)* form definite salts containing 1, 2, or 3 moles of acid.

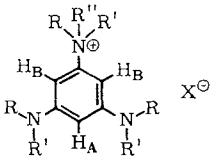
Depending on the substituents R and R′, stable *N*- or *C*-protonation products, *(4)* and *(5)* respectively, are formed on monoprotonation. *N*-protonation of tripiperidinobenzene [*(3)*, R and R′ = $(CH_2)_5$] for example leads to the formation of *(4)*, whilst with tripyrrolidinobenzene [*(3)*, R and R′ = $(CH_2)_4$] a crystalline compound of the type *(5)* is produced. (Physical properties: *e.g. (5)*, X = BF_4, yellow needles. m. p. 254–257 °C).

Assignment of structure was based on ^1H–NMR-spectroscopic data. The ^1H–NMR spectrum of tripyrrolidinobenzene hydroiodide [*(5)*, R and R′ = $(CH_2)_4$, X = I] in $CDCl_3$ showd H_B as a singlet at τ = 5.17 and H_A as a singlet at τ = 6.20 (relative intensities 1:1).

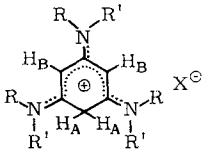
Particular structural characteristics can be gleaned from the ^1H–NMR spectra of tripiperidinobenzene monoperchlorate [*(4)*, R and R′ = $(CH_2)_5$, X = ClO_4]. In polar solvents (*e.g.* $(CD_3)_2CO$ or $(CD_3)_2SO$) the three nuclear protons appear as a singlet at τ = 3.6, whilst the proton attached to the nitrogen (whose presence can be seen only on integration) indicates rapid proton exchange among the amino groups. On the other hand, in $CDCl_3$ this proton is fixed on an amino function and the signals of the three nuclear protons are widely separated in the spectrum (1 H at τ = 2.10 [N–H], 2 H at τ = 3.38 and 1 H at τ = 4.63). A *meta* coupling of the ring protons H_A and H_B was not observed. The comparable *N*-methyl compound [*(6)*, R and R′ = $(CH_2)_5$, X = ClO_4], however, shows only a small amount of splitting of the nuclear protons (τ-values centered at 3.5) and a distinct *meta* coupling (J_{AB} = 2 Hz).

We conclude from the NMR spectra that there is a strong electronic disturbance of the aromatic π-electron system in tripiperidinobenzene monoperchlorate. An alternative to the benzenoid structure *(4)* is a valence isomer with a "Dewar structure"; although this would certainly agree with the NMR spectrum, we have no other evidence to support this structure.

Further investigations, in particular X-ray structural analysis of the tripiperidinobenzene monoperchlorate, are in progress.



(4), R″ = H
(6), R″ = CH_3



(5)

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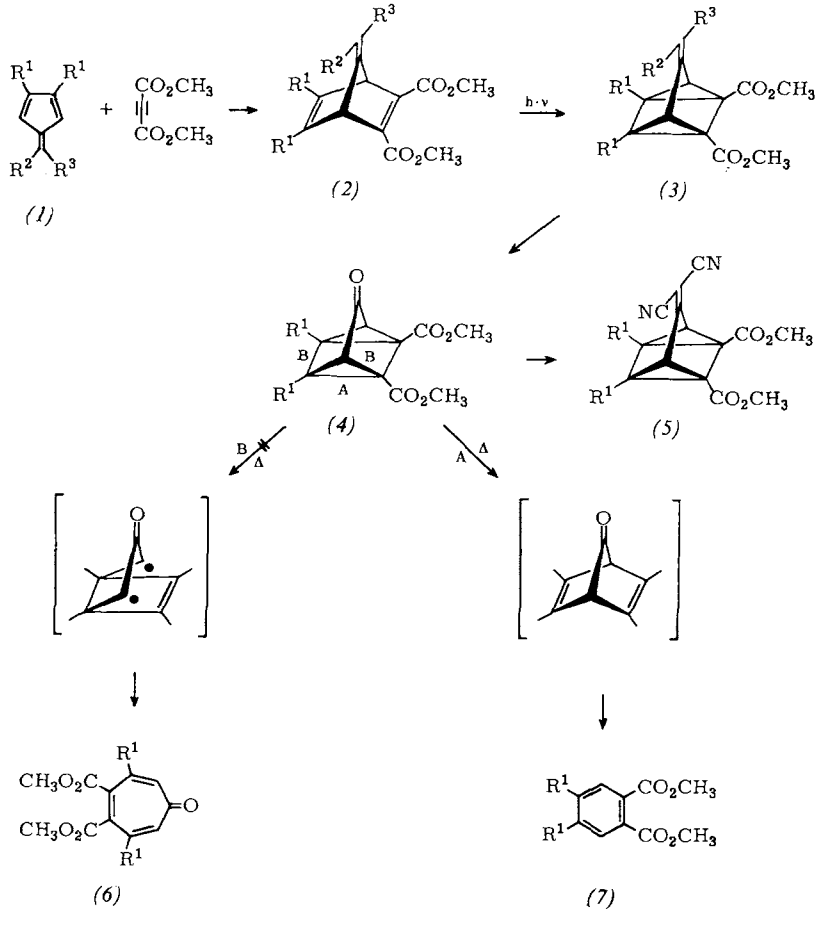
[*] Dr. F. Effenberger and R. Niess
Institut für Organ. Chemie
der Techn. Hochschule
Azenbergstr. 14/16
7 Stuttgart (Germany)

[1] The preparation of the aminobenzenes was reported at the *Chemiedozententagung* in Würzburg on April 29th, 1966.

A New Route to the Tetracyclo[3.2.0.0^{2,7}0^{4,6}]-heptan-3-one System [1]

By *H. Prinzbach* and *J. Rivier* [*]

Syntheses hitherto available [2] for the tetracyclo-[3.2.0.0^{2,7},0^{4,6}]heptan-3-one system ("quadricyclanone") have been very devious and unsatisfactory. In the reaction series *(1)* → *(2)* → *(3)* → *(4)* we have found a new route which, according to results to date, is very productive. Many variations are known for the step *(1)* → *(2)*; according to the nature of the substituent at position 8, the photochemical valence isomerization of the homotriene *(2)* to the methylenetetracyclene *(3)* can be effected in good to very good yield by direct or sensitized excitation [3]. The oxidation *(3)* → *(4)* also occurs almost quantitatively under controlled conditions.



(a), $R^1 = H$, $R^2 = R^3 = CH_3$
(b), $R^1 = H$, $R^2 = R^3 = C_6H_5$
(c), $R^1 = R^2 = H$, $R^3 = C_6H_5$
(d), $R^1 = CO_2CH_3$, $R^2 = R^3 = CH_3$

As first examples we have prepared the crystalline quadricyclanones *(4a)* and *(4d)* by degrading the methylenequadricyclane derivatives *(3a)* and *(3d)* by ozone. Spectroscopic data (see Table) show that the oxidation proceeds without skeletal rearrangement; the structures *(4a)* and *(4d)* are also proved by numerous reactions, cycloadditions [4] or condensations [*e.g.* with malonitrile to give *(5a)*]. In the pyrolysis (> 120 °C), the 3σ → 3π-process which predominates for 3-oxa- [1] and 3-aza-tetracyclene [5] plays no part, since the tropones *(6a)* and *(6d)* could not be detected by NMR spectroscopy. As with the analogously substituted 3-methylene compounds [3], and in at least formal agreement with the markedly different resonance stabilization of free radicals by *O*- and *N*-substituents or carbonyl groups [6], the bonds A are cleaved exclusively, with simultaneous or subsequent elimination of CO, to yield the aromatic compounds *(7a)* and *(7d)*. Mass spectra indicate that the radical cations produced at 70 eV from *(4a)* and *(4d)* decompose analogously. We are at present studying the stabilization of *(4a)* and *(4d)*, and of quadricyclanones containing additional substituents on the bridgeheads, after selective n→π*excitation.

Experimental

An O_2 stream containing 23 mg of O_3 per liter was passed slowly into a CH_2Cl_2 solution (−10 °C) of *(3a)*, *(3b)*, or *(3c)* (27 mmoles in 120 ml), until the KI indicator was distinctly colored. After removal of the excess of ozone in a stream of N_2 and addition of 180 ml of glacial acetic acid, a total of 5 g of zinc powder and 1.5 ml of water was added in portions. On extraction with ether, drying, and removal of the solvent by distillation there remained *(4a)* (yield, 90 to 100 %) as a slowly crystallizing oil. *(4d)* was obtained (yield, 90–100 %) similarly from *(3d)* [**].

	M.p. (°C)	UV λ_{max} (nm); ε	NMR [τ, TMS = 10; J(Hz)]	Molecular ion [M$^+$] at (*m/e*)
(4a)	39.5–40.5	307; 195 [a] 222 (s); 1808	6.27 (6,S) [c] 7.07 (2,D; 4.8) 8.05 (2,D; 4.8)	weak compared with (M−CO)$^+$
(4d)	102–103	302; 115 [b] 245 (s); 730	6.10 (12,S) [c] 7.33 (2,S)	338
(5a)	139 (dec.)	247 [a]	6.16 (6,S) [d] 6.6–7.1 (4; A_2B_2)	

S = Singlet; D = doublet.

[a] In isooctane. — [b] In acetonitrile. — [c] In CCl_4. — In nitrobenzene.

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[*] Prof. Dr. H. Prinzbach and Ing. chim. dipl. J. Rivier
Université de Lausanne, Laboratoire de Chimie organique
3, Place du Château
CH-1000 Lausanne (Switzerland)

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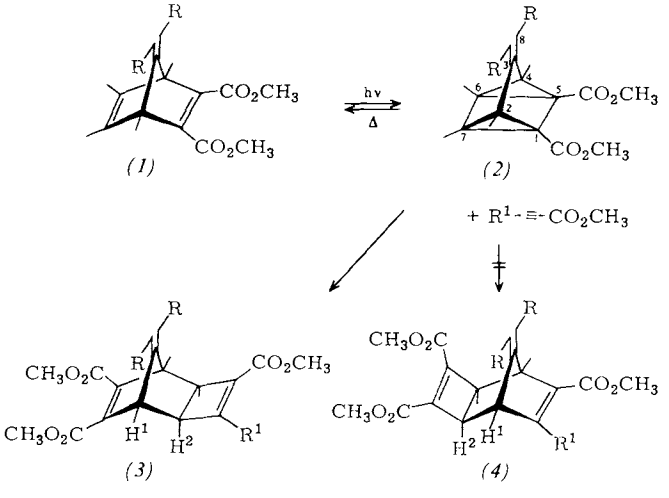
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[**] Note added in proof: The singly methoxycarbonyl-substituted ketone *(4)* can also be obtained in good yields by the same method.

Cycloadditions to Derivatives of Methylenequadricyclane and of Quadricyclanone (Bishomocyclobutadiene) [1]

By *H. Prinzbach* and *J. Rivier* [*]

3-Methylenetetracyclo[3.2.0.0^{2,7}.0^{4,6}]heptane derivatives *(2)*, substituted at position 8, are obtained by photoisomerization of compound *(1)* [2]. These compounds, and the tetracyclic ketones *(5)* [1] obtained from them, behave towards dienophiles formally as if they were bishomocyclobutadienes (C^1–C^2–C^7–C^6–C^4–C^5).



(a), R = C_6H_5, R^1 = CO_2CH_3
(b), R = C_6H_5, R^1 = H
(c), R = CH_3, R^1 = CO_2CH_3
(d), R = CH_3, R^1 = H

Heating *(2a)* with a five- to ten-fold excess of dimethyl acetylenedicarboxylate (DMA, 1 h, 130 °C) or methyl propiolate (MP, 6 h, 125 °C, bomb tube) affords the 1:1 adducts *(3a)* (*ca.* 90 %) and *(3b)* (*ca.* 60 %), respectively. The "forbidden" process *(2)* → *(3)* [3] is irrelevant under these conditions. The structure *(3)*, which was expected from earlier findings [4], is proved by the data collected in the table. Since these results prove the *exo*-arrangement of the four-membered ring ($J^{12} \leqslant 1.2$ Hz in *(3a)* and *(3b)*) stereospecific *exo*-attack [5] is established. That addition occurs at positions 6/7, to give *(3)*, and not at positions 2/4, to give *(4)*, is convincingly demonstrated by the fact that the olefinic

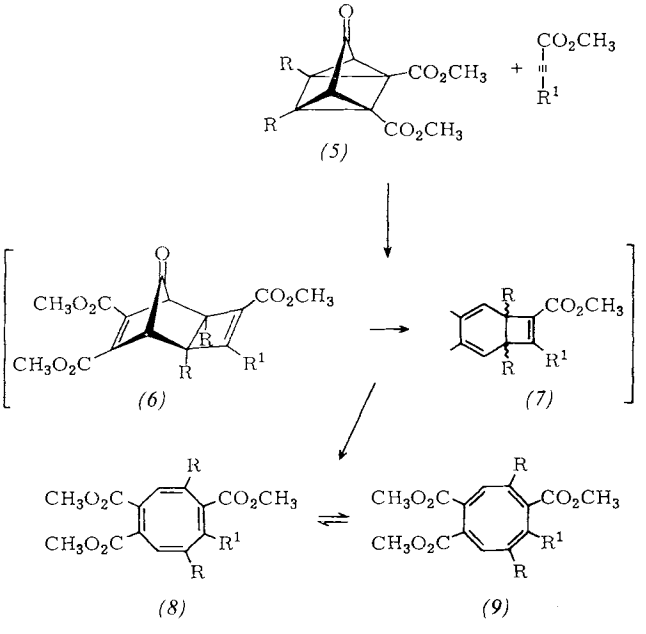
	M.p. (°C)	UV λ_{max} (nm)	UV ε	NMR (τ, TMS = 10)
(3a)	170–171	235 (s) 222 (s)	20800 [a] 24500	2.1–3.0 (10,M) [c] 5.83 (2,S) 6.61 (12,S) 6.98 (2,S)
(3b)	148	238 (s) 220 (s)	19000 [b] 23500	2.4–2.9 (10,M) [c] 3.00 (1,dD), J < 1.0 Hz 5.80 (1,T), J = 1.2 Hz 6.14 (1,T), J = 1.2 Hz 6.48 (3,S) 6.64 (6,S) 6.78 (1,dT), J = 4.0; 1.2 6.78(1,dT),J=4.0;1.2 Hz) 7.32(1,dT),J=4.0;1.2 Hz)

[a] In Isooctane. – [b] In Acetonitrile. – [c] In C_6D_6.

proton of the propiolic ester adduct (R^1) couples with the singly allylic proton H^2 *(3b)* and not with the doubly allylic proton H^1 *(4b)*.

The importance of the substituents at position 8 is illustrated by the fact that, for example, the dimethyl compound *(2c)*, even when in excess, always reacts with two equivalents of DMA or MP, giving 1:2 adducts. The structure of these products is not yet established unambiguously; it is possible that *(2c)* reacts primarily as a monohomodiene (C^1–C^7–C^2–C^3–C^8) [6].

Under the conditions of the addition *(2)* → *(3)*, the ketone *(5a)* affords the cycloctatetraene derivatives *(8, 9)*, which, according to the NMR spectra (see table), at 30 °C exist almost exclusively as the compound designated *(9)* [7]. It is reasonable to formulate the addition leading to *(9)* as analogous to that for *(3a)* and *(3b)*, *i.e.* as proceeding by way of *(6)* and *(7)* (it must be left an open question as to whether the individual steps are or are not synchronous). It would then be understandable why the ketone *(5c)*, which is substituted by acceptor groups at positions 6 and 7 and is sterically shielded, is resistant to DMA and MP under conditions that are sufficient for reaction of *(5a)* and *(5b)*.



(a), R = H, R^1 = CO_2CH_3
(b), R = H, R^1 = H
(c), R = CO_2CH_3, R^1 = CO_2CH_3
(d), R = CO_2CH_3, R^1 = H

	M.p. (°C)	UV λ_{max} (nm)	UV ε	NMR (τ, TMS = 10)
(9a)	187	232	24800 [a]	2.62 (4,S) [b] 6.24 (12,S)
(9b)	108	230	19100 [a]	2.66 (3,S) [b] 3.66 (2,S) 6.18 (3,S) 6.20 (3,S) 6.27 (3,S)

[a] In Methanol. – [b] In CCl_4.

It is doubtful whether the bishomocyclopentadienone system *(5)* has the same importance for the synthesis of derivatives of cyclooctatetraene as cyclopentadienones have for the preparation of substituted benzene derivatives[8]. Experiments with cycloctatetraene, methyl 1,2-dimethylcyclopropene-1-carboxylate, and dimethyl 1-cyclobutene-1,2-dicarboxylate as dienophilic reagents for *(5a)* did not give decisive results, even under drastic conditions.

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[*] Prof. H. Prinzbach and Ing. chim. dipl. J. Rivier
Université de Lausanne, Laboratoire de Chimie organique
3, Place du Château
CH-1000 Lausanne (Switzerland)

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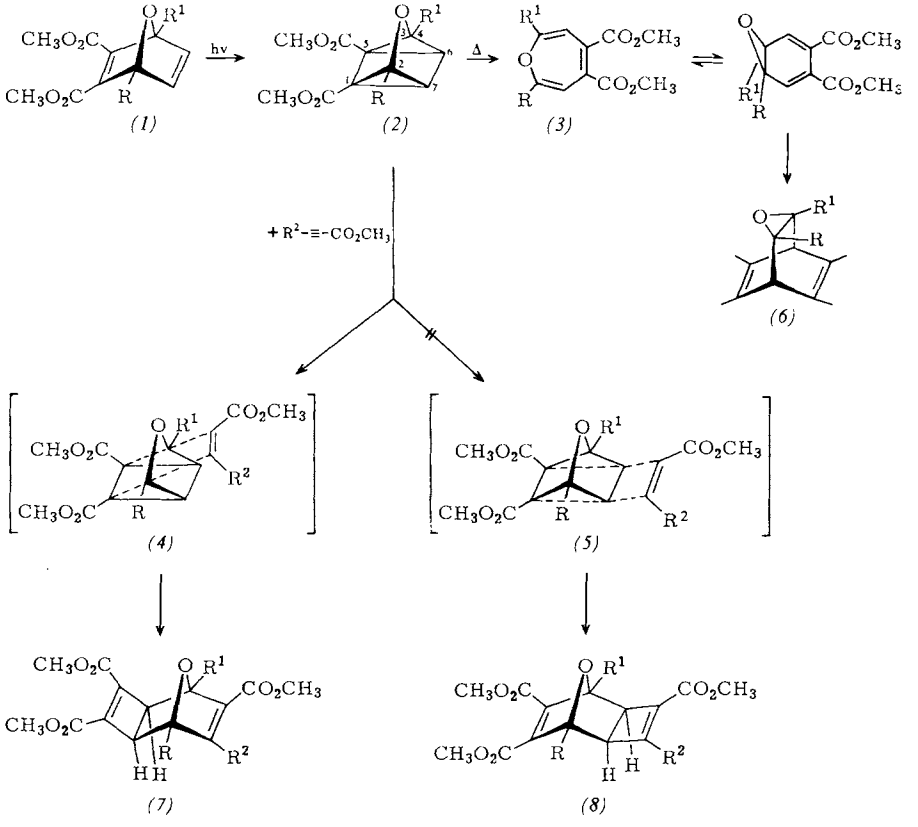
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Cycloadditions to Derivatives of Oxaquadricyclanes (Bishomofuran) [1]

By *H. Prinzbach*, *M. Argüelles*, *P. Vogel*, and *W. Eberbach* [*]

The tetracyclic ethers *(2)* are readily accessible from oxanorbornadiene derivatives *(1)* by photochemical valence isomerization and can be pyrolysed to oxepins *(3)* under very mild conditions[2]. We have used the strain energy indicated by this pyrolysis of system *(2)* to advantage for a series of cycloadditions. In the temperature region where the change *(2)* → *(3)* plays only a subordinate role [small proportions of *(6)* can be separated by crystallization], the tetracycles *(2)* afford 1:1 adducts with reactive dienophiles.



(a), R = R^1 = H, R^2 = CO_2CH_3
(b), R = R^1 = H, R^2 = H
(c), R = R^1 = CH_3, R^2 = CO_2CH_3
(d), R = R^1 = CH_3, R^2 = H

For this purpose, the bishomodiene *(2)* is heated with a five- to ten-fold excess of dimethy lacetylenedicarboxylate (DMA), methyl propiolate (MP), or maleic anhydride (MA). Depending upon the substituents in *(2)* and the reactivity of the dienophile, temperatures between 80 and 110 °C and reaction times between 30 min and 9 h are necessary. The

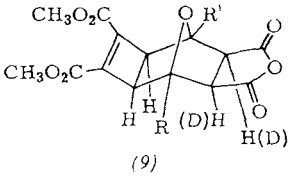
adducts *(7)* and *(9)/(10)* are obtained in good to very good yield. The physical data relevant to proof of structure are given in the Table[3].

That addition to *(2)* occurs at positions 2/4 [giving *(7)* or *(9)/(10)*], and not, as with the isocyclic analogues[1] and their 3-methylene[1] and 3-oxo derivatives[1], at positions 6/7 [to give *(8)* or *(11)/(12)*], is shown, at least for *(7b)* and

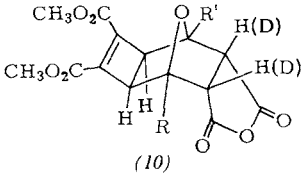
	M.p. (°C)	UV λ_{max} (nm)	UV ε	Molecular ion at *m/e* [5]	NMR (τ, TMS = 10)
(7a)	157–158	230 (br.s)	11400 [a]	352	4.95 (2, S) [a] 6.13 (12,S) 6.91 (2, S)
(7b)	80	265 (s) 218	2100 7400 [a]	294	2.78 (1,D), J = 2.0 Hz 5.05 (1,S) 5.17 (1,D), J = 2.0 Hz 6.10 (3,S) 6.15 (3,S) 6.20 (3,S) 7.20 (2,S)
(7c)	106	226 (s)	9900 [b]	380	6.18 (6,S) [c, d] 6.19 (6 S) 6.96 (2,S) 8.42 (6,S)
(7d)					2.93 (1,S) 6.12 (6,S) 6.19 (3,S) 7.12 (2,S) 8.36 (3,S) 8.47 (3,S)

[a] In CH_3OH. — [b] In isooctane. — [c] In $CDCl_3$. — [d] In CCl_4.

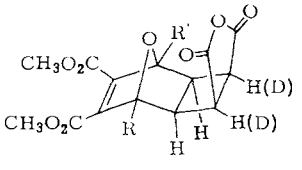
(10a), as follows: The alternative formula *(8b)* is excluded by the vicinal coupling, shown in the NMR spectrum of the MP adduct *(7b)*, between the olefinic proton (τ = 2.78) and the proton R in the α-position to the bridging oxygen atom (τ = 5.17). Similarly, formulae *(11)/(12)* are excluded by the coupling existing in the MA adduct *(10a)* between the protons introduced by MA (τ = 6.10) (assigned with the aid of $[D_2]$-MA) and the bridgehead protons R/R' (τ = 5.00). Evidence in favor of the structure *(9a)* (which then becomes probable for the second MA adduct) and against *(11a)/(12a)*[6] is provided by the singlet character of the signal of the MA protons (τ = 6.72), which also proves the *exo*-arrangement of the anhydride ring in *(9a)*. A second indication of the correctness of this assignment is the finding that the signals of the MA protons *cis* to the O atom in *(10a)* are shifted paramagnetically by 0.62 ppm in relation to those of *(9a)*[7].



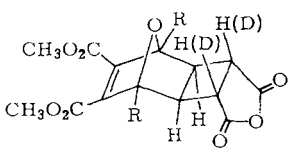
(9)



(10)



(11)



(12)

(a), R = R' = H
(b), R = R' = CH_3

	M.p. (°C)	UV λ_{max} (nm)	UV ε [a]	Molecular ion at *m/e* [5]	NMR (τ, TMS 10) [b]
(9a)	239–240	234	3200	308	4.95 (2,S) 6.11 (6,S) 6.72 (2,S) 6.81 (2,S)
$[D_2]$–*(9a)*	240	234	3200	310	4.95 (2,S) 6.11 (6,S) 6.81 (2,S)
(9b)	199.5	234 (S)	4800	336	6.07 (6,S) 6.78 (2,S) 6.81 (2,S) 8.37 (6,S)
(10a)	215–219	230	5100	308	5.00 (2,M) 6.08 (6,S) 6.10 (2,M) 6.65 (2,S)
$[D_2]$–*(10a)*	216–219	230	5100	310	5.00 (2,S) 6.08 (6,S) 6.65 (2,S)
(10b)	177.5	234 (S)	5300	336	6.08 (6,S) 6.38 (2,S) 6.64 (2,S) 8.32 (6,S)

[a] In CH_3CN. — [b] In $CDCl_3$.

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[*] Prof. H. Prinzbach, Ing. chim. dipl. M. Argüelles, Ing. chim. dipl. P. Vogel, and Dr. W. Eberbach
Université de Lausanne, Laboratoire de Chimie organique
3, Place du Château
CH-1000 Lausanne (Switzerland)

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[5] We thank Dr. *B. Willhalm*, Firmenich Co., Geneva, and Dr. *H. Achenbach*, Universität Freiburg/Brsg., for the mass spectra.

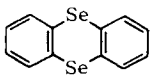
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Formation of Selenanthrene from Diphenyl Selenide and of Dipotassium Triimidotellurite from Diphenyl Telluride

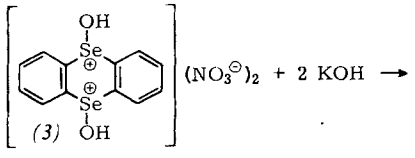
By *O. Schmitz-DuMont* and *B. Ross*[*]

Whereas diphenyl sulfide $S(C_6H_5)_2$ in liquid ammonia containing KNH_2 undergoes partial ammonolysis with formation of C_6H_5SK and aniline[1], reaction of diphenyl selenide $Se(C_6H_5)_2$ *(1)* under the same conditions leads to selenanthrene *(2)*, the yield thereof depending on the amount of KNH_2 present; byproducts are K_2Se_x ($x \geq 2$) and C_6H_5SeK.

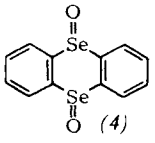


(2)

Diphenyl selenide is treated with about one equivalent of KNH_2 in liquid ammonia at −70 °C in a pressure apparatus [2] On warming to 0 °C. all the diphenyl selenide dissolves. After a few hours, colorless needles separate from the yellow solution. These are filtered off and washed several times at 0 °C with liquid ammonia. The compound is then pure (m.p. 181–182 °C) and agrees in all its properties with the selenanthrene described previously [3]. The reaction with HNO_3, which is said [3] to lead to an addition compound $C_6H_4Se_2C_6H_4 \cdot 2HNO_3$, is particularly characteristic. We have found that this compound, when treated with aqueous potassium hydroxide, yields selenanthrene dioxide *(4)*, which regenerates selenanthrene with evolution of O_2 when heated above its melting point. To accord with this, the compound *(3)* and its reaction with KOH is to be formulated as:



(3) $(NO_3^{\ominus})_2$ + 2 KOH →



+ 2 KNO_3 + 2 H_2O

(4)

When two equivalents of KNH_2 are used the yield of selenanthrene decreases from 50 to 30 %; and there is no reaction in pure liquid ammonia at room temperature.

The reaction of diphenyl telluride $Te(C_6H_5)_2$ *(5)* with liquid ammonia in the presence of KNH_2 leads, however, by complete ammonolysis to formation of benzene and dipotassium triimidotellurite $K_2[Te(NH)_3]$ *(6)*. In this salt, Te has oxidation state +4 as a result of valency disproportionation of the Te^{2+} present in *(5)*:

$$7\ Te(C_6H_5)_2 + 10\ KNH_2 + 2\ NH_3 \rightarrow$$
$$4\ K_2[Te(NH)_3] + K_2Te_3 + 14\ C_6H_6$$

The red color of the mixture and the good solubility in liquid NH_3 (K_2Te is insoluble) suggest the formation of K_2Te_3.

Diphenyl telluride is treated at −70 °C with two equivalents of KNH_2 in liquid NH_3 and warmed to 20 °C, whereupon it dissolves with red coloration. The product *(6)* separates as colorless crystals within several hours, and is then filtered off, washed several times with liquid ammonia, and freed from adhering solvent by passing anhydrous N_2 over it. The substance, which is weighed for analysis with exclusion of air and moisture, must be wetted with benzene before it is hydrolysed since otherwise it explodes violently. Hydrolysis with exclusion of air and subsequent addition of acetic acid yields $TeO_2 \cdot H_2O$ as a gelatinous precipitate, which is converted into crystalline TeO_2 by warming.

On reaction of *(6)* with an excess of NH_4NO_3 in liquid NH_3 a highly explosive, yellow deposit is obtained. After being washed with liquid ammonia and freed from adhering NH_3 by passage of anhydrous N_2 at −70 °C, the product has the composition of pure tellurium(IV) nitride Te_3N_4. It could not be weighed out for analysis because of its tendency to explode. Instead, the whole material was hydrolysed in a stream of moist N_2 (absorption of the NH_3 evolved in 2 % boric acid solution, removal of the residual NH_3 by heating of the hydrolysis product with water to the boiling point, and titrimetric determination of the NH_3). The residue from the hydrolysis is TeO_2, which is weighed as elemental Te. Since the substance contains only Te and N (H can be excluded because of the exact ratio Te:N = 3:4 and the proved oxidation state +4 of the Te), the amounts of Te and N found indicate the composition Te_3N_4 unambiguously. Analysis, hydrolysis, and reaction with NH_4NO_3 accord with formulation of product *(6)* as potassium triimidotellurite. The product is formally derived from K_2TeO_3 by replacement of the O atoms by NH.

The electronegativity of the element bound to C is decisive for the course of hydrolysis of the diphenyl compounds of S, Se, and Te. If this is lower than that of the phenyl-C atom, then the ammonolysis occurs with formation of benzene and a N-compound of the element in question (cf. the ammonolysis of the phenyl compounds of phosphorus [4] and of arsenic, antimony, and bismuth [5]).

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[*] Prof. Dr. O. Schmitz-Du Mont and Dr. B. Ross
Anorganisch-Chemisches Institut der Universität
Meckenheimer Allee 168
53 Bonn (Germany)

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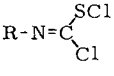
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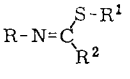
Preparation of *S*-Aminoisothioureas by Nucleophilic Substitution of *S*-Chloroisothiocarbamoyl Chlorides [1]

By *G. Ottmann* and *H. Hooks, jr.* [*]

N-Alkyl and *N*-aryl-*S*-chloroisothiocarbamoyl chlorides *(1)* are conveniently prepared by chlorination of isothiocyanates [2]. We have found that compounds *(1)* react very readily with primary and secondary, aliphatic and aromatic amines to form *S*-aminoisothioureas *(2)* [3] in high yields. These compounds are obtained in satisfactory purity if the reaction is performed below 0 °C and in absence of moisture.



(1)

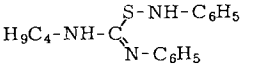


(2)

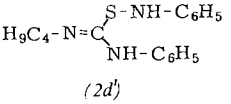
The stability of compounds *(2)* depends on the substituents: phenyl groups stabilize, whereas alkylamino groups weaken the structure. Thus, *(2a)* is stable above its melting point, while *(2b)* decomposes slowly to a tar at *ca.* 25 °C. On heating *(2c)*, 2-dibutylamino benzthiazole *(3)* was formed alongside other products by elimination of dibutylamine.

The structures of compounds *(2)* are confirmed by synthesis, elemental analysis, molecular-weight determination, and NMR spectroscopy. A migration of the C=N double bond anticipated for reactions of *(1)* with primary amines, was detected by NMR spectrometry in the case of the reaction of *(1d)*, R = C_4H_9, with aniline, which gave *(2d)* and not *(2d')*. In contrast, the original $C_6H_5N{=}C$ structure of *(1b)*, R = C_6H_5, was maintained in the reaction with butylamine.

The NMR spectrum of *N*,*N*^{1},*N*^{2}-tributyl-*S*-aminoisothiourea *(2e)* shows 2 triplets with an intensity ratio of 2:1, which



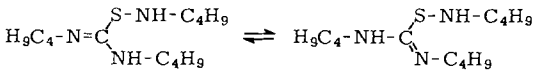
(2d)



(2d')

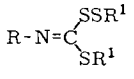
	R	R^1	R^2		Yield (%)	δ-^{1}H Relative intensity α-CH_2 in C_4H_9—N (ppm)			λmax (mμ)
						R^1	R^2	R	
(2a)	C_6H_5	C_6H_5NH	C_6H_5NH	m.p. 150—150.5 °C	71				257
(2b)	C_6H_5	C_4H_9NH	C_4H_9NH	oil, not distillable	83	2.70 (1)	3.35 (1)		249
(2c)	C_6H_5	$(C_4H_9)_2N$	$(C_4H_9)_2N$	oil, not distillable	88	2.38 (1)	3.39 (1)		244
(2d)	C_6H_5	C_6H_5NH	C_4H_9NH	m.p. 149.5—150.5 °C	84		3.33		240
(2e)	C_4H_9	C_4H_9NH	C_4H_9NH	oil, not distillable	89	3.20 (1)	3.46 (2)		
(2f)	C_4H_9	$(C_4H_9)_2N$	$(C_4H_9)_2N$	b.p. 138—139 °C/0.14 mm	71	2.91 (2)	3.29 (2)	3.49 (1)	

represent two equivalent and one non-equivalent CH_2N_{butyl} group. The triplet of relative intensity 2 has a chemical shift between those of $-CH_2NH$ and $-CH_2N=$; this indicates a delocalization of the double bond of the butylimino group and the proton of the butylamino group in *(2e)*.



(2e)

Contrary to their reactions with amines, the reactions of *(1)* with sodium thiolates did not lead to stable products, but gave isothiocyanates and diaryl disulfides instead of the desired compounds *(4)*.



(4)

The reactions of *(1)* with sodium *O,O*-diethyl dithiophosphate also afforded isothiocyanates.

Syntheses:

(a) A solution of 42.0 g of *N*-phenyl-*S*-chloroisothiocarbamoyl chloride in 100 ml of ether was added dropwise at 0 °C to a stirred solution of 74.4 g of aniline in 300 ml of ether. The reaction mixture was stirred overnight at 25 °C and then filtered. The filter cake was extracted with cold water to dissolve aniline hydrochloride. The water insoluble portion was dried, and recrystallized from toluene and finally from alcohol to give 46 g of pure *S*-anilino-*N,N'*-diphenylisothiourea.

(b) The reaction mixture obtained from 37.2 g of *N*-butyl-*S*-chloroisothiocarbamoyl chloride and 113 g of dibutylamine was filtered and the solvent evaporated. The residue was extracted with 1200 ml of pentane. Distillation of the crude reaction product in 6 portions in a high vacuum yielded 52 g of pure *S*-dibutylamino-*N*-butyl-*N'*-dibutylisothiourea in the form of yellow oily liquid, and 10 g of a resinous distillation residue.

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[*] Dr. G. Ottmann[**] and H. Hooks, jr.
Olin Mathieson Chemical Corporation Research Center
275 Winchester Avenue
New Haven, Connecticut 06504 (U.S.A.)

[**] Present address:
Dr. Kurt Herberts und Co.,
56 Wuppertal-Barmen
Christbusch 25 (Germany)

[1] Chlorination of Isothiocyanates, Part VII. – Part VI: *G. Ottmann* and *H. Hooks, jr.*, Angew. Chem. *79*, 470 (1967); Angew. Chem. internat. Edit. *6*, 455 (1967).

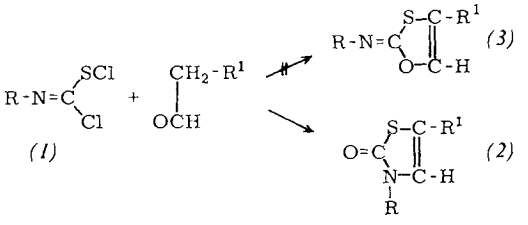
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[3] *K. Ley* and *U. Eholzer*, Angew. Chem. *78*, 672 (1966); Angew. Chem. internat. Edit. *5*, 674 (1966).

Preparation of 5-Alkyl-1,3-thiazolin-2-ones by Reaction of *S*-Chloroisothiocarbamoyl Chlorides with Aldehydes and Vinyl Ethers [1]

By *G. Ottmann*, *H. Hoberecht*, and *H. Hooks, jr.* [*]

The chlorination product of isothiocyanates, *S*-chloroisothiocarbamoyl chlorides *(1)*, react with aliphatic or cycloaliphatic ketones to form 2-imino-1,3-oxathioles or 4-alkyl- and 4,5-dialkyl-1,3-thiazolin-2-ones [2]. Thiazolin-2-ones *(2)*, mono-substituted at C-5 or unsubstituted at both C-4 and C-5, cannot be prepared by this reaction, nor have they been obtained by any other method.



(1) *(3)* *(2)*

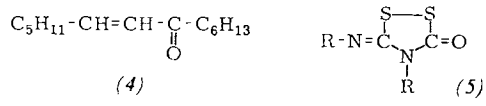
	R	R^1	M.p. (°C)	B.p. (°C/mm Hg)	n_D^{25}	Yield (%)	^{1}H Chemical Shift δ in ppm (Multiplicity; *J* in Hz)			
							δ (=CH—)	δ (CH_3)or δ (CH_2R^1)	δ (C_6H_5)	δ (CH_2N)
(2a)	C_6H_5	H	70—71	—	—	25 [a] 81 [b]	6.20 (2; 5.5) 6.80 (2; 5.5)	—	7.41 (1)	—
(2b)	C_6H_5	CH_3	83.5—84.5	—	—	87	6.48 (4; 1.4)	2.14 (2; 1.4)	7.46 (1)	—
(2c)	C_6H_5	n-C_5H_{11}		—	—	69	6.50 (3; 1.3)	2.50 (3; broad)	7.40 (1)	
(2d)	n-C_4H_9	CH_3	—	94 (0.4)	1.5089	26 [c]	6.36 (4; 1.4)	2.13 (2; 1.4)	—	3.65 (3; 6.4)
(2e)	n-C_4H_9	n-C_5H_{11}	—	140 (0.2)	1.5016	27 [c]	6.32 (3; 1.3)	2.47 (3; 6.6)	—	3.64 (3; 6.6)

[a] From *(1)* and acetaldehyde.
[b] From *(1)* and vinyl ethyl ether.
[c] The 3-alkyl substituted derivatives of *(2)* were obtained in a pure state only by vapor phase chromatography (column: 30 % SE 30 on Chromosorb, W 60—80 mesh). Fractional distillation over a spinning band column gave products of only 80—85 % purity.

We have now synthesized compounds *(2)* by the reaction of *N*-alkyl- and *N*-aryl-*S*-chloroisothiocarbamoyl chlorides with primary aliphatic aldehydes as well as with vinyl alkyl ethers; the expected isomeric iminooxathioles *(3)* were not obtained.

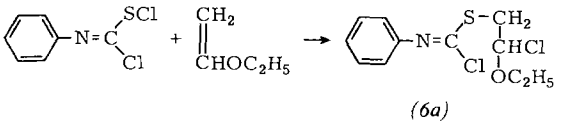
Isothiocyanates, condensation products of the aldehydes, *e.g.* *(4)* from heptaldehyde, and adducts which, upon treatment with water, give 3-imino-1,2,3-dithiazolidin-5-ones *(5)*, are obtained as by-products [3].

Thiazolin-2-ones *(2)*, R^1 = H, carrying no substituents on C-4 and C-5 can be prepared readily and in high yields from *S*-chloroisothiocarbamoyl chlorides and vinyl ethyl ether [4]. This reaction is superior to that of *(1)* with acetaldehyde. For

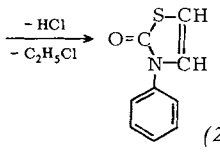


(4) (5)

instance, compound *(1)* and vinyl ethyl ether give at, or below, 0 °C *S*-(2-chloro-2-ethoxyethyl)-*N*-phenylisothiocarbamoyl chloride *(6a)*, which is only stable in the cold or in solution. At room temperature *(6a)* undergoes an exothermic ring closure reaction with elimination of ethyl chloride and hydrogen chloride to form 3-phenyl-1,3-thiazolin-2-one *(2a)* in 81 % yield. The conversion of *(6)* to *(2)* is also effected by treatment with water[5].



(6a)



(2a)

The structure of compounds *(2)* is supported by elemental analysis, by NMR, IR, and (in some cases) mass spectroscopy The fragmentation patterns of *(2a)*, *(2b)*, and *(2c)* upon electron bombardment are very similar, with $(C_6H_5NCH)^+$ at *m/e* 104 being the common principal fragment. Other major fragments observed were $(C_6H_5NCHCHS)^+$ at *m/e* 149 in case of *(2a)*, and $(C_6H_5NCHC(CH_3)S)^+$ at *m/e* 163 for *(2b)*. The proton magnetic resonance spectra of *(2)* are in agreement with the chemical shifts established recently[2] for 4-alkyl- and 4.5-dialkyl-1,3-thiazolin-2-ones.

5-Pentyl-3-phenyl-1,3-thiazolin-2-one

103 g of *N*-phenyl-*S*-chloroisothiocarbamoyl chloride is added dropwise with stirring to 72 g of n-heptaldehyde in 250 ml of dry ether over a period of 2 h at 20–25 °C. When the reaction becomes exothermic, the addition is continued at 0–5 °C. After several hours at 10 °C, the reaction mixture is filtered and low boiling components distilled. The residue is dissolved in 150 ml of cold, dry n-pentane. After storage for several hours at −20 ° to −25 °C, 85 g (69 %) of 3-phenyl-5-pentyl-1,3-thiazolin-2-one was obtained in form of white needles m.p. 40–41 °C (from methanol).

3-Phenyl-1,3-thiazolin-2-one

206 g of *N*-phenyl-*S*-chloroisothiocarbamoyl chloride *(1)* is added slowly to 79 g of vinyl ethyl ether in 150 ml of carbontetrachloride at 0–5 °C. The clear solution is then concentrated *in vacuo*. Upon standing at room temperature, an exothermic evolution of C_2H_5Cl and HCl commences after a short time to yield a solid product which is freed from contaminating oil (porous plate) and recrystallized from heptane. Yield: 143 g of 3-phenyl-1,3-thiazolin-2-one. The latter product is also obtained by adding the original reaction mixture (CCl_4-solution) slowly to water. Vigorous agitation and efficient cooling is essential. Yield: 79 %.

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[*] Dr. G. Ottmann [**], H. Hoberecht, and H. Hooks, jr.
Olin Mathieson Chemical Corporation Research Center
275 Winchester Avenue
New Haven, Connecticut 06504 (U.S.A.)

[**] Present address:
Dr. Kurt Herberts und Co.
Christbusch 25
56 Wuppertal-Barmen (Germany)

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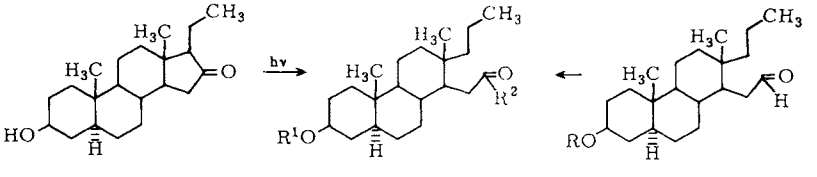
[4] *G. Ottmann* and *H. Hooks, jr.*, Angew. Chem. *78*, 210 (1966); Angew. Chem. internat. Edit. *5*, 250 (1966).

[5] Compounds *(2)*, like 4-alkyl- and 4,5-dialkyl-1,3-thiazolin-2-ones [2], do not form hydrochlorides.

Photolysis of 3β-Hydroxy-5α-pregnan-16-one [1]

By *G. Adam* [*]

In order to clarify the photochemical behavior of 16-oxo steroids a 0.025 M solution of 3β-hydroxy-5α-pregnan-16-one *(1)* [2] in aqueous dioxane was irradiated externally, under argon, by means of a 500 W high-pressure mercury lamp (3 h, 25 °C, quartz apparatus, distance from the flask 6 cm). Separation and purification by way of the well crystalline piperidine salt (m.p. 118 °C) gave a 61 % yield of a steroidal carboxylic acid $C_{21}H_{36}O_3$ [m.p. 178–180 °C, $[\alpha]_D^{20}$ −15.7 ° ($CHCl_3$)], giving IR bands (Nujol) at 1683, 1718, 1743 (acid-carbonyl), and 3460 cm^{-1} (hydroxyl) and, in the electron-addition mass spectrum [3], principal fragments at *m/e* = 355 (M−1) and 317 (M−1−18, removal of water).



(1)

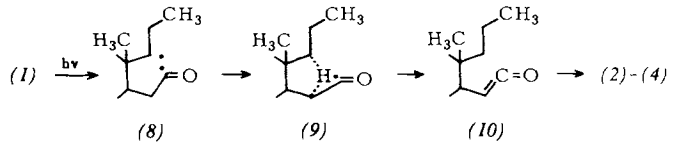
(2), R^1 = H, R^2 = OH
(3), R^1 = H, R^2 = OCH_3
(4), R^1 = H, R^2 = NH-$(CH_2)_3$-CH_3
(5), R^1 = Ac, R^2 = OH

(6), R = H
(7), R = Ac

The 3β-hydroxy-16,17-seco-5α-pregnan-16-oic acid structure *(2)* of the photoproduct was proved by synthesis from 3β-hydroxy-16,17-seco-5α-pregnan-16-al *(6)* [2]: acetylation of *(6)* with acetic anhydride/pyridine (15 h, 20 °C) gave almost quantitatively the amorphous *O*-acetyl derivative *(7)*, $[\alpha]_D^{20}$ = −14.9 °, with IR bands at 1245 and 1748 (*O*-acetyl) as well as 1732 and 2720 cm^{-1} (aldehyde), which was converted in 60 % yield by oxidation with chromic acid in acetone/dilute sulfuric acid to the seco acid *(5)*, m.p. 148–150 °C, $[\alpha]_D^{20}$ = −23.0 °, IR bands at 1245 (*O*-acetyl), 1697, 1718, 1745 (acid- and ester-carbonyl), and 3475 cm^{-1} (acid-OH). Hydrolysis by 2.5 % methanolic potassium hydroxide (1 h, 80 °C) affords the acid *(2)* in 81 % yield [4].

Corresponding carboxylic acid derivatives are formed on UV irradiation of the 16-ketone *(1)* in other protic solvents. For instance, photolysis in anhydrous methanol affords, after chromatography on Al_2O_3, a 52 % yield of the amorphous methyl 3β-hydroxy-16,17-seco-5α-pregnan-16-oate *(3)*, $[\alpha]_D^{18}$ =

$-28.3°$, IR bands (CCl_4) at 1155, 1748 (methyl ester), and 3629 cm^{-1} (hydroxyl), electron-addition mass spectrum m/e = 349 (M−1) and 331 (M−1−18). UV irradiation of *(1)* in n-butylamine gives analogously a 49 % yield of the amide *(4)*, m.p. 218–220 °C, $[\alpha]_D^{20} = -5.0°$, IR bands (Nujol) at 1555, 1660 (sec. amide), and 3315 cm^{-1} (hydroxyl), electron-addition mass spectrum m/e = 390 (M−1).



As proved for other cyclic ketones[5], a homolytic α-fission of the $n \rightarrow \pi^*$ excited 16-ketone to give the alkyl-acyl diradical *(8)* is to be assumed as responsible for the UV-induced formation of the 16,17-seco compounds *(2)–(4)*, the radical disproportionating by intramolecular migration of hydrogen to give *(10)* by way of *(9)*. Addition of nucleophilic solvent molecules affords *(2)–(4)*. Intermediate occurrence of the ketene *(10)* was confirmed by a characteristic IR band at 2108 cm^{-1} on UV irradiation of *(1)* in benzene.

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[*] Dr. G. Adam
Institut für Kulturpflanzenforschung der Deutschen Akademie der Wissenschaften zu Berlin
DDR 4325 Gatersleben, Kreis Aschersleben (Germany)

[1] Part XI of Photochemical Reactions. – Part X: *G. Adam*, Chem. Ber., in press.

[2] *G. Adam* and *K. Schreiber*, Liebigs Ann. Chem., in press.

[3] I thank Dr. *R. Tummler*, Dresden, for measurement of the electron-addition mass spectra.

[4] R_F = 0.44 on Kieselgel G (Merck), eluant $CHCl_3/CH_3OH$ 9:1. Detection by iodine.

[5] Cf. *G. Quinkert*, Angew. Chem. 77, 229 (1965); Angew. Chem. internat. Edit. 4, 211 (1965).

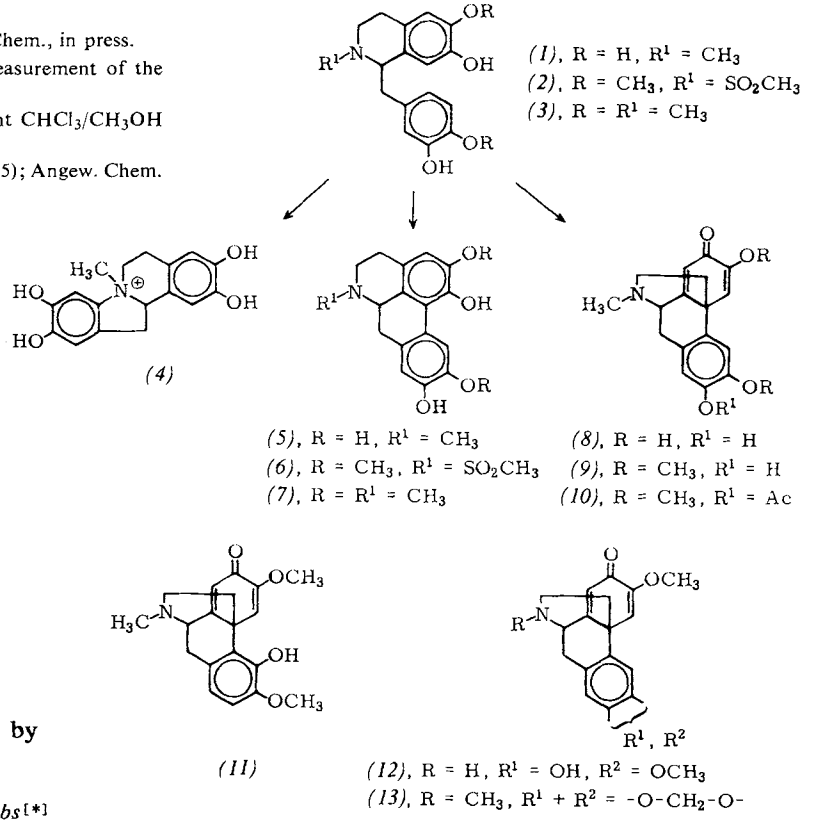
Synthesis of a Morphinan Derivative by Oxidative Ring Closure [1]

By *B. Franck*, *G. Dunkelmann*, and *H. J. Lubs*[*]

Earlier attempts to obtain aporphine *(5)* and morphinan alkaloids *(8)* from laudanosoline by biogenetic-type condensation led to the formation of pyrrocoline *(4)*[2]. Later we showed that aporphines were also formed from laudanosoline, in good yield, if during the oxidation the nitrogen was quaternized[3] or the pyrocatechol groups were protected as complexes[4]. By using isotope dilution analysis *Barton et al.*[5] were able to prove that a morphinan derivative, salutaridine *(11)*, was formed in 0.024 % yield on oxidation of the dimethyllaudanosoline, reticuline *(3)*, by MnO_2.

We now report the preparative synthesis of the morphinan derivative *(9)* by oxidative condensation of reticuline *(3)*. Experience with oxidative condensations of other alkaloid precursors[3] indicates that in order to obtain higher yields it is necessary to prevent oxidative side reactions on the nitrogen, and intramolecular condensation and polymerization. Since oxidation on nitrogen can be prevented by acylation, *N*-mesylnorreticuline *(2)* (m.p. 205 °C) was first prepared and was oxidized with MnO_2 in $CHCl_3$. This led to the formation of crystalline *N*-mesylnorisoboldine *(6)*[6] (yield 40 %, m.p. 238 °C), whose mass spectrum at 70 eV showed fragments at m/e = 391 (M), 311 (M−CH_3SO_2H), and 283 (base peak, M−$CH_2{=}\overset{\oplus}{N}H{-}SO_2CH_3$), and whose UV spectrum in CH_3OH gave λ_{max} (log ε) = 220 (4.57), 282 (4.06), and 305 nm (4.16). Thus condensation of *N*-mesylnorreticuline *(2)* gives the aporphine preferentially. Morphinan derivatives could not be detected in the oxidation mixture by chromatographic investigation.

The tertiary reticuline *(3)* was then oxidized by MnO_2 in $CHCl_3$ using a heterogeneous variant of the Ziegler dilution principle. To keep the concentration of reticuline molecules on the surface of the oxidizing agent low and the distance between them large, an additional active adsorbing surface was provided by mixing the MnO_2 with three times its weight of silica gel (particle size < 0.08 mm, E. Merck). By chromatography of the reaction mixture on silica gel with benzene/methanol (5:1) as eluant a 4 % yield of the morphinan derivative, isosalutaridine *(9)*, was isolated as its crystalline acetate *(10)*: m.p. 203 °C; mass spectrum at 70 eV, m/e = 369 (M) (base peak), 341 (M−CO), 326 (M−$COCH_3$), 298 (326−CO), 284 (326−$CH_2{=}\overset{\oplus}{N}{=}CH_2$); UV spectrum in CH_3OH, λ_{max} (log ε) 204 (4.51), 232 (4.15), 283 nm (3.81); IR spectrum in KBr, 1760 (ester), 1666, 1641, 1620 cm^{-1} (dienone); NMR spectrum in $CDCl_3$, δ = 6.33 (H on C-8), 6.36 (H on C-1), 6.92 and 6.83 (H on C-5 and C-4), 2.30 ($COCH_3$), 2.47 (NCH_3), 3.81 (OCH_3). The structure of the isosalutaridine is derived unambiguosuly from these data, and it is confirmed by proton-catalysed rearrangement by acetic anhydride/conc. H_2SO_4, which, as with morphine, leads to a crystalline aposphine.



The oxidation utilizing the heterogeneous dilution principle, which led to the first isolation of a morphinan derivative after oxidation of the reticuline, probably comes particularly close to conditions in the cell. Crystalline isoboldine *(7)* (m.p. 124 °C)[7] (6 % yield) (but no salutaridine *(11)*) was isolated from the oxidation mixture alongside isosalutaridine *(9)*. Since isosalutaridine *(9)* differs only slightly from the two alkaloids, flavinine *(12)*[8] and amurine *(13)*[9], isolated from *Croton* and *Papaver* species, preparation of *(9)* can be regarded as the first, almost complete, total synthesis of these two new alkaloids *(12)* and *(13)*.

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[*] Prof. Dr. B. Franck, Dipl.-Chem. G. Dunkelmann, and Dipl.-Chem. H. J. Lubs
Institut für Organische Chemie der Universität
Neue Universität
23 Kiel (Germany)

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Effect of Pressure on the Equilibrium between Hydrogen and Solvated Electrons in Potassium Amide-Ammonia Solutions. The "Volume" of Solvated Electrons.

By *U. Schindewolf*, *R. Vogelsgesang*, and *K. W. Böddeker*[*]

Solvated electrons are formed by the reversible reaction of alkali amides with hydrogen in liquid ammonia[1]; they are detected by their strong absorption in the near infrared and by electron spin resonance (ESR).

$$^1/_2\,H_2 + KNH_2 \rightleftharpoons e^-_{sol} + NH_3 + K^+ \qquad (1)$$

The equilibrium constant $K = 2\times10^{-5}$ (25 °C) and the enthalpy $\Delta H = 16$ kcal/mole of the reaction, derived from the temperature dependence of K, agree reasonably well with the values calculated from thermodynamic data.

If the pressure dependence of the equilibrium constant is known, the change of volume, ΔV, associated with the reaction can be calculated according to

$$d \ln K/dp = -\Delta V/RT \qquad (2)$$

From this, in conjunction with the molar volumina of all other reacting species, the "volume" of the solvated electrons in ammonia can be estimated. This quantity is of significance to the theory of the solvated electron[2] and has not hitherto been determined experimentally. The published density measurements of alkali metal-ammonia solutions afford information only as to the volume of the spin-compensated electron pairs, e_2^-, predominating in solutions of medium concentration which still permit a meaningful evaluation of density measurements ($V_{e_2^-} = 65$ to 93 ml/mole at −33 °C[2,3]).

For the determination of the pressure dependence of the reaction, a 0.23 M solution of potassium amide in liquid ammonia was saturated, at room temperature, with hydrogen (100 atm) in an autoclave. The solution was transferred *via* a high pressure capillary into a high pressure optical cell fitted with sapphire windows (distance between windows 0.4 ± 0.01 cm), in which the pressure could be raised to 2000 atm and the temperature to 150 °C. The cell was located in the light path of a spectrophotometer with which the absorption spectrum of the solution in the pertinent interval of 1.0 to 2.3 μ was recorded. For comparison, the same solution after the hydrogen had been pumped off was measured under otherwise identical conditions. Concurrently, the spin concentration of the solutions was followed ESR-spectrometrically up to 500 atm and 50 °C. The solutions were contained in a heavy walled quartz capillary fitted into the resonator cavity of the spectrometer; connection to a pressure generator was made by means of the pressure coupling described by *Eucken* and *Suhrmann*[4].

The difference in optical density between the hydrogen-saturated and the hydrogen-free solutions yields the broad absorption spectrum of the solvated electrons[5], the intensity of which, as shown in Fig. 1, decreases with increasing pressure and increases with increasing temperature. The intensity of the ESR signal of the hydrogen-saturated solution shows the same pressure- and temperature dependence. No ESR signal is observed with the hydrogen-free solution.

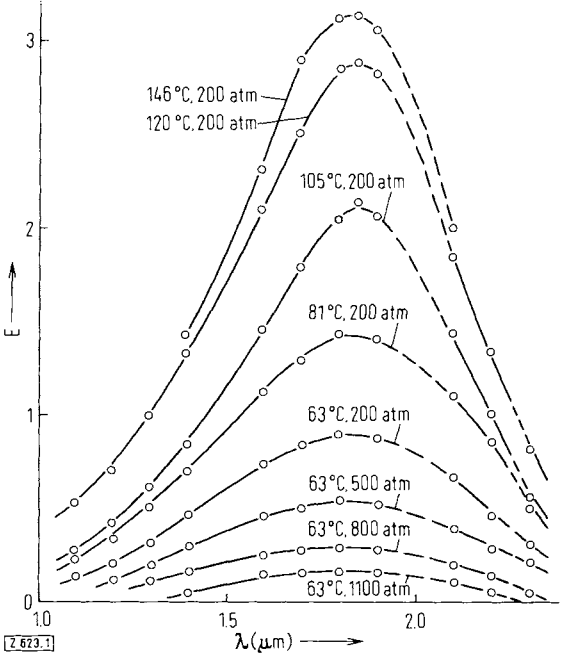


Fig. 1. Absorption spectrum of the solvated electrons as function of pressure at 63 °C and of temperature at 200 atm (0.23 M KNH_2–NH_3 solution saturated with 100 atm of H_2 at 23 °C).

The equilibrium concentration of solvated electrons of the hydrogen-saturated solution, calculated from the intensity of the absorption maximum (molar extinction coefficient 4.8×10^4 l mol^{-1} cm^{-1}[6]) between 200 and 1100 atm, and between 23 and 146 °C lies between 5×10^{-7} and 2×10^{-4} mole/l[7]; it is thus small enough to exclude the presence of spin-compensated electron pairs.

The temperature dependence of the electron concentration in the range of 23 to 63 °C at 200 atm results in an enthalpy,

ΔH, of 12 ± 1 kcal mole^{-1} for reaction (1); this value is somewhat smaller than that reported[1], without error limits, for 100 atm. From the pressure dependence at 23 °C, in conjunction with Eq. (2), a volume change, ΔV, associated with the reaction of 64 ± 3 ml/mole is obtained. Both ΔH and ΔV decrease with increasing temperature.

The apparent molar volume of KNH_2 and H_2 in ammonia are 10 ± 2 and 110 ± 20 ml/mole, respectively, as determined by density measurements at 23 °C and 100 atm. The molar volume of ammonia under these conditions is 27.8 ml. The apparent molar volume of the K^+ ions is reported as 3 ml/mole[3b]. With these values and

$$V_{e^-} = \Delta V - V_{NH_3} - V_{K^+} + V_{KNH_2} + {}^1/_2 V_{H_2} \qquad (3)$$

an apparent "volume" of the solvated electrons of 98 ± 15 ml/mole at 23 °C and 100 atm is obtained. By taking into consideration the temperature dependence of the volume of the solvated electrons, estimated from the variation of absorption frequency with temperature[8], a value of 84 ml/mole at −33 °C results; within the limits of error, this value is the same as that for the spin-compensated electron pairs.

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[*] Doz. Dr. U. Schindewolf, Dipl.-Phys. R. Vogelsgesang and, Dr. K.W. Böddeker
Institut für Kernverfahrenstechnik
der Technischen Hochschule
Postfach 947
75 Karlsruhe (Germany)

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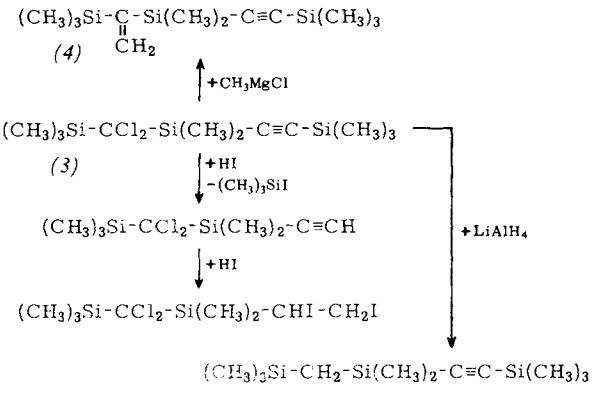
Reaction of Perchloro-1,3,5-trisilacyclohexane with Methylmagnesium Chloride

By *G. Fritz* and *N. Szczepanski*[*]

1,1,3,3,5,5-Hexachloro-1,3,5-trisilacyclohexane $(SiCl_2{-}CH_2)_3$ *(1)* reacts at the $SiCl_2$ group[1] without change in the ring skeleton. Reactions at the skeletal C atom require substitution at the CH_2 group, *e.g.* by photochlorination to give $(SiCl_2{-}CCl_2)_3$ *(2)*[2]. Chlorine on the bridging C atom of carbosilanes is extremely reactive, and this can be recognized also with $(SiH_2{-}CCl_2)_3$[3]. Reactions of $(Cl_3Si)_2CCl_2$ with CH_3MgCl lead to $[(CH_3)_3Si]_2C{=}CH_2$, $[(CH_3)_3Si]_2CH_2$, and $[(CH_3)_3Si]_2CH(CH_3)$[4].

With an excess of CH_3MgCl, perchloro-1,3,5-trisilacyclohexane *(2)* gives a mixture of several compounds[5], the three major components of which, having formulae $Si_3C_{11}H_{24}Cl_2$ *(3)*, $Si_3C_{12}H_{26}$ *(4)*, and $Si_3C_{12}H_{26}$ *(5)* (verified by mass spectrometry) were isolated by gas chromatography.

Compound *(3)* forms white crystals, m.p. 35 °C. The structure illustrated follows from the NMR spectrum and reactions with HI, $LiAlH_4$, and CH_3MgCl. The C≡C group was recognized by the Raman line at 2105 cm^{-1}[6], and excludes cyclic structural formulae.



The structure illustrated for compound *(4)* follows from the fission reaction with HBr, as well as from the NMR and Raman spectra; and was confirmed by synthesis. The course of the fission of *(4)* by HBr depends on the reaction conditions: in CCl_4 the first product is

$$(CH_3)_3Si{-}CH(CH_2Br){-}Si(CH_3)_2{-}C{\equiv}C{-}Si(CH_3)_3;$$

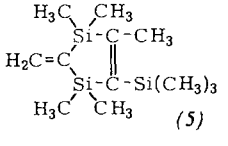
on passage of HBr into the solvent-free substance one obtains

$$H_2C{=}CH{-}Si(CH_3)_2{-}C{\equiv}C{-}Si(CH_3)_3$$

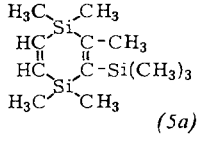
and

$$BrH_2C{-}CH_2{-}Si(CH_3)_2{-}C{\equiv}C{-}Si(CH_3)_3.$$

According to its Raman spectrum, compound *(5)*, which is isomeric with *(4)*, does not contain an acetylene group. All our observations indicate a cyclic structure, for which all except *(5)* and *(5a)* can be excluded. Structure *(5)* is considered the more probable.



(5)



(5a)

All the other compounds obtained from *(2)* are linear and contain three Si atoms. In none of the products from *(2)* is the ring skeleton intact.

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[*] Prof. Dr. G. Fritz and Dr. N. Szczepanski
Institut für Anorganische Chemie der
Technischen Hochschule
Englerstr. 11
75 Karlsruhe (Germany)

[1] *G. Fritz, H. J. Buhl*, and *D. Kummer*, Z. anorg. allg. Chem. *327*, 165 (1964).

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Reactions of Silylphosphines. — Formation of Lithium Tris(diethylphosphinyl)silicide

By *G. Fritz* and *G. Becker* [*]

Chlorosilanes such as $HSiCl_3$ which contain SiH groups react with $LiP(C_2H_5)_2$ to give large amounts of $(C_2H_5)_2PH$ together with silylphosphines. $(C_2H_5)_2P{-}P(C_2H_5)_2$ is formed from chlorosilanes such as $SiCl_4$ which do not contain SiH groups, provided that an excess of $LiP(C_2H_5)_2$ is present [1]. In addition, red polymers containing Si–Si groups are formed. These side reactions are almost completely suppressed if an excess of the chlorosilane is maintained during the whole reaction, as can be done by adding dropwise an ethereal solution of the phosphide to the chlorosilane [2]. Thence it can be assumed that a silylphosphine formed as intermediate is reactive towards the strongly nucleophilic phosphide. We have therefore prepared silyl- and methylsilyl-phosphine and have studied their behavior towards $LiP(C_2H_5)_2$ in diethyl ether. The course of the reaction was followed by measurement of the NMR spectrum.

We found that $(CH_3)_3Si{-}P(C_2H_5)_2$ and $LiP(C_2H_5)_2$ do not react with each other, even during a long period. However, SiH-containing silylphosphines do react, giving phosphorylated products:

$$H_3SiP(C_2H_5)_2 + LiP(C_2H_5)_2 \rightarrow H_2Si[P(C_2H_5)_2]_2 + LiH \quad (a)$$

$$H_3Si{-}P(C_2H_5)_2 + 2\,LiP(C_2H_5)_2 \rightarrow HSi[P(C_2H_5)_2]_3 + 2\,LiH \quad (b)$$

$$(CH_3)_2HSi{-}P(C_2H_5)_2 + Li(P(C_2H_5)_2 \rightarrow (CH_3)_2SiP[(C_2H_5)_2]_2 + LiH \quad (c)$$

$$(CH_3)HSi[P(C_2H_5)_2]_2 + LiP(C_2H_5)_2 \rightarrow CH_3Si[P(C_2H_5)_2]_3 + LiH \quad (d)$$

Since reaction (a) is the fastest, it is understandable why the compounds $H_2Si[P(C_2H_5)_2]_2$ and $HSi[P(C_2H_5)_2]_3$ always occur as by-products in the preparation of $H_3Si{-}P(C_2H_5)_2$ from H_3SiBr and $LiP(C_2H_5)_2$. Reaction of LiH with H_3SiBr gives SiH_4.

Reactions (c) and (d) are appreciably slower. Reaction (d), the slowest, requires several days for completion.

$HSi[P(C_2H_5)_2]_3$ and $LiP(C_2H_5)_2$ react quite differently. If the two compounds are mixed in ether in an NMR tube and the NMR spectrum is measured immediately, the following observations can be made: The quartet of the SiH resonance, which arises by spin-spin coupling with the three phosphorus atoms, has almost disappeared and simultaneously the multiplet of the phosphorus-hydrogen resonance of diethylphosphine appears. After about 2 hours the Si–H resonance can hardly be seen at all in the spectrum. The color of the ethereal solution has changed from pale yellow to bright red. The reaction occurs in accordance with

$$HSi[P(C_2H_5)_2]_3 + LiP(C_2H_5)_2 \rightarrow LiSi[P(C_2H_5)_2]_3 + HP(C_2H_5)_2 \quad (e)$$

The diethylphosphine formed can be distilled off with the solvent in a vacuum and oxidized by iodine solution to diethylphosphinous acid. This analysis shows 80% of the $HP(C_2H_5)_2$ expected for the complete reaction.

$$LiSi[P(C_2H_5)_2]_3 + CH_3Cl \rightarrow CH_3{-}Si[P(C_2H_5)_2]_3 + LiCl \quad (f)$$

$$LiSi[P(C_2H_5)_2]_3 + (CH_3)_3SiCl \rightarrow (CH_3)_3Si{-}Si[P(C_2H_5)_2]_3 + LiCl \quad (g)$$

$$LiSi[P(C_2H_5)_2]_3 + (CH_3)_2SiHCl \rightarrow (CH_3)_2HSi{-}Si[P(C_2H_5)_2]_3 + LiCl \quad (h)$$

$$LiSi[P(C_2H_5)_2]_3 + H_3SiBr \rightarrow H_3Si{-}Si[P(C_2H_5)_2]_3 + LiBr \quad (i)$$

Lithium tris(diethylphosphinyl)silicide, $LiSi[P(C_2H_5)_2]_3$, cannot be isolated in crystalline form. It is obtained as a red resinous substance which redissolves completely in ether. It reacts with CH_3Cl, $(CH_3)_3SiCl$, $(CH_3)_2SiHCl$, and H_3SiBr according to equations (f)–(i). In reaction (f) a Si–C bond is formed, but in (g)–(i) phosphinyl derivatives of disilane are obtained.

Experimental: $HSi[P(C_2H_5)_2]_3$ was mixed with the stoichiometric amount of $LiP(C_2H_5)_2$ in ether, then kept at 20 °C for about 5 h, after which the diethylphosphine was pumped off with the solvent. There remained the red resinous $LiSi[P(C_2H_5)_2]_3$, which dissolved without residue on renewed addition of ether. The halogen compound was condensed on to the frozen solution, in which it dissolved at about −90 °C. Reaction occurs only between −50 ° and −60 °C, the solution being decolorized and the appropriate amount of lithium halide precipitated. The products were isolated by distillation. Yields are 30–40%.

The products indicated in equations (f)–(i) are accompanied by less volatile products containing Si–Si bonds and by simple silylphosphines such as diethyl(trimethylsilyl)phosphine, which is formed by reaction of $LiSi[P(C_2H_5)_2]_3$ with $(CH_3)_3SiCl$. Thus substitution of the lithium [eq. (g)] is accompanied by fission of the Si–P bond by the halogen compound [eq. (k)].

$$[(C_2H_5)_2P]_3SiLi + ClSi(CH_3)_3 \rightarrow (C_2H_5)_2P{-}Si(CH_3)_3 + [(C_2H_5)_2P]_2ClSiLi \quad (k)$$

This product, which contains lithium and halogen on the same Si atom, gives substances of high molecular weight with loss of LiCl.

In contrast to reaction (e), $HSi[P(C_2H_5)_2]_3$ and butyllithium in pentane do not react with metalation of the Si atom:

$$HSi[P(C_2H_5)_2]_3 + 3\,LiC_4H_9 \rightarrow HSi(C_4H_9)_3 + 3\,LiP(C_2H_5)_2$$

Metalation in accord with equation (e) occurs only with $HSi[P(C_2H_5)_2]_3$. If either one or two $(C_2H_5)_2P$ groups are attached to the Si atom, then reaction occurs with formation of LiH [eq. (a)–(d)]. Apparently the Si–H hydrogen loses its hydride character as the number of $(C_2H_5)_2P$ on the Si atom increases, so that the exchange for lithium becomes understandable in the case of $HSi[(C_2H_5)_2]_3$. Similar conclusions can be drawn from the NMR spectra of the SiH-containing compounds of this series.

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[*] Prof. Dr. G. Fritz and Dipl.-Chem. G. Becker
Institut für Anorganische Chemie
der Technischen Hochschule
Englerstr. 11
75 Karlsruhe (Germany)

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Resolution of Racemates of Asymmetric Phosphinylacetic Acids, Model Compounds for Reactions of Phosphinate Carbanions

By *J. Michalski* and *St. Musierowicz* [*]

Dedicated to Professor G. Wittig on his 70th Birthday

In connection with our work on the stereochemistry of reactions of the carbanions formed from phosphonates [1] and thiophosphonates [2], we have synthesized phosphinylacetic

acids $R(R_1O)P(O)CH_2COOH$ in which the phosphorus atom is an asymmetric center, and we have resolved them into optical antipodes.

Starting materials were t-butyl phosphinylacetates $R(R_1O)P(O)CH_2COOC_4H_9$-t, which we prepared by the Arbusov reaction from equimolar amounts of t-butyl chloroacetate and dialkyl phosphinites $RP(OR_1)_2$ at 140 °C and isolated by distillation.

R	R_1	B.p. (°C/mm)	n_D^{20}	Yield (%)
C_6H_5	C_2H_5	92/0.01	1.5008	70
C_6H_5	CH_3	108/0.1	1.5050	76
C_2H_5	C_2H_5	80/0.03	1.4430	66

Selective removal of the t-butyl group by 5% hydrochloric acid at 100 °C gives the free phosphinylacetic acids, which were obtained pure by extraction with benzene, evaporation of the solvent, and crystallization.

R	R_1	M.p. (°C)	Yield (%)	Solvent
C_6H_5	C_2H_5	88–91 [3]	80	Acetone
C_6H_5	CH_3	83–85 [3]	70	Acetone/ether
C_2H_5	C_2H_5	48–52	73.5	Ether

The racemic phosphinylacetic acids were separated into their antipodes by fractional crystallization of the quinine and cinchonidine salts from acetone or acetone/ether. The optically active acids, which were liberated from the alkaloid salts on an ion-exchange column (Amberlite IR 120), are yellow viscous oils. Their reaction with diazomethane led to the optically active methyl esters. Esters with rotations of $[\alpha]_{589}^{25} = -10.1°$ (acetone, $c = 5.064$), and $[\alpha]_{589}^{25} = +10.4°$ (acetone, $c = 5.537$) were obtained from the (−)- and (+)-acids with $R = C_6H_5$ and $R' = CH_3$ respectively.

(1)		Salt			Acid
		M.p. (°C)	Solvent	$[\alpha]_{589}^{25}$ (in ethanol); c	$[\alpha]_{589}^{25}$; c
$R = C_6H_5$	Cinchonidine	149–150	Acetone	− 81.5°; 3.777	− 8.8°; 5.42 (benzene)
$R_1 = C_2H_5$		154–155	Acetone	− 59.2; 2.5124	+ 9.1; 3.0 (benzene)
$R = C_6H_5$	Quinine	124–125	Acetone	−126.6; 4.578	−25.9°; 3.265 (water)
$R_1 = CH_3$		93–95	Acetone/ether	− 87.4°; 4.827	+26.6; 2.081 (water)
$R = C_2H_5$	Quinine	134–135	Acetone	−136.3°; 4.724	+24.1°; 5.142 (benzene)
$R_1 = C_2H_5$		86–88	Acetone/ether	−124.0°; 4.885	−24.5°; 6.088 (benzene)

All the products gave correct elemental analyses.

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[*] Prof. J. Michalski and Dr. St. Musierowicz
Institute for Organic Synthesis,
The Technical University (Politechnika)
Żwirki 36
Łódź 40 (Poland)

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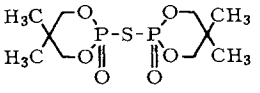
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[3] *Kabatschnik et al.* [Ž. obš. Chim. *37*, 695 (1967)] recently reported another method for the preparation of these racemic acids.

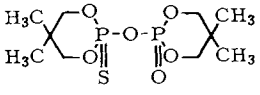
Synthesis of Bis(5,5-dimethyl-2-oxo-1,3,2-P^V-dioxaphosphorinanyl) Sulfide

By *J. Michalski, M. Mikołajczyk, B. Młotkowska*, and *A. Zwierzak* [*]

In 1963, *Edmundson* [1] reported the synthesis of the isomeric thiopyrophosphates *(1)* and *(2)* containing cyclic groups which stabilized the rather unstable thiol form *(1)*.



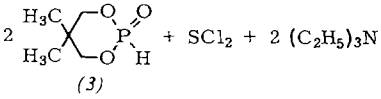
(1)



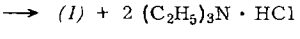
(2)

Our attempts to synthesize the isomer *(1)* in the pure state by *Edmundson*'s method always led to a difficulty separable mixture of comparable amounts of *(1)* and *(2)* [**].

In the treatment of 5,5-dimethyl-2-oxo-1,3,2-P^V-dioxaphosphorinane *(3)* with sulfur dichloride in the presence of triethylamine we have found a new procedure for the synthesis of *(1)*.

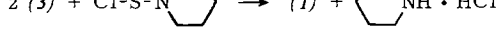


(3)



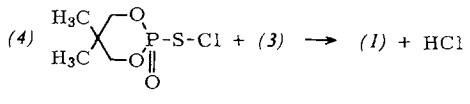
Treating *(3)* with piperidinesulphenyl chloride also leads to *(1)*.

In both cases the desired thiopyrophosphate *(1)* is obtained chemically pure in good yield. The purity of *(1)* was determined chromatographically [silica gel G (E. Merck); benzene/acetone/chloroform (3:2:1); R_F values, 0.64 for *(1)* and 0.88 for *(2)*].



Compound *(1)* is completely stable at room temperature and is unchanged in boiling benzene; however, it rearranges to *(2)* when boiled for *ca.* 10 hours in xylene.

It is remarkable that *(1)* is also formed by the action of *(3)* on 2-(chlorothio)-5,5-dimethyl-2-oxo-1,3,2-P^V-dioxaphosphorinane *(4)*, which is assumed to be an intermediate in the above-mentioned reactions [2].



It is thus proved that oxophosphoranesulfenyl chlorides >P(O)SCl and esters of tervalent phosphorus acids <P–O–R(H) give first the thiol form *(3)* of the monothiopyrophosphate system [3].

Synthesis of bis(5,5-dimethyl-2-oxo-1,3,2-P^V-dioxaphosphorinanyl)sulfide (1):

A solution of sulfur dichloride (2.06 g, 0.02 mole) in benzene (20 ml) was added dropwise to a solution of 5,5-dimethyl-2-oxo-1,3,2-dioxaphosphorinane *(3)* (6.0 g, 0.04 mole) and triethylamine (4.04 g, 0.04 mole) in benzene (50 ml) at 20 to 30 °C (ice cooling). The whole was stirred at room temperature for 1 h and the crystal mass was filtered off with suction, washed with benzene (2 × 50 ml) and water (2 × 50 ml), and dried. Yield, 4,0 g; m.p. 162–167 °C; m.p. 185–188 °C after recrystallization from benzene/chloroform.

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[*] Prof. J. Michalski, Dr. M. Mikołajczyk, B. Młotkowska, and Dr. A. Zwierzak
Institute of Organic Synthesis,
The Technical University (Politechnika),
and the Institute of Organic Chemistry of the Polish Academy of Sciences
Łódź 40 (Poland)

[1] *R. S. Edmundson*, Chem. and Ind. *1963*, 784.

[**] Note: The compound *(1)* is not produced in the reaction of bis(5,5-dimethyl-2-oxo-1,3,2-P^V-dioxaphosphorinanyl) disulfide with triphenylphosphine [*R. S. Edmundson*, J. chem. Soc. (London) *B 1967*, 1635].

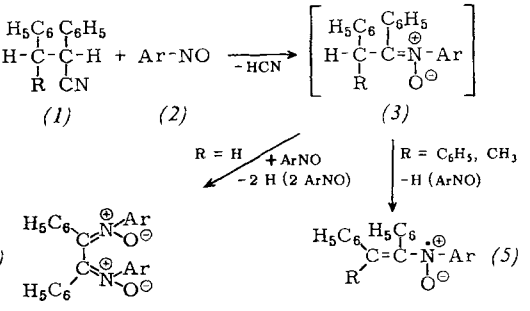
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Detection of Aryl(vinyl)nitroxides by ESR Spectroscopy

By *H. G. Aurich* and *F. Baer* [*]

If 2,3-diphenylpropionitrile *(1)*, R = H, is treated with an aromatic nitroso compound *(2)* in methanol containing sodium methoxide, the expected nitrone *(3)*, R = H, is not obtained because it reacts at once with further nitroso compound, giving the α,α',*N*,*N*'-tetraphenyldinitrone [benzoin bis(phenylimide *N*-oxide)] *(4)* by dehydrogenation [1].



The second step in the reaction is blocked if the starting material is a nitrile with a secondary β-carbon atom, as *(1)*, R = C_6H_5 or CH_3; but even then the reaction proceeds beyond the nitrone stage *(3)*, giving the aryl(vinyl)nitroxides *(5)*, which can be detected by their ESR spectra.

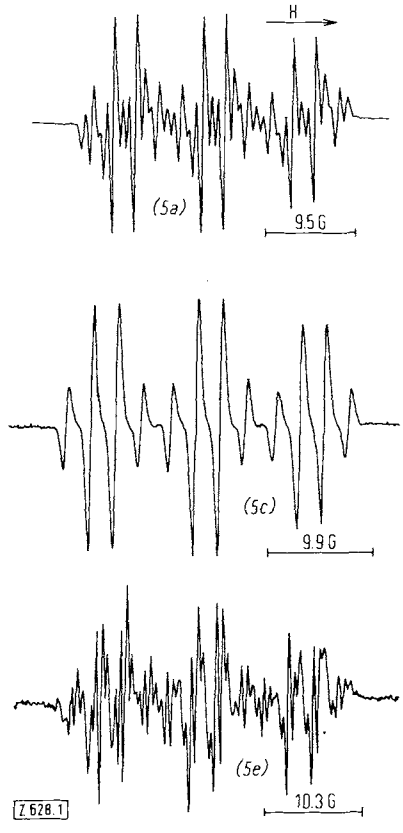


Fig. 1. ESR spectra of the aryl(vinyl)nitroxides *(5a)*, *(5c)*, and *(5e)*.

A solution of a nitrile *(1)* (1 mmole) and a nitroso compound *(2)* (1 to 2 mmoles) in t-butyl alcohol (20 ml) is added to a solution of potassium t-butoxide (5 mmoles) in t-butyl alcohol (20 ml) under nitrogen. The dark red mixture is stirred for 45 min at room temperature. Glacial acetic acid is added to give a weakly acid reaction, the solvent is distilled off in a rotary evaporator, and the solid residue is taken up in benzene (50 ml) and water (50 ml). The benzene phase is separated, washed several times with water, and dried. For determination of the ESR spectra samples of the benzene solutions were further diluted.

In accord with the coupling of the unpaired electron with the nitrogen atom, the ESR spectra of these nitroxides consist of three line groups of about the same intensity [2]. Quadruplet splitting of the individual line groups (approximate intensity ratio 1:3:3:1) in the spectrum of *(5c)* is caused by the three equivalent *o*- and *p*-protons of the phenyl nucleus on the nitroxide group. In the spectrum of *(5a)* each of these lines is additionally split three-fold by the *m*-protons of this phenyl nucleus.

The density of the unpaired electron in the vinyl group and the three neighboring phenyl nuclei is apparently too small for visible splitting by these phenyl protons to arise. On the

	R	Ar	Coupling constants (gauss)			
			a_N	a_H (*o*,*p*-Ar)	a_H (*m*-Ar)	a_H (CH_3)
(5a)	C_6H_5	C_6H_5	9.5	2.37	0.82	–
(5b)	C_6H_5	4-$(CH_3)_3C$–C_6H_4	9.8	2.37	0.82	–
(5c)	C_6H_5	3,5-[$(CH_3)_3C$]$_2$–C_6H_3	9.9	2.33	–	–
(5d)	CH_3	C_6H_5	10.0	2.62	0.95	0.6
(5e)	CH_3	3,5-[$(CH_3)_3C$]$_2$–C_6H_3	10.3	2.64	–	0.62

other hand, coupling with the protons of the methyl group in *(5d)* and *(5e)* increases the number of lines. Although the spectrum of *(5d)* is thus rendered very complex, the quadruplet splitting by the methyl protons can be readily recognized on comparison of the spectra of *(5e)* and *(5c)*.

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[*] Doz. Dr. H. G. Aurich and Dr. F. Baer
Institut für Organische Chemie der Universität
Bahnhofstr. 7
355 Marburg (Germany)

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μ-Cyanogenbis(pentacarbonylmetal) Complexes

By *J. F. Guttenberger* [*]

Cyanogen reacts photochemically with hexacarbonylmetals with formation of intensely colored compounds of composition $[(OC)_5MNC]$ *(1)*, that are not attacked by oxygen.

Determination of the molecular weights of these products gives values that correspond to twice the molecular weights of *(1)*. It is therefore assumed that the C–C bond in $(CN)_2$ remains intact and that this substance links two pentacarbonylmetal fragments as a bifunctional donor, so that μ-cyanogenbis(pentacarbonylmetal) complexes

$$(OC)_5MNC{-}CNM(CO)_5 \qquad (2)$$

are formed. This behavior is in agreement with the high dissociation energy (145 kcal/mole[1]) of the C–C bond in cyanogen and is supported by calculations of electron density distribution[2] according to which the external bonds in $(CN)_2$ are barely changed by conjugation. Further, the spectroscopic data given in the Table accord with structure *(2)*.

Preparation of the Complexes:

An apparatus described by *Strohmeier*[3] was used for irradiation of the substances. Cyanogen was prepared and purified as described in[4]. It was carried into the irradiation cuvette in a slow N_2 stream that passed through the $(CN)_2$ production apparatus and the cuvette during the irradiation.

1. μ-Cyanogenbis(pentacarbonylchromium): 2 mmoles (440 mg) of $Cr(CO)_6$ in 25 ml of tetrahydrofuran was irradiated for 2 h under a stream of N_2 and $(CN)_2$. Then the solvent was removed in a rotary evaporator at 40 °C/40 mm, and the residue was dried in a vacuum at 40 °C/10^{-2} mm. The compound was freed from decomposition products by dissolution in benzene, filtration, and removal of the solvent. After renewed drying in a vacuum 139 mg [32% calc. on $Cr(CO)_6$] of the reddish-violet complex was isolated.

2. μ-Cyanogenbis(pentacarbonylmolybdenum): Preparation as for 1, but benzene was used as solvent for the irradiation. Yield: 115 mg (22%).

3. μ-Cyanogenbis(pentacarbonyltungsten): Preparation as for 1. Yield: 252 mg (36%).

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[*] Dr. J. F. Guttenberger
Institut für Physikalische Chemie der Universität
Marcusstr. 9/11
87 Würzburg (Germany)

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Preparation and Properties of Diammonium Dioxodiselenomolybdate(VI)

By *A. Müller, B. Krebs*, and *E. Diemann* [*]

If hydrogen selenide is led into a saturated solution of molybdenum trioxide in 25% aqueous ammonia until a deep red color appears, and the solution is then saturated with oxygen-free carbon dioxide with strong cooling (ice-salt mixture), olive-green crystals of the compound $(NH_4)_2MoO_2Se_2$ *(1)* separate after a short time. The $MoO_2Se_2^{2-}$ ion has not been previously observed either in solution or in the crystalline state. Substance *(1)* was identified by elemental analysis and by its IR and UV spectra.

Compound *(1)* dissolves in water with an intense orange-red color and is almost insoluble in ether or alcohol. Like the corresponding tetraseleno salt it is extraordinarily sensitive to oxygen, and all operations with it must therefore be carried out in a closed system with an atmosphere of a protecting gas.

The IR spectrum of the solid between 4000 and 250 cm^{-1} shows the internal vibrations of the NH_4^+ ion at *ca.* 3200 cm^{-1} [$\nu_3(F_2)$] and 1395 cm^{-1} [$\nu_4(F_2)$]. The absorption frequencies of the dioxodiselenomolybdate(VI) ion can be assigned approximately on the basis of point group C_{2v}: 830 cm^{-1}: $\nu_s(MoO) \wedge \nu_1(A_1)$; 790 cm^{-1}: $\nu_{as}(MoO) \triangleq \nu_6(B_1)$; also 362, 344, and 285 cm^{-1}: $\nu_s(MoSe) \wedge \nu_2(A_1)$, $\nu_{as}(MoSe) \wedge \nu_8(B_2)$, and $\delta(MoO_2)\ \nu_3(A_1)$. $\wedge$ The assignment $\nu_s(MoO) > \nu_{as}(MoO)$ can be regarded as certain since the bands of higher vibration in the IR spectrum occur with lower intensity and since only this assignment leads to a reasonable value for the length-length interaction force constant. Not much can be said about the series $\nu_2(A_1)$, $\nu_3(A_1)$, and $\nu_8(B_2)$; exact assignment is not possible without a knowledge of the Raman spectrum.

$(OC)_5MNC{-}CNM(CO)_5$

	M = Cr	M = Mo	M = W
IR [a] ν_{CN}(cm^{-1})	2263 vw, 2118 vw	2267 vw	2267 vw, 2107 vw
ν_{CO}(cm^{-1})	2067 w, 2038 m, 1980 s, 1959 m	2075 w, 2043 m, 1985 s, 1960 m	2069 w, 2027 m, 1975 s, 1955 m
Mol. wt. [b]	425 (436)	*ca.* 600 (524)	*ca.* 900 (700)
Color	Reddish-violet	Dark brown	Violet
Stability	The benzene solutions are stable in air for a few hours, the solid substance for several days.		
Solubility	The compounds are insoluble in water, difficulty soluble in CH_3OH, slightly soluble in aliphatic hydrocarbons, and moderately soluble in benzene and acetone.		
M.p.	The complex compounds do not melt.		

[a] In CCl_4; accuracy ±3 cm^{-1}; vw = very weak; w = weak; m = medium; s = strong.

[b] Osmometric in benzene. The low solubility of the molybdenum and tungsten compounds prevented accurate measurement. The theoretical values are given in parantheses.

On the basis of our previous studies [1], bands at *ca.* 300 cm^{-1} are characteristic of transition metal-selenium bonds with π-bond contributions.

The Table lists the absorption maxima in the UV spectrum of an aqueous solution of the $MoO_2Se_2^{2-}$ ion. As expected, the maxima are shifted to longer wavelengths in comparison with those of $MoO_2S_2^{2-}$ and $WO_2Se_2^{2-}$. It seems remarkable that $MoO_2Se_2^{2-}$ has the same color as MoS_4^{2-}, and correspondingly that $WO_2Se_2^{2-}$ has the same color as WS_4^{2-} (cf. the longest-wavelength bands). It is difficult to assign all the bands found for $MoO_2Se_2^{2-}$. Probably, however, the band at 455 nm corresponds to a transition $3b_2 \rightarrow 5a_1$, *i.e.* to an electron transition that represents a charge transfer Se→Mo (cf. [2]).

	Band 1 nm	Band 2 nm	Band 3 nm	Band 4 nm	Ref.
$MoO_2Se_2^{2-}$	455	352	313	245	
$MoO_2S_2^{2-}$	394	319	288	219	[2]
$WO_2Se_2^{2-}$	370	293	264		[3]
$WO_2S_2^{2-}$	327	273	244		[2]
MoS_4^{2-}	463	316	241		[4]
WS_4^{2-}	391	276	222		[4]

The MoO stretching force constant can be estimated from equations given by us [5]:

$f_{MoO} = 5.3$ mdyn/Å ($f_{MoO/MoO} = 0.5$).

As expected, it is somewhat smaller than the values for MoO_4^{2-} [5] and $MoO_2S_2^{2-}$ [5].

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[*] Dr. A. Müller, Dr. B. Krebs, and E. Diemann
Anorganisch-Chemisches Institut der Universität
Hospitalstr. 8–9
34 Göttingen (Germany)

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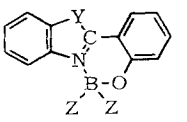
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Boron Chelate Compounds in the 2-(*o*-Hydroxyphenyl)benzazole Series

By *F. Umland* and *E. Hohaus* [*]

We have synthesized fused six-membered heterocycles of type *(1)* containing O–B–N groups where Y = S, O, NH, or CH_2 and Z = C_6H_5, F, or Cl.



(1)

The compounds behave as metal chelates where the BZ_2^+ group takes the place of a coordinatively bidentate metal cation.

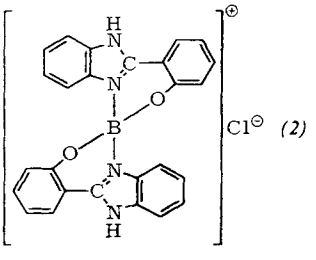
The chelating agents used were the 2-(*o*-hydroxyphenyl) derivatives of benzothiazole, benzoxazole, benzimidazole, and indole. In the last case the indole-indolenine tautomeric equilibrium was shifted to the indolenine side by the chelate formation: the C=N stretching vibration at *ca.* 1610 cm^{-1} occurs only weakly in free indole, but in the indolenine-BZ_2 chelates it is in the same strength as for the other chelates.

Experimental: The chelating agent was dissolved in benzene, dioxane, or ether and mixed with a slight excess of a solution of the boron compound (tetraphenyldiboron oxide, BF_3, or BCl_3), and the whole was heated under reflux for 1–2 hours. The boron chelates crystallize after evaporation of the solvent and cooling. They were recrystallized or (for Y = NH) were reprecipitated by addition of toluene and evaporation. Compounds with Z = Cl can be purified only by washing with ether or dioxane. The compound with Y = CH_2 and Z = Cl has been prepared at −40 °C.

Y	Z	M.p. (°C)	Color	Fluorescence [a]
S	C_6H_5 [1]	220	Intense yellow	Strong yellowish-green
	F	280	Pale yellow	Weak pale blue
	Cl [b]	330–340 (decomp.)	Yellow	Weak blue
O	C_6H_5	195	Colorless to pale greenish	Blue to pale blue
	F	218–219	Colorless	Bluish-violet
NH	C_6H_5	400–440 (decomp.)	Colorless	Dark blue
	F	356–357	Colorless	Blue
	Cl	240–245 (decomp.)	Colorless to pale violet	Pale blue
CH_2	C_6H_5	227–229	Strong yellowish-green	Strong yellowish-green
	F	280 (decomp.)	Yellowish	Pale blue
	Cl [b]	200–205 (decomp.)	Yellow	Pale yellow

[a] In the solid state. [b] Sensitive to hydrolysis.

It was not possible to isolate a compound of type *(1)* after treatment of 2-(*o*-hydroxyphenyl)benzimidazole with BCl_3 in dioxane; the salt-like compound *(2)* was formed at once. This colorless substance neither melts nor decomposes below

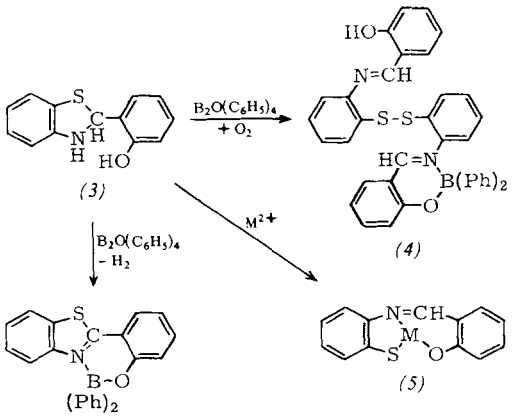


(2)

370 °C, and is difficultly soluble in the usual organic solvents and in water, but it is slowly hydrolysed when kept in water, as shown by the increase in conductivity.

Diphenylboron and difluoroboron chelates of 2-(*o*-hydroxyphenyl)benzothiazole are formed, with evolution of hydrogen, also from 2-(*o*-hydroxyphenyl)benzothiazoline *(3)* and tetraphenyldiboron oxide or BF_3. In the presence of oxygen the reaction involves also formation of *ca.* 25% of a disulfide, in which with tetraphenyldiboron oxide only one [cf. *(4)*] (m.p. 130–135 °C, yellow) but with BF_3 both chelating groups react (m.p. 276–277 °C, yellow, fluorescence blue green).

The reaction of the thiazoline *(3)* with boron compounds contrasts with its reaction with metal cations (Cu, Zn, Cd); in the latter case the thiazoline reacts as a tridentate chelating agent with fission of the C–S bond and formation of an azomethine chelate *(5)* [2]. It is known [3] that, in the reaction of boron compounds with tridentate chelating agents that contain only O and N as ligating groups, a reaction analogous to that with metal chelates and involving loss of a second Z group is possible; therefore, the cause of the differing behavior of the thiazoline may lie in the lower stability of the B–S bond. This view is supported by the fact that it is also impos-



sible to obtain aphenyl boron-azomethine chelate $[B(C_6H_5)^{2+}]$ in which with tetraphenyldiboron oxide only one [cf. *(4)*] (m.p. 130–135 °C, yellow) but with BF_3 both chelating groups react (m.p. 276–277 °C, yellow, fluorescene blue green).

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[*] Prof. Dr. F. Umland and Dipl.-Chem. E. Hohaus
Anorganisch-chemisches Institut der Universität
Hindenburgplatz 55
44 Münster (Germany)

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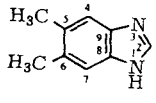
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Biosynthesis of 5,6-Dimethylbenzimidazole [1]

By *P. Renz* and *K. Reinhold*[*]

Anaerobically, in the presence of cobalt, *Propionibacterium shermanii* forms cobinamide. Aerobically, on addition of lactic acid, mainly cobalamine [α-(5,6-dimethylbenzimidazolyl)cobamide] is formed. Since lactic acid is converted by propionic acid bacteria into acetyl-coenzyme A[2], it was possible, by using sodium [2-^{14}C]-D,L-lactate and [2,3-$^{14}C_2$]-D,L-lactate, to determine whether the 5,6-dimethylbenzimidazole *(1)* contained in cobalamine is formed from acetate units as are numerous other aromatic compounds.



(1)

For this purpose, the moist bacterial mass from *P. shermanii* was harvested by centrifugation after two days' anaerobic growth. Ten 25 g batches of this material (cobinamide content 1–2 mg/25 g) were slurried in 400 ml of sterile 1/15 M phosphate buffer (pH 7.0) and treated with 8 ml of a 50% sodium lactate solution that contained 10 μCi of radioactive lactate. The batches were shaken for 50 h at 30 °C. After isolation, the vitamin B_{12} formed was degraded to *(1)* by HCl[3]. For determination of the radioactivity of the two methyl groups and of C-5 and C-6, the compound *(1)* was degraded by the *Kuhn-Roth* method[4], yielding 2 molecules of acetic acid per 1 molecule of *(1)*. The acetic acid was further degraded to methylamine and CO_2[5]. Since the remaining C atoms are oxidized to CO_2 in the *Kuhn-Roth* degradation, the radioactivity at C-4, C-7, C-8, and C-9 was determined by degradation of *(1)* to 4,5-imidazoledicarboxylic acid (as in the method due to *Efros et al.*[6]) and this acid was decarboxylated to imidazole[7]. The radioactivity at C-2 was not determined separately.

Distribution of radioactivity in labeled 5,6-dimethylbenzimidazole (counts min^{-1} $mmole^{-1}$)

	[2-^{14}C]Lactate	[2,3-$^{14}C_2$]Lactate
(1)	4230	12000
CH_3	146	1170
C-5 + C-6	730	1170
C-4 + C-7	0	2090
C-2 + C-8 + C-9	1022	730
Total	1898	5160
% of original radioactivity	45 [a]	43 [a]

[a] That only 45 or 43% of the original radioactivity was found in the fragments is due to the fact that *(1)* was measured in ethanol/dioxane/toluene, and the fragments in hyamine/toluene.

The Table shows that mainly C-2, C-5, C-6, C-8, and C-9 are labeled on introduction of [2-^{14}C]lactate, but that all the fragments are labeled when [2,3-$^{14}C_2$]lactate is used. This distribution is the same as *Plaut*[8] found for the dimethylbenzene ring of riboflavin. Formation of this ring thus occurs by the same route in cobalamine as in riboflavin.

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[*] Dr. P. Renz and Dipl.-Chem. K. Reinhold
Institut für Biochemie und Biotechnologie der Universität
Azenbergstr. 14
7 Stuttgart N (Germany)

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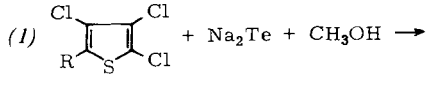
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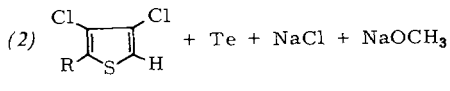
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Reductive Dehalogenation of Organic Compounds by Sodium Telluride

By *W. Mack*[*]

As a rule it is not easy to substitute hydrogen for halogen in aromatic compounds[1]. In Na_2Te a reducing agent has been found that makes this exchange possible. In particular perhalogeno aromatic compounds, which are often easy to prepare, can be converted by this reagent, smoothly and in good yield, into partially halogenated compounds which are not easy to obtain by other methods.





(a), R = Cl, 91%
(b), R = H, 96%
(c), R = OC_6H_5, 91% [2]
(d), R = Piperidino, 82% [3]

The organic compound is heated with a stoichiometric amount of Na_2Te[4] in aqueous-methanolic solution until separation of Te is complete, and the mixture is worked up after filtration from the Te/NaCl precipitate. Hexachlorobenzene is thus converted into 1,2,4,5-tetrachlorobenzene, and octachloronaphthalene into heptachloronaphthalene.

Perhalogenated olefins also undergo this reaction. Tetrachloroethylene affords 51% of trichloroethylene, which in turn can be reduced to *cis*-1,2-dichloroethylene in 12% yield. A variant of the reaction consists of using, in place of Na_2Te, elemental Te with a reducing agent, *e.g.* Rongalite[5], which converts Te into telluride.

Experimental:

Tetrachlorothiophene (333 g) is heated under reflux with Rongalite (485 g), Te (192 g), and NaOH (330 g) in 50% aqueous methanol (4.2 l) under N_2 for 33 h. This affords *(2a)* (208 g, 74%) as well as *(2b)* (5.4 g) and unused *(1a)* (30 g). The products are separated by distillation. The tellurium used is recovered quantitatively.

Na_2Te (1980 g, 11.4 moles) in methanol (10 l) and then water (3 l) are added to a solution of compound *(1a)* (1280 g), 5.77 moles) in boiling methanol (2 l), and the whole is boiled for 42 h. Then O_2 is passed in for a short time, the mixture is neutralized with gaseous HCl, and Te and NaCl are filtered off. Pouring the filtrate in water (20 l) and distillation affords *(2b)* (907 g, 84%) together with *(2a)* (162 g, 13%). 99% (1434 g) of the Te is recovered.

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[*] Dr. W. Mack
Consortium für Elektrochemische Industrie GmbH
Zielstattstr. 20
8 München 25 (Germany)

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[2] M.p. 36 °C – 3,4,5-Trichloro-2-phenoxythiophene is obtained from *(1a)* and Na phenoxide in dimethylformamide during 5 h at 150 °C, 72%, m.p. 14 °C.

[3] B.p. 106 °C/0.1 mm. – 3,4,5-Trichloro-2-piperidinylthiophene is obtained from *(1a)* and piperidine during 20 h at 200 °C, 55%, m.p. 53 °C.

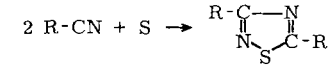
[4] Liquid ammonia (5 l) is poured over powdered Te (756.4 g) in a 6-liter flask, then Na (273.2 g) is added slowly at −60 °C with stirring. For further detail see *G. Brauer*: Handbuch der präparativen anorganischen Chemie. Enke-Verlag, Stuttgart 1960, p. 399.

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Synthesis of 1,2,4-Thiadiazoles from Nitriles and Sulfur

By *W. Mack*[*]

1,2,4-Thiadiazoles *(1)* are formed by reaction of aromatic nitriles with sulfur in the presence of basic catalysts. Alkylamines are particularly suitable for this purpose, their catalytic activity increasing with increasing chain length. For



(1a), R = Phenyl
(1b), R = ß-Naphthyl
(1c), R = *p*-Tolyl

instance, tri-n-octylamine is five times as active as the same molar proportion of triethylamine.

Synthesis of (1a)

0.6 mole of benzonitrile is heated with 0.2 mole of sulfur and 1.8 mmole of tri-n-octylamine in a bomb tube for 42 h at 250 °C. Subsequent distillation affords 35.7 g (75%) of *(1a)*, b.p. 156–160 °C/0.2 mm, m.p. 90 °C (from ethanol).

Synthesis of (1b)

60 mmoles of 2-naphthonitrile, 30 mmoles of sulfur, and 0.3 mmole of tri-n-octylamine are heated in a bomb tube for 158 h at 250 °C. All the volatile materials are then sublimed off in a high vacuum and the alcohol-insoluble portion of the sublimate is recrystallized from benzene. Yield 3.2 g (28%) of *(1b)*, m.p. 180 °C.

Synthesis of (1c)

200 mmoles of *p*-tolunitrile, 100 mmoles of sulfur, and 0.1 mmole of tri-n-octylamine are heated in a bomb tube for 21 h at 250 °C. Then all the material that volatilizes from the reaction mixture at about 200 °C/10^{-3} mm is recrystallized from ethanol. Yield: 3.2 g (12%) of *(1c)*, m.p. 128 °C.

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[*] Dr. W. Mack
Consortium für Elektrochemische Industrie GmbH.
Zielstattstr. 20
8 München 25 (Germany)

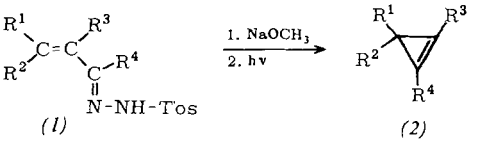
Photochemical Synthesis of Alkyl- and Aryl-cyclopropenes [1]

By *H. Dürr*[*]

Dedicated to Professor B. Eistert on his 65th Birthday

Bamford and *Stevens*' reaction[2] can be used to prepare alkylcyclopropenes by thermal decomposition of the sodium salts of tosylhydrazones of α,β-unsaturated carbonyl compounds[3,4], but the method fails with the tosylhydrazones of aryl-substituted ketones.

However, photolysis of the alkali salts of the tosylhydrazones *(1)* affords both alkyl- and aryl-cyclopropenes *(2)*.



(1) *(2)*

	R¹	R²	R³	R⁴	Solvent	Photolysis conditions [a]	Yield (%) Photochem.	Thermal
(2a)	CH_3	CH_3	H	CH_3	Diglyme	I	42 [b]	39 [3]
(2b)	CH_3	CH_3	CH_3	CH_3	Diglyme	II	28 [b]	22 [4]
(2c)	C_6H_5	H	H	C_6H_5	Dioxane	I	19	0
(2d)	C_6H_5	H	C_6H_5	C_6H_5	Dioxane	II	21	–

[a] Photolysis conditions: I. One Philips HPK 125W lamp and one Hanau-Q-81 lamp. – II. Two Philips HPK 125W lamps. [b] Determined by gas chromatography.

Experimental: 3,4-Dimethyl-3-penten-2-one tosylhydrazone *(1b)* 16.50 g) and sodium methoxide (3.63 g) (molar ratio 1:1) are stirred in anhydrous diglyme[5] with exclusion of moisture for 18 h at atmospheric pressure, then for $^1/_2$ h at water-pump vacuum, and finally for $^1/_2$ h at oil-pump vacuum (all at room temperature) and are thus dried. The solution is irradiated for 6 h at 14–16 °C in a Duranglas 50 apparatus by means of two high-pressure Hg lamps[6], whereupon 91% of the theoretical amount of N_2 is evolved. The mixture is treated with 50 ml of ethanol and then distilled. The distillate is shaken with H_2O and toluene, the tetramethylcyclopropene passing into the toluene phase.

The structures of *(2a)*, *(2b)*, and *(2d)* were proved by mixed melting points or mixed chromatograms with authentic samples and by comparison of the IR spectra [3, 7].

Alkyl- and aryl-cyclopropenes are stable under the above conditions, but on longer irradiation, particularly in the presence of sensitizers, are converted into tricyclohexanes [4, 8].

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[*] Dr. H. Dürr
Institut für Organische Chemie der Universität
66 Saarbrücken 15 (Germany)

[1] Part IV of Photochemistry of Small Rings. – Part III: *H. Dürr*, Liebigs Ann. Chem., in press.

[2] *W. R. Bamford* and *T. S. Stevens*, J. chem. Soc. (London) *1952*, 4735.

[3] *G. L. Closs*, *L. Closs*, and *W. Böll*, J. Amer. chem. Soc. *85*, 3796 (1963).

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[7] *R. Breslow* and *H. W. Chang*, J. Amer. chem. Soc. *83*, 2367 (1961); *R. Breslow* and *P. Dowd*, *ibid. 85*, 2729 (1963).

[8] *H. Dürr*, Tetrahedron Letters *1967*, 1649.

Organic Compounds in Fossil Plants (Equisetum; Horsetails) [1]

By *H. Knoche* and *G. Ourisson* [*]

Chemotaxonomic classification of fossil plants would be particularly interesting since it could be carried out on mutilated and incomplete specimens, and because conclusions could be drawn about the history of the fossils from comparison of the constituents of fossil and fresh plants.

We have begun experiments designed to isolate organic compounds, in particular hydrocarbons, from fossil plants from the bunter sandstone of the Northern Vosges (Trias, 2×10^8 years old) and to compare them with the compounds in present-day plants. Of the fossils available to us a horsetail *Equisetum brongniarti* [2] was especially interesting because numerous *Equisetum* species still grow today. The stems of the plants were approximately 30 mm in diameter. In addition, horsetails have few parasites [3], which diminishes the danger of the compounds found originating from foreign organisms. Great attention was paid to purity during the collection, and contamination during working up was excluded by control experiments. The *Equisetum* described here came from a clay inclusion in the bunter sandstone of the Northern Vosges (Hangvillier, Moselle).

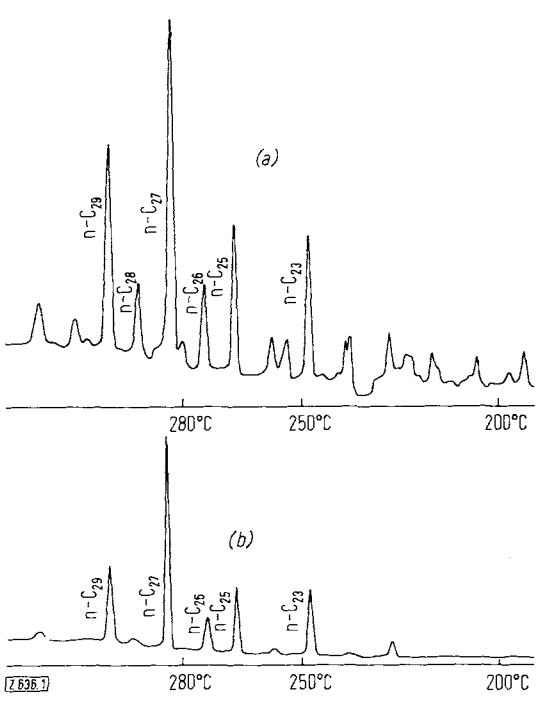


Fig. 1. Gas chromatograms [5] of the hydrocarbon fractions from (a) fossil and (b) fresh *Equisetum*.

400 g of dried rock containing *ca.* 20% of fossil plants (further separation from the rock is rather difficult and unnecessary since the surrounding material contains very little organic material [4]) were ground and extracted with 400 ml of a benzene/methanol mixture (3:1 v/v) using an ultrasonic technique (25 kHz). Centrifugation, decantation, and removal of the solvent by distillation gave 3 mg of residue, which was desulfurized in a small column by 100 mg of active copper and then separated on 2 g of silica gel (Merck, 0.05–0.2 mm). Elution with 50 ml of petroleum ether gave the hydrocarbon fraction (*ca.* 0.5 mg). The gas chromatogram (Fig. 1a) showed four main components in the ratio 1:1:2.4:2 [5].

50 g of fresh, dried *Equisetum sylvaticum* (wood horsetail) was extracted with 500 ml of benzene (ultrasonically). The hydrocarbon fraction (18 mg) was isolated from the extract by column chromatography. The gas chromatogram of this fraction (Fig. 1b) showed the same four main components in almost the same proportions, namely, 1:1:2.4:1.3 [**].

The products were identified as the normal hydrocarbons n-$C_{23}H_{48}$, n-$C_{25}H_{52}$, n-$C_{27}H_{56}$, and n-$C_{29}H_{60}$ by their gas-chromatographic retention times [6], mass spectra, and inclusion in Linde molecular sieves (5 Å, 6 h in boiling isooctane). The extract of the fresh plant does not contain the numerous minor components of the fossil plant.

In this work the same compounds have been isolated for the first time from a living and a fossil plant and it has been proved that hydrocarbons can remain unchanged in a fossil for 200 million years.

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[*] Prof. G. Ourisson and Dr. H. Knoche
Université de Strasbourg, Institut de Chimie,
Laboratoire attaché au C.N.R.S.,
1, rue Blaise Pascal
Strasbourg (France)

[**] Note added in proof: *K. Stransky*, *M. Streibl*, and *V. Herout*, Collect. czechoslov. chem. Commun. *32*, 3213 (1967), have recently found the ratio of alkanes n-C_{23}:n-C_{25}:n-C_{27}:n-C_{29} to be approximately 1:1:3:0.5 in the wax of fresh *Equisetum palustre* L.

[1] Part I. – This work forms part of the research program D.G.R.S.T. No. 64-FR-058. – We thank Messrs. *L. Grauvogel* and *J.-C. Gall* for help in collection of the fossils, and Dr. *Vetter*, Hoffman-La Roche, Basel, for determination of the mass spectra.

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[4] *R. Brandt* and *G. Ourisson*, unpublished work.

[5] Conditions: Perkin-Elmer gas chromatograph 226, 1.5% of SE-30 on Aeropack 30, 80/100 mesh, 1.80 long, 3 mm in diameter, program 6.25 °C/min, 100–290 °C, 30 ml of He per min.

[6] Perkin-Elmer gas chromatograph 226, capillary column 0.025 mm, 50 m, SE-30, 240 °C, 1.6 mol of He per min; retention times: benzene 3.9 min., *n*-C_{23} 9.3 min, n-C_{25} 13.5 min, n-C_{27} 31 min, n-C_{29} 33.8 min.

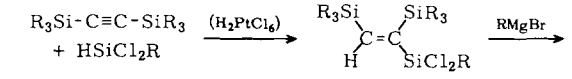
Ionization Energies of Silyl- and Alkyl-ethylenes [**]

By *H. Bock* and *H. Seidl* [*]

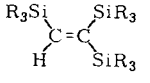
The differing properties of simple π-electron systems containing R_3Si- and R_3C-substituents can be considered as being due to the different inductive polarization ($+I_{SiR_3} >$

$+I_{CR_3}$) and additional conjugative back-donation of electrons $Si_d \leftarrow C_\pi$. The relative energy changes of the highest occupied and lowest unoccupied molecular orbitals caused by interaction with the substituents can be measured individually be means of *e.g.* half-wave potentials[1], electron spin densities[2], or charge-transfer band maxima[3], while the resulting total energy differences can be determined from the corresponding transitions in the electronic spectra[2,3]. Of the cross-conjugated[1], cyclic[2,3], and linear π-electron systems containing R_3Si-groups, ethylene derivatives were the first for which we were able to determine ionization energies by mass spectroscopy[4] and thence to obtain, by means of the *Koopman* theorem[5], direct information about the highest occupied (π)-levels[6].

The hitherto unknown[7] tris(trimethylsilyl)ethylene *(2)* can be prepared as shown:



R = CH_3 *(1)*



(2)

60 mmoles of dichloro(methyl)silane is added dropwise and slowly to an equimolar amount of bis(trimethylsilyl)acetylene to which has been added 0.3 ml of a 0.1 N solution of H_2PtCl_6 in 2-propanol. After 20 hours' boiling under reflux, distillation affords 13% of *(1)*, b.p. 57–60 °C/0.5 mm, which affords 47% of *(2)*, b.p. 43–45 °C/0.5 mm, by a Grignard reaction. The product is purified by gas chromatography (SE-30 column). The ^1H–NMR-spectrum contains three singlets in the ratio 1:18:9 at τ = 2.67, 9.86, and 9.91; the C=C stretching frequency appears at 1499 cm^{-1}. Comparison with the corresponding data for trimethyl ethylene[8] (^1H–NMR signal of the ethylene proton: 4.83 τ; C=C stretching frequency 1667 cm^{-1}) illustrates to what extent characteristic properties of the ground state of simple R_3Si- and R_3C-substituted π-electron systems may differ.

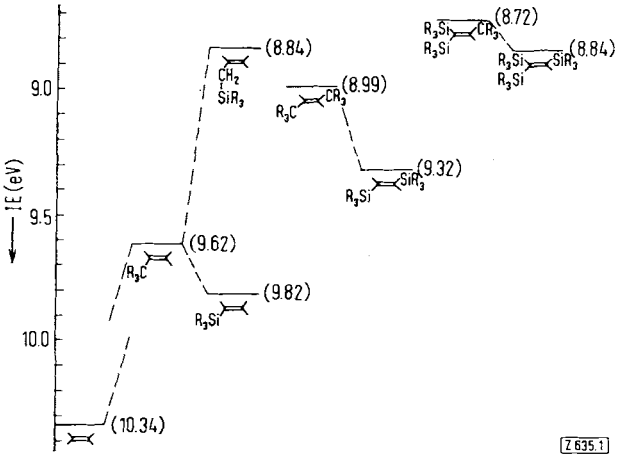


Fig. 1. Ionization energies (IE) of silyl- and alkyl-ethylenes.

The diagram (Fig. 1) for the highest occupied (π)-molecular orbitas[6] of silyl- and alkyl-ethylenes permits the following conclusions: (+I)-Substituents such as R_3Si- and R_3C-groups lower the ionization energy of the ethylene π-electron system, corresponding to a rise of the π-level, which for the silyl derivatives $C_nH_{4-n}(SiR_3)_n$ is linearly proportional, within a good approximation, to the number of substituents. The effect of the R_3Si-groups is, however, in all cases less than required for inductive polarization ($I_{SiR_3} > +I_{CR_3}$), and applying the usual model of the $Si–C_{sp^2}$ bond this provides further evidence[1–3] in favor of a conjugative $Si_d \rightarrow C_\pi$ electron back-donation. A minimum value for the $+I_{SiR_3}$ effect follows from the ionization energy of t-butylethylene which is 0.8 eV higher than that of 1-trimethylsilyl-2-propene where the β-situated R_3Si group is separated from the π-electron system by a tetrahedral C atom.

The d-orbital interactions demonstrated by the ionization energies for the ground state of silylethylenes were used previously to explain why the NMR signals of the ethylene protons are shifted to lower field in comparison with the alkyl derivatives[9] and why the C=C stretching frequencies are lowered[10]. In this connection, extreme differences are shown by the values for tris(trimethylsilyl)- and trimethylethylenes, where a difference of 5000 cm^{-1} ≙ 14 kcal/mole in the $\pi \rightarrow \pi^*$ excitation energies also indicates considerable π^*/d splitting[11]. Smaller, but similar, differences between the properties of silyl- and alkyl-polyenes and -polyynes[11] confirm the d-orbital effects for silyl substituted linear π-electron systems.

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[*] Priv.-Doz. Dr. H. Bock and Dipl.-Chem. H. Seidl
Institut für Anorganische Chemie der Universität
Meiserstr. 1
8 München 2 (Germany)

[**] Part IV of d-Orbital Effects in π-Electron Systems Containing Silicon Substituents. – Part III [3].

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[7] *R. West* and *G. R. Husk* synthesized the compound by a similar route (personal communication at the IUPAC Symposium on Organometallic Chemistry, München (Germany) 1967).

[8] Possibly, non-bonding interactions between the bulky *cis* $(CH_3)_3Si$-groups play a part. It is impossible to build a Stuart-Briegleb model for a tris(t-butyl)ethylene, in the model of the tris(trimethylsilyl) derivate ($d_{R_3Si-C} > d_{R_3C-C}$) rotation of the *cis*-R_3Si groups is sterically hindered.

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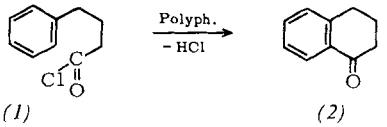
[10] *J. Knizek*, *M. Horak*, and *V. Chvalovsky*, Coll. czechoslov. chem. Commun. *28*, 3097 (1963).

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Cyclization of Acid Chlorides by Polyphosphoric Acid

By *A. Bhati* and *N. Kale*[*]

We have cyclized arylalkanecarbonyl chlorides *(1)*, namely, 4-phenylbutyryl, 5-phenylvaleryl, 4-(2-chloro-5-methoxyphenyl)butyryl, and 4-(5-chloro-2-methoxyphenyl)butyryl chloride, with polyphosphoric acid and thus obtained the cyclic ketones *(2)* in excellent yield.



(1) *(2)*

Synthesis of 1-tetralone (2):

The acid chloride obtained from 1.65 g of 4-phenylbutyric acid and thionyl chloride was treated with 23 g of freshly prepared[1] polyphosphoric acid with exclusion of moisture, and the whole was stirred at 70 °C for 15 min. HCl was evolved. The mixture was poured into water and extracted with ether. After washing with 10 % sodium hydroxide solution and drying, the ether was removed, leaving 1.38 g (94.6 %) of 1-tetralone.

Under the same conditions 1-indanone is formed from 3-phenylpropionyl chloride, but with only 57.3 % yield.

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[*] Dr. A. Bhati and N. Kale
Department of Chemistry and Biology,
Regional College of Technology
Byrom Street
Liverpool 3 (England)

[1] *S. Dev*, J. Indian chem. Soc. *32*, 262 (1955).

Irregularities in the Partial Molar Enthalpies of Mixing of Water and Water-Alcohol Mixtures at Constant Temperature

By *G. Kortüm* and *K. A. Steiner*[*]

In the neighborhood of specific temperatures, irregularities (called "kinks" in the Anglo-Saxon literature) occur in the temperature-dependance of numerous properties of water and aqueous solutions[1]. They are interpreted as indicating that such systems contain various mixed phases that are arranged in the manner of clathrates and are transformed into one another at specific temperatures. The best known example of such a liquid structure if the "water hydrate" $(H_2O)_{21}$ proposed by *Pauling*, in which one molecule is surrounded by 20 other molecules, after the manner of a clathrate; as in gas hydrates, these 20 molecules form the corners of a dodecahedron. The transition temperatures are considered to depend on the nature and concentration of the material dissolved in the water, whence it is concluded that the anomalies denote sudden changes in the structure of the water and have nothing to do with interactions between water and the solutes.

Using a very sensitive differential calorimeter[2] we have measured the intermediate enthalpy of mixing of water with water-alcohol mixtures at 30 °C, and from the results have determined the partial molar enthalpies of mixing as a function of the molar fraction of the components. In contrast to the measurements by other authors the molar fraction was varied by very small amounts. Surprisingly, we observed numerous irregularities which exceeded the experimental error in the measurements by an order of magnitude. Figure 1 shows some of our results. From them there is no doubt that structured mixed phases occur also in ethanol-water mixtures, a fact that may be important for the still little understood structure of liquids.

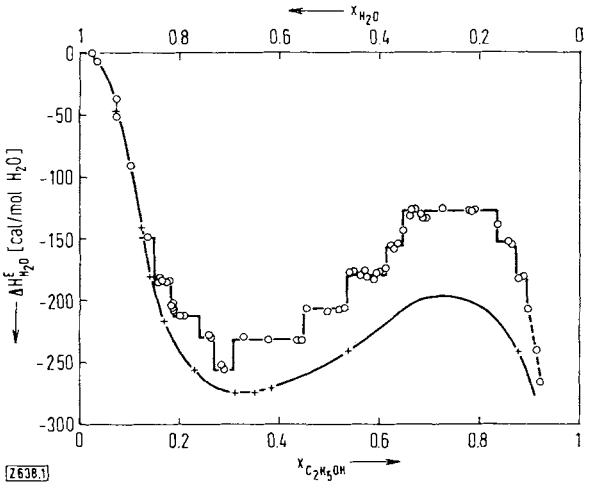


Fig. 1. Partial molar enthalpy of mixing $\Delta H^E_{H_2O}$ of water with water-ethanol mixtures. o = our measurements at 30 °C; + = calculated from measurements by *Bose* [4] at 21 °C. Analogous irregularities were observed at 20 and 40 °C.

It is true that participation of dissolved gases (O_2, N_2) in these structures[3] cannot be excluded with certainty, but such participation is very unlikely at the temperatures selected for our work. Our measurements further show that the iregularities in the properties of aqueous solutions are not determined solely by the structure of the water and its temperature-dependance, since they are observed at almost constant temperatures (temperature variations on mixing amounted to about 0.01 °C).

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[*] Prof. Dr. G. Kortüm and Dipl.-Phys. K. A. Steiner
Institut für Physikalische Chemie der Universität
Wilhelmstr. 56
74 Tübingen (Germany)

[1] *M. J. Blandamer, M. F. Fox*, and *M. C. R. Symons*, Nature (London) *214*, 163 (1967); *C. Salama* and *D. A. I. Goring*, J. physic. Chem. *70*, 3838 (1966); *W. Drost-Hansen*, Ann. N.Y. Acad. Sci. *125*, 471 (1965).

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CONFERENCE REPORTS

Preparation and Properties of Inorganic Halogenoamines

By *J. Jander*[*]

Inorganic halogenoamines have recently been obtained by disproportionation of halogens with ammonia at about −75 °C. That the reddish-brown $NI_3 \cdot NH_3$ isolated, *inter alia*, actually has the structure corresponding to this formula and is not, *e.g.*, a 1:1 adduct of NHI_2 and NH_2I follows from the reaction (studied analytically and by IR spectroscopy) with pyridine or quinoline, in which the ammonia is replaced by the nitrogenous bases without destruction of the NI_3 component[1]. The structure, which was clarified by *Bärnighausen* and *Hartl*[2] by X-ray analysis shows NI_4 tetrahedra which are joined together into chains by common iodine atoms. One iodine atom of each NI_4 tetrahedron is additionally attached to one ammonia molecule by a charge-transfer bond.

In order to explain the decomposition of monochloramine NH_2Cl by way of the unstable imene or nitrene NH, monochloramine was treated with phenyl-lithium in dimethyl-2-butene at −75 °C. The expected α-elimination took place in good yield, as shown by the benzene formed, but only 3 % of 2,2,3,3-tetramethylaziridine was obtained. During the reaction a white precipitate was formed, which evolved N_2 and NH_3 when warmed. The precipitate is moderately soluble in ether at −75 °C; LiCl separates from the clear

solutions on warming. Further study is needed to show whether the precipitate consists of LiNHCl or another compound resulting therefrom[3].

Lecture at Hamburg on July 25th. 1967 [VB 95 IE]
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[*] Prof. Dr. J. Jander
Institut für Anorganische Chemie der Freien Universität
Fabeckstr. 34/36
1 Berlin 33 (Germany)

[1] *J. Jander* and *L. Bayersdorfer*, Z. anorg. allg. Chem., in press.

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[3] *J. Fischer*, Dissertation, Technische Hochschule München, 1967.

Kinetic Studies of the Cyclotrimerization of Butadiene by Ziegler Catalysts

By *W. Ring* [*]

In the presence of a suitable catalyst, the cyclizing trimerization of 1,3-butadiene to 1,5,9-cyclododecatriene, first described by *G. Wilke* [1], occurs with high yield and steric selectivity. Titanium-containing catalyst systems, for example, lead to formation of *cis,trans,trans*-cyclododecatriene in more than 90 % yield with almost complete conversion of the butadiene.

The mechanism of the cyclotrimerization of butadiene on titanium has not hitherto been so thoroughly clarified as has that on the nickel catalyst (*Wilke et al.*). However, it can be regarded as certain that synthesis of the 12-membered ring in presence of titanium also occurs by way of π-complexes of the butadiene or one of its products with the heavy-metal atom. Up to 85 % conversion the reaction displays first-order kinetics with respect to butadiene, but it then becomes slower. When the cyclododecatriene concentration is increased the reaction rate decreases, and at the same time divergences from first-order reaction rate are observed.

Kinetic analysis of the cyclotrimerization of butadiene was supplemented by measurement of the spectral changes in the reacting solutions between 480 and 380 nm as a function of time and of the conversion. The kinetic and spectroscopic results led to the conclusion that the trimerization involves a closed series of partial reactions including a replacement equilibrium (1):

$$\text{K·(Cyclododecatriene)} + \text{Butadiene} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{K·(Butadiene)} + \text{Cyclododecatriene} \quad (1)$$

The expressions K·(cyclododecatriene) and K·(Butadiene) denote π-complexes of the olefins with the heavy-metal atom. The changes of concentration and absorption with time permit the equilibrium constant $K' \equiv k_1/k_{-1}$ to be estimated as about $3 < K' < 10$. The slower reaction with higher concentrations of cyclododecatriene in solution can be quantitatively explained by the effect of the equilibrium on the overall reaction.

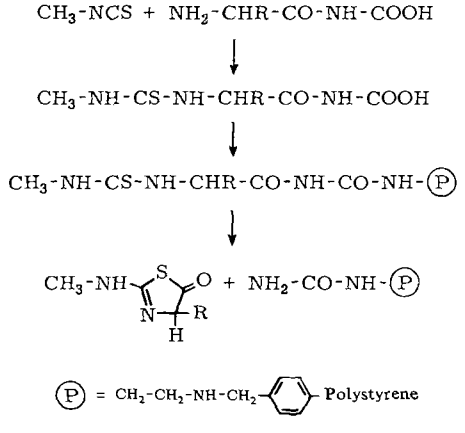
Lecture at Stuttgart on November 2nd, 1967 [VB 96 IE]
German version: Angew. Chem. 79, 1074 (1967)

[*] Dr. W. Ring
Untersuchungsabteilung der Chemische Werke Hüls AG
4370 Marl, Kreis Recklinghausen (Germany)

[1] *G. Wilke*, Angew. Chem. *69*, 397 (1957).

SELECTED ABSTRACTS

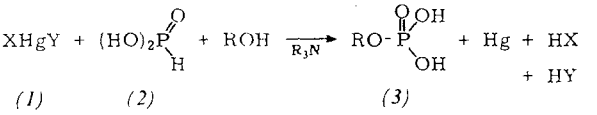
α-Dehydrobiotin *(1)*, which was hitherto unknown, has been isolated by *L. J. Hanka, M. E. Bergy*, and *R. B. Kelly* from the culture filter of *Streptomyces lydicus* and identified by IR and NMR spectrometry; m.p. 238–240 °C, $[\alpha]_D^{25} = 92°$ (0.1 N NaOH). *(1)* is active *in vitro* against a number of gram-positive and -negative bacteria and fungi. The antimicrobial activity is counteracted by biotin. *(1)* is a biotin



antimetabolite. On catalytic hydrogenation with Pd/C, compound *(1)* is converted into (+)-biotin. / Science (Washington) *154*, 1667 (1967) / –Ma. [Rd 644 IE]

Dinonylnaphthalenesulfonic acid has been used as a liquid ion exchanger by *J. Prášilova* and *Z. Satorie*. The reagent is best prepared by alkylation of naphthalene at 164–170 °C with the $BF_3 \cdot 2ROH$ complex of anhydrous nonyl alcohol; the dinonylnaphthalene fraction distilling at 150 to 165 °C is then sulfonated at about 100 °C with 90 % H_2SO_4. The strongly acidic cation exchanger is an approximately 10^{-3} M solution of dinonylnaphthalenesulfonic acid in heptane (readily soluble in nonpolar solvents, practically insoluble in H_2O), which is shaken with an aqueous solution for about 2 hours; the ionic strengths and pH values must be kept constant by the addition of salts and acids. The authors have used this method *e.g.* to determine the stability constant of the thiocyanatoindium species $[In(SCN)]^{2+}$, $[In(SCN)_2]^+$, and $In(SCN)_3$. / Collect. czechoslov. chem. Commun. *32*, 322 (1967) / –Jg. [Rd 735 IE]

A new synthesis of monoalkyl phosphates is reported by *T. Obata* and *T. Mukaiyama*. Monoalkyl dihydrogen phosphates *(3)* are obtained in good yields from alcohols, phosphonic acid *(2)*, and inorganic mercury compounds *(1)* in the presence of tertiary amines.



(1) *(2)* *(3)*

In the absence of amine, mercury(II) acetate and dry phosphoric acid in boiling ethanol give impure monoethyl phosphate *(3a)*, R = C_2H_5. If four molar equivalents of triethylamine are added to the mixture, chromatographically pure *(3a)* can be isolated *e.g.* as the monoanilinium salt (m.p. 164–166 °C, yield 69–92 %) after a few minutes.

The reaction is thought to proceed *via* the deprotonated phosphite ion $PO_3^{3\ominus}$, which is readily oxidized by Hg(II) salts into the metaphosphate anion $PO_3^{\ominus}$. The alcohol adds to this ion. Even solid alcohols such as benzyl alcohol and borneol can be converted, in yields of 80 % and 48 % respectively, into the anilinium salts of the monoalkylphosphates (m.p. 150–152 and 194–196 °C, respectively) in acetonitrile. / J. org. Chemistry *32*, 1063 (1967) / –WG. [Rd 711 IE]

A covalent bond between Pt or Au and Si, Sn, or Pb exists in a number of complexes prepared by *M. C. Baird* in accordance with reactions (a) to (d). Analogous C and Ge compounds are well known. The structures were determined by comprehensive IR measurements. $(P(C_2H_5)_3)_2Pt(H)SiPh_3$

$$(R_3P)_nMCl_x + Ph_3M'Li \rightarrow (R_3P)_nM(Cl_{x-1})\text{-}M'Ph_3 \quad (a)$$
R = Ph, C_2H_5; M = Pt, Au; M' = Si, Sn, Pb

$$(PPh_3)_2PtHCl + Ph_3M'NO_3 \rightarrow (PPh_3)_2Pt(Cl)\text{–}M'Ph_3 \quad (b)$$
M' = Sn, Pb

$$trans\text{-}(PPh_3)_2PtHCl + 2\ SnCl_4 \rightarrow (PPh_3)_2Pt(Cl_2)\ (SnCl_3)_2 \quad (c)$$
(1)

$$trans\text{-}(PPh_3)_2PtHCl + SnCl_2 \rightarrow (PPh_3)_2Pt(H)\text{–}SnCl_3 \quad (d)$$
(2)

(pale yellow; unstable to heat and in $CHCl_3$); $Ph_3PAuSiPh$ (light yellow - brown; ν_{Au-Si} (?) = 305 cm^{-1}); $(PPh_3)_2Pt(Cl)SnPh_3$ (*trans*-isomer: white, stable to light and to air; thermal decomp. > 278 °C; Pt–Sn bond cleaved by anhydrous HCl. *cis*-Isomer: orange); $(PPh_3)_2Pt(Cl)PbPh_3$ (white; easy intramolecular disproportionation by Ph migration; *(1)*, complicated IR spectrum between 350 and 250 cm^{-1}; decomposes on recrystallization into $(PPh_3)_2Pt(Cl)SnPh_3$; 6 Cl very loosely bound toward $AgNO_3$); *(2)*, orange-yellow, *trans*-isomer, m.p. 130–135 °C; *cis* form already known. / J. inorg. nuclear Chem. *29*, 367 (1967) / –Jg. [Rd 752 IE]

The synthesis of acetate from carbon dioxide and Co-methylcobalamin in *Clostridium thermoaceticum*, according to *J. M. Poston* and *E. R. Stadtman*, is ferredoxin-dependent. The strictly anaerobic organism can synthesize acetate from CO_2. An intermediate in this synthesis is Co-methylcobalamin. The incorporation of [^{14}C]-methyl from Co-[^{14}C]-methylcobalamin into acetate is catalysed by two enzyme fractions, which were purified and separated by chromatography on DEAE-cellulose. The reaction also requires the presence of ferredoxin, which was first obtained from *Clostridium pasteurianum*. A corresponding ferredoxin has been concentrated from *C. thermoaceticum*. This ferredoxin catalyses the acetate synthesis in question, and is active in the hydrogenase system from *C. pasteurianum*. The two ferredoxins behave similarly on disk electrophoresis, and have very similar spectra. / Biochem. biophysic. Res. Commun. *26*, 550 (1967) / –Hö. [Rd 717 IE]

The collinearity of the amino-acid sequence and the gene map of the structural gene has been demonstrated by *C. Yanofsky et al.* for the α-subunit of tryptophan synthetase from *E. coli*. The amino-acid sequence of this protein was elucidated (267 amino acids). In eleven tryptophan-deficient mutants with point mutations in the α-subunit of the tryptophan synthetase, it was possible to locate the positions of the point mutations within the amino-acid sequence. The relative distances between the codons for the exchanged amino acids could be determined by recombination analysis. Comparison of the relative distances with the lengths of the peptide chains between the mutated amino acids shows an exact agreement between the gene map and the amino-acid sequence. / Proc. nat. Acad. Sci. USA *57*, 296 (1967) / –Hö. [Rd 718 IE]

The torsional vibrations of the chlorinated ethanes have been assigned in the IR and Raman spectra by *G. Allen*, *P. N. Brier*, and *G. Lane*. For molecules having a symmetrical rotor (CH_3–, CCl_3–) the height of the energy barrier to internal rotation was calculated from the torsional frequencies (80 to 250 cm^{-1}); the result varies from 3.3 (1,1-dichloroethane) to 14.2 (pentachloroethane) kcal/mole. The energy barriers calculated from the torsional frequencies of molecules with asymmetric rotors do not appear to be so reliable, but their sequence is reasonable. The energy barrier is greatest when a Cl atom on C-1 is situated between two Cl atoms on C-2. In the molecules $CH_3CH_xCl_{3-x}$, the steric hindrance is evidently more than compensated for by the opposite polarities of the two halves of the molecule: the (thermodynamically calculated) height of the energy barrier in 1,1,1-trichloroethane is smaller (2.8 kcal/mole) than in ethylene itself. / Trans. Faraday Soc. *63*, 824 (1967) / –Hz. [Rd 719 IE]

Solutions of potassium amide in liquid ammonia show an absorption band at about 335 nm, which *R. E. Cuthrell* and *J. J. Lagowski* assign to the amide ion or to ion associations that contain the amide ion. The position and extinction coefficient of this band vary relatively strongly with temperature, as can be seen from the table (last column: extinction coefficient corrected for the density change). On the other hand, Beer's law is valid over a wide range of concentrations (from about 0.4 to 2.5 × 10^{-4} mole/l). These observations were interpreted with the aid of a model, according to which the absorption corresponds to the transfer of an electron from the amide ion to the solvent cage. / J. physic. Chem. *71*, 1298 (1967) / –Hz. [Rd 720 IE]

T (°C)	λ_{max} (nm)	ε_{max}/D
–30	339	3.17×10^3
–60	334	3.35×10^3

BOOK REVIEWS

Quantenchemie für Chemiker. Elementare Einführung in die mathematischen und wellenmechanischen Grundlagen. (Quantum chemistry for chemists. Elementary introduction to mathematical and wave-mechanical fundamentals.) By *H. Preuß*. Verlag Chemie GmbH., Weinheim/Bergstr. 1966. 1st Edit., xii, 159 pp., 50 figures, 3 tables, paperback DM 24.–.

The subtitle of the book – elementary introduction to mathematical and wave-mechanical fundamentals – characterizes the content of the book better than its main title. 94 of the 148 pages of text are devoted to a discussion of fundamental mathematical concepts. Justification for this step is to be found in the many gaps generally left in the mathematical training of chemists.

The book begins with admirable thoroughness by discussing number sequences and follows with an explanation of the concept of a function by means of elementary examples. Matrices, determinants, vector analysis, and coordinate

systems are dealt with in the next two chapters. The treatment of these concepts, which are generally skimped in mathematics lectures for chemists, is of particular value to the prospective quantum chemist. The introduction to mathematical fundamentals concludes with a discussion of differential and integral calculus.

The second part of the book deals with the fundamentals of wave mechanics and quantum-mechanical approximation procedures. A consideration of the wave function, electron spin, and the Pauli exclusion principle leads to a treatment of the time-dependent and time-independent Schrödinger equations. Some information about operator equations is given in the following chapter. The Schrödinger equation, the angular momentum, and the electron spin are formulated with the aid of operators. Subsequently the Born-Oppenheimer approximation, energy hypersurfaces, and nucleus motion are discussed. The chapter dealing with approximation procedures is devoted to a treatment of the variation principle and of the calculus of perturbation theory.

Certain special procedures for solving electron problems are described in the third part of the book. The various quantum-mechanical methods are distinguished on the basis of the differences between the Hamiltonian operators used. In logical manner, the procedures for solving the Schrödinger equation with the use of exact Hamiltonians (H atom, CI, SCF, LCAO methods) are contrasted with the procedures that use a modified Hamiltonian (Hückel's procedure, free-electron model). It is unfortunate that this chapter, which contains the methods for the treatment of molecular problems that are so important to the chemist, is very short. While three pages are devoted to the treatment of number sequences, the Hückel procedure, for example, is dealt with in a few lines. Because of this brevity of treatment the reader is merely able to appreciate certain fundamental aspects underlying the various approximation procedures. Suitable references are given to more extensive treatments or for the application of the various methods to chemical problems. The book can thus serve as a useful introduction.

The reader can test his progress by means of practice exercises. A few misprints, for example those that have crept into the superscripts of eq. (70) on p. 111, should be amended in the next edition. As an elementary introduction, the book is intended mainly for undergraduates. Considering this it is regrettable that the price is relatively high.

H. Zimmermann [NB 629 IE]

Physical Organic Chemistry. By *O. H. Wheeler*. Principles of Modern Chemistry, Monograph 2. Elsevier Publishing Company, Amsterdam-London-New York 1966. 1st Edit., ix, 172 pages, 42 tables, Dfl. 27.50; paperback Dfl. 15.00.

The present introduction to physical organic chemistry is claimed to be the first so far that "achieves a balanced treatment of the two principal aspects – the empirical study of mechanisms and the fundamental theoretical background". This claim is not entirely justified. The author has failed to stress important principles and to confine himself to important points. The attempt to cover the entire field in 160 pages was bound to lead to a superficial treatment. Some examples are:

Even fundamental concepts such as "transition state" and "intermediate" are not clearly defined (no mention is made of the reaction coordinates), and are frequently confused (pages 59, 72, 106, 133); the difference between bond energy and dissociation energy is not explained (page 19).

The fundamentals of spectroscopy are not discussed, though spectra are occasionally used in the discussion of mechanisms. The classification of reaction mechanisms does not include multi-center reactions. Diels-Alder syntheses and the Claisen rearrangement are formulated as involving "cyclic intermediates", and pyrolytic *syn* eliminations as proceeding *via* "free radicals or ion pairs". Both $C_6H_5COO\cdot$ and $C_6H_5CO\cdot$ are described as benzoyl radicals (pages 141 and 145).

The formulae are generally clear. The two-page index is too short and 36 references are inadequate. Many recent results have not been referred to. The last chapter, which is entitled "New Frontiers", seems completely out of place. The book cannot be recommended. *C. Rüchardt* [NB 615 IE]

Glas im Laboratorium. Eine Einführung für den Laborpraktiker. (Glass in the Laboratory. An Introduction for the Laboratory Worker). By *E. Deeg* and *H. Richter*. Volume 6 of the series "Der pharmazeutische Betrieb" (Pharmaceutical Practice). Edition Cantor KG., Aulendorf i.Württ. 1965. 1st Edit., 160 pp., 74 illustrations, DM 36.–.

This 160-page book could easily carry a more ambitious title, perhaps "All about Glass Laboratory Apparatus". There is hardly a question connected with the use, care, and manufacture of glass apparatus that it does not deal with. The authors have compiled much useful information which would otherwise require a laborious search.

After a chapter on glass as a material, glass apparatus and glassware are described in detail. Many illustrations of apparatus are included, and their properties are described in numerous tables. Special emphasis is laid on the details given in the DIN standards. The types of bottles for stocking varions substances, how to free stuck ground-glass joints and glass taps, precautions to be taken during glass cutting and glass blowing – all are described in an easily understandable form. The volume concludes with a section on glass-to-metal joints, hints on laboratory practice, and a subject index. *H. Grünewald* [NB 644 IE]

The Chemistry of Selenium, Tellurium and Polonium. By *K. W. Bagnall*. No. 7 of the Series of Monographs 'Topics in Inorganic and General Chemistry', edited by P. L. Robinson. Elsevier Publishing Company, Amsterdam-London-New York 1965. 1st Edit., viii, 190 pp., 11 diagrams, 25 tables, Dfl. 35.00.

The author, who, by virtue of his own investigations, is an expert on the chemistry of the extremely rare element polonium, has attempted to present the chemical properties of this element briefly and comprehensively in close comparison with those of the two lighter elements of the same group, tellurium and selenium. In view of the hitherto unsatisfactory treatment of the chemistry of these main-group elements, this attempt has met with great success in a small, well presented, and comprehensible volume. The modern literature is almost completely covered. The book provides a useful review for those concerned with the chemistry of the heavy elements of group VI b (a quarter of the book is devoted to the organic derivatives of Se, Te, and Po) and it may also be recommended generally as a source of stimulating information. Quite justifiably, most chemists will regard the book as too specialized since it considers the three elements alone and not in conjunction with the characteristic Group VI element sulfur. As a result of the high price, the book will probably only be found in libraries, where, however, it should on no account be absent. *Max Schmidt* [NB 627 IE]

Modern Approach to Inorganic Chemistry. By *C. F. Bell* and *K. A. K. Lott*, Butterworth and Co. Ltd., London 1966. 2nd Edit., xiii, 331 pp., numerous figures and tables, 45 s.

The book covers the "Higher National Certificate" syllabus and is intended for "General Degree" students. Its plan departs markedly from that of conventional German textbooks, in that the principles fundamental to inorganic chemistry are emphasized. This is clear also from the chapter headings: (1) Atomic structure I, (2) Atomic structure II, (3) Valency, (4) The structure of the elements and their compounds, (5) Reactions in water and in non-aqueous solvents, (6) Coordination chemistry, (7) Distribution and

extraction of the elements, (8) Extraction with solvents and ion exchange, (9) Comparative chemistry of representative elements, (10) Comparative chemistry of the transition elements. Each chapter has an appended list of references for further study.

Generally speaking, there is a need for a short and modern introduction to inorganic chemistry in the German language, and a German translation of *Bell* and *Lott's* book could fill this gap were it not for the assumption of too much prior knowledge. For example, the use of radioisotopes in elucidating the course of chemical reactions is discussed on p. 21, without previously introducing the reader to the chemical symbolism or to the formulation of reaction equations. Surprising use is made of Bohr's model of the atom, while subsequent discussion suggests that the exclusive use of the wave-mechanical model is considered suitable. The general principles are clearly brought out and the discussion is on a relatively high level. Ionic and covalent bonds are treated in detail and with clarity. The relationships involved in metal bonding are discussed separately, and, together with van der Waals forces, are postponed until Chapter 4.

The structural chemistry of solids is discussed on classic examples, but many classes of compounds, *e.g.* the silicates, are dealt with too summarily. Some recent developments have been ignored. For example, the acid-base theories contain no reference to the Schwarzenbach-Pearson definitions. In the same way, the $Na-NH_3$ system has not been treated according to the most recent results..

Only about a third of the book is devoted to "descriptive chemistry". Thus, for example, ammonia synthesis is dealt with in four lines. Nonetheless, these sections similarly contain many interesting cross-references.

The book cannot be recommended unreservedly as an "introduction" to inorganic chemistry, but certainly as a supplement to standard textbooks. In this respect the study of "Bell-Lott" is likely to be of considerable value to students of chemistry and especially to aspiring chemistry teachers.

H. Nöth [NB 641 IE]

The Chemistry of Organic Sulphur Compounds, Vol. 2. By *N. Kharasch* and *C. Y. Meyers*. Pergamon Press, Symposium Publications Division, Oxford 1966. 1st Edit., vii, 465 pp., numerous figures and tables, bound £7.

Volume 2 of this series of monographs on organosulfur chemistry deals predominantly with rather specialized subjects in its 15 chapters. The following are discussed, in the order given: Electron relationships and bond properties of selected sulfur compounds (*H. A. Bent*), mechanisms of desulfurization by Raney nickel (*W. A. Bonner* and *R. A. Grimm*), isomerization of organic thiocyanates (*A. Fava*), newer aspects of the chemistry of olefinic sulfides (*L. Goodman* and *E. J. Reist*), desulfonylation (*J. L. Kice*), polyfluoroalkyl derivatives of sulfur (*R. E. Banks* and *R. N. Haszeldine*), properties of 1-alkynylthioethers (*W. Drenth*), anionic oxidation of thiols and cooxidation of thiols with olefins (*A. A. Oswald* and *T. J. Wallace*), radical addition of thiols to olefins and acetylenes (*A. A. Oswald* and *K. Griesbaum*), the chemistry of the 1,2-dithiol ring (*N. Lozac'h* and *J. Vialle*), thiohydantoins (*J. T. Edward*), thiophosgenes (*H. Tilles*), alkaline decomposition of aliphatic disulfides (*J. P. Danehy*), reactions of cyanides with cystines and cystine peptides (*O. Gawron*), and finally oxidation of disulfides with special reference to cystine (*W. E. Savige* and *J. A. Maclaren*).

This survey demonstrates that the authors were not restricted in the choice of their subject matter the consequently somewhat fragmentary character of the work was deliberately allowed for, because the issue of further volumes (volume 3 is already in the press) is intended to fill in some of the gaps. The very welcome list of literature references in the appendix deals with important work of the past few years. Anyone interested in these special fields will undoubtedly benefit by reading the book.

J. Gosselck [NB 630 IE]

Elementary Practical Organic Chemistry. Part 1: Small Scale Preparations. By *A. I. Vogel*. Longmans, London 1966. 2nd Edit., xx, 435 pp., numerous figures, bound 35s.

No change has been made in the basic conception of the book for the second edition. The first chapter deals with the theoretical principles of procedures such as distillation, crystallization, and sublimation, as well as the mode of action of drying agents.

This is followed by a detailed description of experimental techniques (about 125 pages). Numerous instruments are illustrated and their use is described, and even the bending of glass tubes and the use of air driers are not forgotten. The various types of stirrers are described, as well as methods for the determination of melting points.

The preparations are divided in the usual manner into aliphatic (Chapter 3) and aromatic compounds (Chapter 4). As a result of this arrangement, the aliphatic and aromatic carbonyl compounds are discussed separately, and too little space is devoted to the effects of substituents on the reactivity of the CO group. Reactions and compounds that do not fit into the above scheme are described in Chapter 5, which ends with some very good experiments on chromatographic methods and electrophoresis. Most of the preparations are preceded by a short description of the relevant reaction mechanisms. The selection of the preparations and reactions could have been rather more up-to-date.

The present book is what students call a cookery book in the best sense of the word. The procedures given are well proven, and can be carried out even by beginners. A number of preparations from Vogel should be carried out by every student, as is already usual in many places. However, it can be recommended as a practical handbook only if used in conjunction with a second book that includes spectroscopic methods for structural elucidation and for the characterization of substances used and prepared, as well as more modern preparative methods.

H. J. Bestmann [NB 592 IE]

Elementary Practical Organic Chemistry. Part 2. Qualitative Organic Analysis. By *A. I. Vogel*. Longmans, London 1966. 2nd Edit., xv, 431 pp. numerous figures and tables, 35s.

The book opens with a short introduction on the qualitative analysis of organic compounds and the determination of physical constants.

The text begins with the determination of melting point in all its aspects with *Vogel's* well known thoroughness, including illustrations and a discussion of the most common apparatus. Whether it is necessary to describe the drawing out of a melting-point tube at epic length is debatable. The determination of boiling point follows. Here the mention of the Siwoloboff method for small amounts of liquid is welcome, because it is no longer generally known to the probationer. Measurement of density and refractive index is then discussed. The chapter concludes with the determination of optical rotation followed by an unfortunately rather short section on rotatory dispersion.

Chapter 2 is devoted to the qualitative analysis of the elements, but only C, H, N, S, and the halogens are described. A useful chapter on the solubility of different classes of substances in diverse solvents follows. 120 pages are then devoted to the reactions and characteration of various organic compounds. The characterization of a substance by the preparation of a derivative has unfortunately come into some disrepute today. This chapter is warmly recommended for constant use to all demonstrators. The preparation of crystalline derivatives of olefins by reaction with 2,4-dinitrophenylsulfenyl chloride is likewise described, as is the often very useful cleavage reaction of ethers with 3,5-dinitrobenzyl chloride in the presence of zinc chloride. In many cases a procedure is given for preparing the reagents. These 120 pages are a rich source for every chemist who does not wish to rely solely on spectral results.

Whether the following Chapter 5, in which classification reactions, *i.e.* reactions for identifying certain functional groups, are discussed, is necessary at all needs careful consideration. Extensive overlapping and repetition of Chapter 4 are the rule. For instance, the preparation of a 2,4-dinitrophenylhydrazine solution is described both on p. 118 and on p. 189. A combination of the table on pp. 215 and 216, listing the principal identification reactions, with Chapter 6, which once more lists the principal derivatives, would be adequate.

Following an introduction to the qualitative analysis of mixtures of substances, Chapter 8 discusses spectroscopic methods (UV, IR, NMR, and mass spectrometry). In every case a short theoretical introduction is given, the relevant apparatus is sketched in ready-for-use arrangement, and the possible applications of the spectra are discussed with examples. This chapter, which is introduced for the first time in this edition, is a very valuable contribution to the book, which concludes with a number of tables containing the physical characteristics for a large number of compounds. Chromatographic methods are not discussed here but are described in Volume 1; however, pages 237 and 238 contain a bibliography of the various chromatographic methods. The volume represents a successful compilation of chemical and physical methods of analysis. It can be recommended without reservation, even if one would like to see a condensation of certain sections and an extension of the spectroscopic methods. No organic chemical laboratory should be without it.

H. J. Bestmann [NB 636 IE]

Technique of Inorganic Chemistry. Vol. IV. Edited by *H. B. Jonassen* and *A. Weissberger*. Interscience Publishers, a Division of John Wiley and Sons, New York-London-Sydney 1965. 1st Edit., 400 pp., 98 illustrations, 115s.

Five contributions of varying scope, weight, and level go to make up the fourth volume of the series which was started in 1963, and the unfortunate title of which gave rise to serious doubts when the first volume was reviewed [*].

In view of the scope and quality of discussions of the theory and practise of ion exchange which have already been published, the first article headed "Ion Exchange Techniques" (30 pp., with only 16 references, six of which refer to books and reviews) would appear rather superfluous. In contrast, the second contribution "The growth of oxide single crystals from the fluxed melt" (33 pp., 67 references) is a successful comprehensive presentation of the development of a relatively new experimental technique which has proved extraordinarily useful in special cases. The third article "High-temperature Techniques" (70 pp., 316 references) deserves particular attention as a very welcome review of the newest methods of investigating chemical reactions at high temperatures – a field of study which will certainly assume ever increasing interest in the future. The fourth article "Magnetochemistry" (105 pp., 142 references gives a good idea of the eminent importance of magnetic measuremonts in gaining information about the nature of the bonding in a given substance, with particular reference to the recent rapid developments in the complex chemistry of transition metals. Only 33 pages are devoted to the "technique" as such, whereas 66 pages deal with theory and a further six pages are taken up by results of experiments conducted on the lanthanides and actinides. Who would consider looking for these 72 pages under the heading given?

The same applies to the last article "Techniques of optical rotatory dispersion and circular dichroism" (108 pp., 448 references) in which only 18 pages are devoted to the methods of measurement, the rest being reserved for general theory, procedures for preparing optically active substances, and results of measurements. The general impression given by this contribution is no less than "very good". However, for this reason it is to be regretted all the more that such papers are undeservedly camouflaged by the unsuitable title of the series. A comforting thought is, however, that the excellently presented volume will certainly take its place in all libraries and for this reason its full value will be exploited, even if only indirectly. The reviewer would hesitate to recommend the purchase of such a heterogeneous collection of articles to the individual chemist.

Max Schmidt [NB 626 IE]

[*] Cf. Angew. Chem. *76*, 799 (1964).

Chemistry and Physics of Carbon, Vol. 1 and 2. Edited by *P. L. Walker jr.* Marcel Dekker, Inc., New York 1966. Vol. 1, xv, 382 pp., numerous figures and tables, $ 13.75. Vol. 2, xiv, 384 pp.

Carbon is often described as one of the most long-established, and yet newest materials to be used in technology. This observation is made in the light of, firstly, the classical use of diamond, activated charcoal and carbon blacks, artificial carbon as refractory material, and artificial graphite as electrode material; secondly, its novel use in nuclear technology and as a rocket material; finally, its use as a reinforcing agent in future composite materials, with a potential scope that must at present remain a matter for conjecture. As a result of its industrial importance, carbon has during the past 20 years again assumed a key position in the chemistry and physics of solids. The number of books written on the subject has not kept pace with this development. Apart from a monograph about reactor graphite and a French collective work on carbon, no modern monographs exist. A book on the physics and chemistry of carbon, therefore, meets an urgent need.

The present two initial volumes of a four-volume series are each divided into six chapters written by authors of international standing. Volume 1 contains a chapter by *S. Amelinckx* on "Dislocations and stacking faults in graphite", which, by means of excellent electron micrographs of natural graphite introduces the reader to the results of this technique. In Chapter 2, *G. F. Hewitt* discusses the "Gaseous mass transport within graphite". This section, containing extensive literature references and a discussion of technical problems, is of technological significance. *J. M. Thomas*, in Chapter 3, describes the results, mainly his own, of "Microscopic studies of graphite oxidation'. Chapter 4, by *S. Ergun* and *M. Mentser*, gives an exhaustive ssuvey of the "Reactions of carbon with carbon dioxide and steam". "The formation of carbon from gases" is discussed, fundamentally rather than exhaustively, by *H. B Palmer* and *C. F. Cullis* in Chapter 5. This section contains a good review of the literature. Chapter 6 consists of a rather specialized treatise on "Oxygen chemisorption effects on graphite thermoelectric power" by the editor, P *L. Walker*, and his coworkers.

The second volume continues the series of individual chapters. Chapter 1, by the late *G R. Henning*, gives an excellent account of "Electron mictoscopy of reactivity changes near lattice defects in graphite". The subject matter in the chapter is related to that dealt with in Chapters 1 and 3 of Volume 1 In Chapter 2, *M. M. Dubinin* discusses the problems invelved in the "Pore structure and adsorption properties of active carbons". Particular reference is made to the author's own work, and to Soviet literature in general. *W. N. Reynolds*' chapter on "Radiation damage in graphite" largely follows the recently published monograph by *Simmons*. This section deals predominantly with the problems of Radiation damage in graphite at medium temperatures (a point of interest to British reactor development), and to a lesser extent with irradiation at high temperatures. A comprehensive bibliography is appended. Chapter 4 by *A. C. Zettlemoyer* and *K. S. Narayan* deals with the "Absorption from solution by graphite surfaces", a narrow, specialized field. Chapter 5 by *C. R. Klein* likewise has a specialized character. The author deals with the "Electronic transport in pyrolytic graphite and boron alloys of pyrolytic graphite", mainly on the basis of his own investigations. Finally, Chapter 6 of Volume 2 contains a description of

the "Activated diffusion of gases in molecular sieve materials" by the editor and his co-workers. This chapter covers a very wide scope.

In attempting to formulate an overall opinion on the two published volumes one is immediately struck by the topical choice of subject of most chapters, and by the international eminence of the contributors. The modern and in parts particularly lucid presentation of the most recent research results as well as some excellent illustrations also deserve mention. This new series differs in the above respects from the collective work of French scientists on carbon that appeared two years ago.

The depth of treatment varies between the individual chapters. It ranges from a comprehensive survey and critical comparison of all available data, *e.g.* Chapters 2 and 4 in Volume 1, to excessively concise treatment of important subjects, *e.g.* Chapter 5 in Volume 1; elsewhere incomplete treatments under too general a title are given alongside excellent detailed descriptions of specialized subjects (*e.g.* Vol. 1, Chapter 3). Literature reference are also abstracted with varying thoroughness. Some chapters provide a valuable scientific basis for the study of complex technological problems, others are restricted to simplified models which, nevertheless, provide a stimulant for further research.

Subsequent Volumes of this series will show whether the editor of this work succeeded in presenting a self-contained monograph on current knowledge of the physics and chemistry of carbon by a skilful choice of the individual subjects. Even now the present two volumes may be regarded as important chronicles of progress in the field of carbon. They are very warmly recommended to every scientist and technologist with an interest in this subject. *E. Fitzer* [NB 652 IE]

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